

# Promoting the Quality of Medicines (PQM) Program

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

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

As of December 2018, USAID supports PQM's work in 19 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
CTD	common technical document
DTL	Drug Testing Laboratory
EAC	East Africa Community
FPP	finished pharmaceutical product
GCP	good clinical practices
GLP	good laboratory practices
GMP	good manufacturing practices
ILT	inter-laboratory testing
M&E	monitoring and evaluation
MDR-TB	multidrug-resistant tuberculosis
MedRS	Medicine Risk Surveillance
MNCH	maternal, newborn, and child health
MQDB	Medicines Quality Database
MQM	medicines quality monitoring
MRA	medicines regulatory authorities
MRH	medicines registration harmonization
NEPAD	New Partnership for Africa's Development
NQCL	national quality control laboratory
NTD	neglected tropical diseases
PQM	Promoting the Quality of Medicines (program)
QA	quality assurance
QMS	quality management systems
SOP	standard operating procedure
TB	tuberculosis
USAID	U.S. Agency for International Development
USP	U.S. Pharmacopeial Convention
WAHO	West Africa Health Organization
WHO	World Health Organization

# Executive Summary

The Promoting the Quality of Medicines (PQM) program helps low- and middle-income countries strengthen the systems that ensure the quality and increase the supply of priority medicines. PQM's assistance helps to build the capacity of medicines regulatory authorities (MRAs) and quality assurance (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 first quarter (Q1) of FY 2019, from October 1 to December 31, 2018.

In FY 2019 Q1, PQM advanced the objective to strengthen quality assurance systems to sustainably ensure medical products quality and safety and to protect public health. Access to medicines quality test results from laboratories that operate according to international standards is important for medicines regulation. The Bangladesh National Control Laboratory was assessed by the ANSI-ASQ National Accreditation Board and received accreditation for ISO 17025:2017. PQM provided technical assistance to the Intergovernmental Authority on Development (IGAD) Expert Working Group (EWG) to finalize the post-marketing surveillance (PMS) protocol and conducted a workshop on the risk-based PMS approach and the Medicine Risk Surveillance tool (MedRS). The workshop, which was held October 1–5, 2018, in Entebbe, Uganda, was designed to build the capacity of IGAD medicines registration harmonization (MRH) member states on conducting surveys of medicines quality.

The Mozambique National Laboratory made progress in its effort to ensure that all national quality control laboratory (LNCQM) laboratory equipment is qualified and functional. With PQM support, LNCQM categorized the laboratory equipment using a risk-based analytical instrumentation qualification approach, USP <1058>. This integrated risk-based approach promotes efficiency and cost savings for laboratories.

PQM supported Jiangsu Chengxis Pharma to achieve World Health Organization (WHO) prequalification for the active pharmaceutical ingredient (API) praziquantel. This new source of quality-assured micronized and non-micronized API will contribute to increase the availability of the praziquantel medical product, which WHO recommends for the treatment of schistosomiasis. In Benin, the adoption of risk-based PMS helped reduce the burden on the laboratory to conduct quality control (QC) testing activities and the time needed to complete these activities. The laboratory was able to provide actionable results to the Department of Pharmacy and Medicines (DPMED) in a timely manner to protect the public from the harm of substandard and falsified medicines. This and other PQM accomplishments were well acknowledged as the program closed out in December 2018. DPMED, LNCQ, USAID, and other stakeholders appreciated PQM's support to the laboratory and expressed continued support to quality assurance systems strengthening in Benin. The PQM report recommended that strategies should be developed to finance PMS through user fees. In addition, risk-based approaches should be implemented to ensure adequate allocation of resources for sustainable implementation of regulatory functions. Finally, PQM recommended that future pharmaceutical regulatory authorities' mandate should cover all regulatory functions.

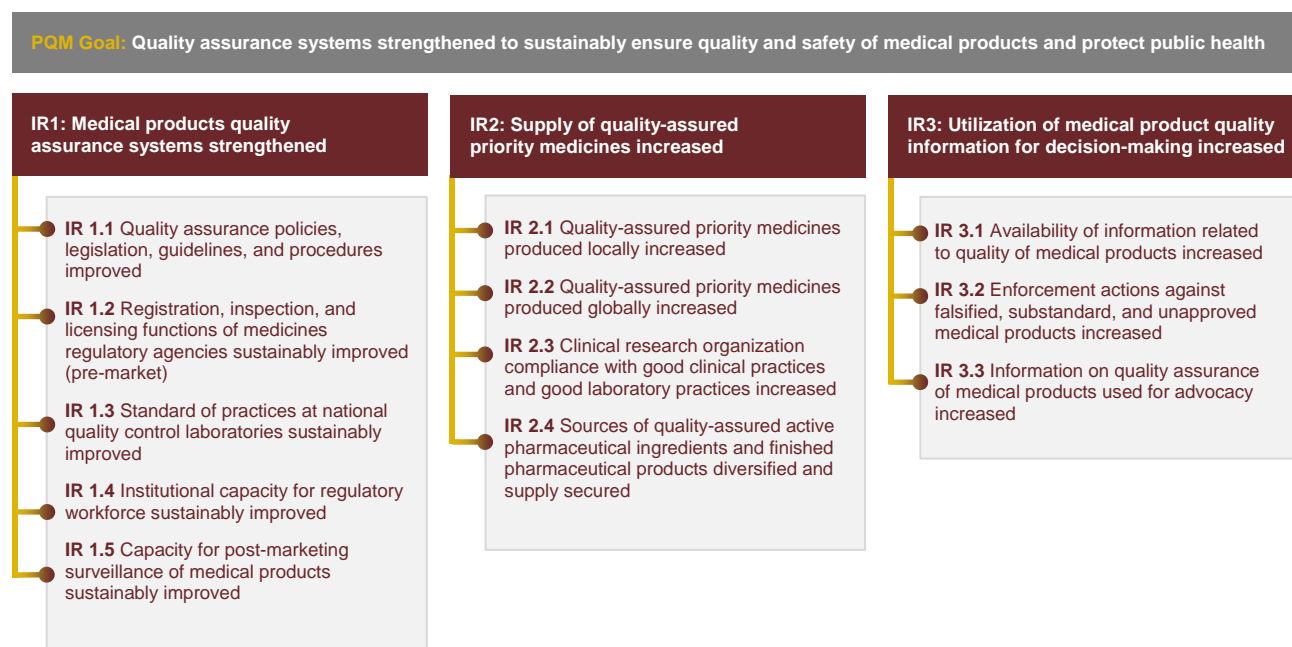
# Program Background

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 MRAs and QA systems in countries with weak health systems. PQM also provides technical support to manufacturers of quality-assured priority medicines for malaria, HIV/AIDS, TB, NTDs, and MNCH.

This quarter, PQM implemented projects for 19 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 that are complementary for strengthening quality assurance systems as a critical part of country's overall health system.



This report highlights PQM's accomplishments, organized by Result Areas representing key activities in multiple countries where the program works, as well as by country and core portfolio for the October–December 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**

WHO defines medicines policy as a commitment to prioritized medium- to long-term goals for the pharmaceutical sector and the strategies for attaining them. It expresses government's commitment to 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 quality assurance 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 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 WHO prequalification.

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

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

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

combining preservice and in-service training interventions and the development of structures and processes necessary for effective QMS, PQM builds a sustainable in-country regulatory and QA workforce.

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

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

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

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## **Overview of FY 2019 First Quarter IR1 Achievements**

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### **Key Results and Highlights**

In Q1, the National Control Laboratory of Bangladesh was assessed by ANSI-ASQ National Accreditation Board and received accreditation for ISO 17025:2017. This was a significant milestone for Bangladesh, as it is the first laboratory with international standards in the country. This will provide the country's regulators and industries with the ability to ensure reliable products and services in relation to medicines quality.

In addition, three laboratories PQM-supported (one in Myanmar and two in Nigeria) were reaccredited. Myanmar's Pharmaceutical Chemistry Laboratory achieved ISO 17025:2017 reaccreditation. In Nigeria, two National Agency for Food and Drug Administration and Control (NAFDAC) laboratories (Agulu and Yaba) achieved ISO 17025:2005 reaccreditation.

In terms of PQM's PMS activities, the program in Burkina Faso added six sentinel sites (Boucle du Mouhoun, Cascades, Centre, Centre-Sud, Est, and Plateau Central), which are now collecting medicines samples and following the process of monitoring and testing their quality.

### **Key IR1 Indicators for FY 2019 Q1**

Number of quality control laboratories accredited or reaccredited	4 – Bangladesh (accredited for ISO 17025:2017), Myanmar, and Nigeria (Agulu and Yaba) reaccredited
Number of sampling sites added for MQM/PMS activities by MRA	6 – Burkina Faso

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

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### **Description of Sub-IRs**

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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 of priority public health medicines that comply with international quality standards threatens supply security and increases the vulnerability of supply chains to shortages, stock-outs, and poor-quality medicines. Furthermore, the lack of economic incentives for manufacturers to produce essential medicines is an obstacle to sustainable

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

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

In some instances, there is only one source of quality-assured essential medicine to supply the global public health market. This makes the medicine vulnerable to substantial price increases for both procurement agencies and countries purchasing the product. It also increases the risk for potential disruptions in supply if the manufacturer sustains any operational setbacks during production. PQM has witnessed companies that manufacture both the API and the finished pharmaceutical product (FPP) become the sole source of a quality-assured product on the market. Interrupting the supply of APIs to other FPP manufacturers allows for price increases in a monopolized FPP market. To prevent this, PQM works to identify API manufacturers that can supply APIs to multiple FPP manufacturers. This increases the number of 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 2019 First Quarter IR2 Achievements**

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### **Key Results and Highlights**

In Quarter 1, PQM supported Jiangsu Chengxis Pharma in the Core NTD program to achieve full WHO prequalification for micronized and non-micronized praziquantel API. This new source of quality-assured praziquantel API will increase the availability of the product on the global market. Praziquantel is the only medicine recommended by WHO for the treatment of schistosomiasis, an NTD caused by parasitic worms.

Through the program in Nigeria, in Q1 PQM was able to support manufacturers in the submission of dossiers to MRAs. PQM supported Drugfield Pharmaceuticals in submission of its dossier for chlorhexidine (CHX) gel to the West Africa Health Organization (WAHO). PQM also provided support to Juhel Pharmaceuticals in the submission of its dossier for magnesium sulfate injection to the Tanzania Food and Drug Agency and to WAHO. Lastly, PQM supported Juhel Pharmaceutical in the submission of its dossier for oxytocin injections to WAHO. The PQM GMP team has been instrumental in providing technical support to these two manufacturers that will lead to the increase of locally manufactured critical MNCH products in Nigeria.

### Key IR2 Indicators for FY 2019 Q1

Number of priority medicines that achieved WHO PQ, SRA or ERP approval	2 – praziquantel API (micronized and non-micronized)
Number of dossier accepted for review by the local MRA	3 – Nigeria (magnesium sulfate, chlorhexidine, and oxytocin – WAHO)

### Number of Manufacturers Provided with Technical Assistance in FY 2019 Q1

Countries/ Core Programs	Number of Manufacturers	Product Types
Core MNCH	1	magnesium sulfate injection
Core TB	13	clofazimine FPP, cycloserine API, rifapentine API, rifapentine FPP, gatifloxacin API, gatifloxacin FPP, kanamycin API, kanamycin FPP, rifampicin/isoniazid/ethambutol/pyrazinamide tablets
Core NTD	7	praziquantel API, praziquantel FPP, albendazole API, albendazole FPP
Bangladesh	1	chlorhexidine solution
Ghana	1	artemether–lumefantrine tablets
Nigeria	9	sulfadoxine–pyrimethamine tablets, chlorhexidine gel, Amoxicillin tablets, zinc sulfate dispersible tablets, artemether–lumefantrine tablets, oxytocin injection, magnesium sulfate injection, ready-to-use therapeutic foods
Indonesia	3	levofloxacin and fixed-dose combination rifampicin 150 mg/isoniazid 75 mg
Kazakhstan	1	levofloxacin
Pakistan	6	amoxicillin dispersible tablets, chlorhexidine gel, zinc sulfate dispersible tablets
Uzbekistan	1	levofloxacin

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

### Description of Sub-IRs

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

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

PQM assists national stakeholders with implementing medicines quality monitoring (MQM) to generate data on the quality of pharmaceuticals circulating in country. To sustain such a critically protective public health activity, PQM supports countries to develop or strengthen PMS as a regulatory function. PQM also supports countries to increase

the body of knowledge generated on the quality of priority essential medicines used in public health programs, particularly medicines used for MNCH, HIV/AIDS, and TB.

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

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

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

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

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

PQM raises awareness about the dangers of substandard and falsified medicines, providing information to the public and government stakeholders by supporting local, regional, and global initiatives on medicines quality. Activities often include hosting and attending partner meetings, developing regional databases and alert systems, advocating for the allocation of resources to improve pharmaceutical quality systems, and encouraging collaboration among stakeholders. PQM develops e-learning courses on medicines 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 societies 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 2019 First Quarter IR3 Achievements**

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### **Key Results and Highlights**

In Quarter 1, PQM engaged in three awareness raising/advocacy in the Africa region. This included a meeting convened in Mali with the National Health Laboratory (Laboratoire National de Sante; LNS), Pharmacy and Drug Division (DPM), Malaria Control Program (PNLP), and Pharmacist Association to finalize a protocol for monitoring the quality of antimalarial medicines that incorporates taking immediate action at the site of sampling. This will lead to increased regulatory action upon the identification of falsified antimalarial medicines.

In the Nigeria program, NAFDAC facilitated a dissemination meeting to discuss the PMS results of the antimalarial study. The meeting was attended by NAFDAC's Director-General, represented by the Director of Registration and Regulatory Affairs, PQM staff, representatives of the Director of Food and Drug Services, Federal Ministry of Health, National Secretary of Pharmaceutical Society of Nigeria, Registrar, Pharmacists Council of Nigeria, Chairman of Association of Community Pharmacists of Nigeria, Pharmaceutical Manufacturing Group of Manufacturers Association of Nigeria, and marketing authorization holders. The outcome of the meeting was six key recommendations for enhanced PMS in Nigeria.

PQM also conducted a workshop with members of the IGAD Expert Working Group on PMS to implement the work plan programmed quality survey to determine the prevalence of substandard and falsified medicines within IGAD cross-border areas. The workshop was designed to build the capacity of IGAD-MRH member states on conducting surveys of medicines quality and to facilitate planning for sample collection during the survey. The workshop was held on October 1–5, 2018, in Entebbe, Uganda, with a focus on training member states on risk-based PMS, finalizing the

PMS protocol, and training sample collectors on the protocol. PQM's risk based PMS approach, including the MedRS, was utilized for the development of the final protocol.

PQM made nine presentations on medical products QA in Q1: Benin (1), Core MNCH (2), Cross Bureau (1), Indonesia (1), IGAD (3) and Ethiopia (1). In the Core MNCH program, PQM contributed to the "Training workshop on key enabling factors for successful local production and supply of quality-assured medicines," which was coordinated by the New Partnership for Africa's Development (NEPAD)/PQM/WHO on December 17–19 in Addis Ababa, Ethiopia. PQM delivered two presentations on "Good products development practices" and "Elements of Sound Technology Transfer" during this workshop.

In Ghana, preliminary data from the PMS of uterotronics (oxytocin and ergometrine injections) conducted by the Food and Drug Administration (FDA) in September 2018 indicated a large number (63%,  $n=105$ ) of unregistered oxytocin injection samples found within the supply chain. This significant finding prompted, as an immediate regulatory action, an FDA letter to the Minister of Health to trigger higher-level discussion, particularly because some of the unregistered products were found in public sector facilities under the control of the Ministry of Health. This is a valuable action to ensure only registered products are procured for the public sector.

#### Key IR3 Indicators for FY 2019 Q1

Number of PQM-supported awareness raising or advocacy events promoting quality of medical products	3 – Mali, Nigeria and IGAD
Number of publications issued and presentations made on medical products quality assurance at national or international level that are presented or authored by PQM	11 – Benin (1), Core MNCH (2), Cross Bureau (1), Indonesia (1), IGAD (3), and Ethiopia (3)
Number of regulatory actions made by the MRA	1 – Ghana

# Africa



# Benin

## I. Quarter 1 Highlights

PQM organized the closeout of the project in Benin. The closeout report was presented at a closeout meeting. The management of the National Quality Control Laboratory (LNCQ) expressed their thanks to PMI and PQM for the support provided to the laboratory. PQM's technical support helped LNCQ to improve the quality of its work and the results it provides. LNCQ management expressed their wish that such technical support continue because Benin greatly benefited from it as the laboratory was able to fulfill its mandate to protect the public from the harm of substandard and falsified medicines.

## 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, with 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 1 Progress by Objective

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### Objective 1 – Sustainably strengthen the NQCL's functions

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PQM organized a meeting for the closeout of the PQM program in Benin. The meeting was held at LNCQ. The day of the meeting coincided with a meeting convened by the Ministry of Health to finalize regulatory provisions for the establishment of a national pharmaceutical regulatory agency. As a result, invitees to the closeout meeting were not able to attend. Dr. Parfait Adjakidje, Director General of LNCQ, gave an opening remark. He thanked USAID and PQM for the support to the laboratory. He wished that the program or a new version of it would continue to support the laboratory and indicated that the laboratory will miss PQM expertise.

PQM presented the closeout report and discussed the way forward, including the transition of PQM support. Emphasis was put on the improvement of the quality of the laboratory work and the results it shared with its clients. The report underlined the success of the laboratory in sharing its acquired expertise with other countries such as training inspectors in Equatorial Guinea on screening of antimalarial medicines.

LNCQ also performed very well in a recent audit, ordered by the government of Benin, to determine the laboratory's technical capacity. Its success in passing the audit could not have been possible without PQM's technical support and expert guidance. The manager of LNCQ's chemical-physical quality control services wondered what would have been the fate of the laboratory without PQM technical support.

Mr. Ricardo Missihoun, USAID manager of the PQM project, added that the end of the PQM program does not mean an end to PMI support to the laboratory. PMI is exploring ways to continue the support that PQM has provided.

A message from Dr. Parfait Adjakidje was received after the closeout meeting in which he expressed his hope that the support the laboratory received through PQM would continue because the laboratory greatly needs it. He also underlined the progress that LNCQ has made toward its organizational goals thanks to PQM's technical support and what could be achieved with additional support.

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

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PQM facilitated analytical testing of the samples collected and tested last quarter. The laboratory reported the result, which showed that 141 total samples were collected. Using a risk-based approach, after visual inspection 71 samples underwent screening with handheld Raman, and a subset of 36 samples were analyzed using thin-layer chromatography (Minilab™). One sample of quinine sulfate failed the screening and underwent further laboratory

testing. The result confirmed that this product was falsified. Interestingly, this product was purportedly produced by a local manufacturer. The laboratory submitted the results to DPMED for further action, including recommendation to follow up with the local manufacturer. The adoption of elements of risk-based PMS has helped reduce the burden on the laboratory to conduct quality control testing activities and the time needed to complete these activities. The laboratory was able to provide actionable results to DPMED in a timely manner to protect the public from the harm of substandard and falsified medicines.

## Burkina Faso

### I. Quarter 1 Highlights

PQM continued to strengthen the technical capacity of the Directorate of Control of Medicines and Non-Food Products (DCM/PNA) laboratory and collaborate with the Sahel Women's Empowerment and Demographic Dividend (SWEDD) project to prepare the laboratory for ISO 17025 accreditation. PQM and SWEDD facilitated training of technical laboratory personnel in methods validation and measurement uncertainty at a training workshop sponsored by SWEDD. As part of the accreditation process, the laboratory must show that its testing is reliable and its personnel are competent in conducting the tests included in the scope of accreditation. This can be achieved through participation in proficiency testing or inter-laboratory testing (ILT) schemes. DCM/PNA completed an ILT organized by USP, and results will be available after the program ends.

Because the laboratory seemed short-staffed, PQM helped with some day-to-day activities, including preparation of testing reports.

To complete the nationwide survey of antimalarial medicines quality, PQM facilitated the sampling and testing of antimalarials in the remaining six regions that were not covered in 2016 or 2017. One hundred samples were collected and screened; four of these are undergoing confirmatory 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 1 Progress by Objective

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

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To continue supporting the DCM/PNA in its preparedness for ISO 17025 accreditation, PQM facilitated the participation of the laboratory in an ILT scheme managed by USP-Ghana. PQM assisted the laboratory with the review and finalization of the results report before submission to USP-Ghana. PQM provided technical support during the organization of a training workshop for the laboratory technical personnel on methods validation and calculation of measurement uncertainty. SWEDD sponsored the workshop. Methods validation and calculation of measurement uncertainty are required for ISO 17025 accreditation. Participation in ILT or proficiency testing is required to show that

the laboratory generates reliable results for the test considered for ISO accreditation and that the personnel are proficient in conducting the test.

In Q1, the laboratory had an unusually high workload and needed support from PQM. The laboratory was at risk of delaying submission of test results to its customers. PQM assisted the laboratory in completing testing result sheets and memos for 77 samples, which allowed it to meet its obligation to its customers. One may anticipate that the demand for medical products testing will increase in the future and a similar situation may occur; DCM/PNA needs to put in place a strategy or plan appropriate staffing.

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

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The PMS activities planned in collaboration with the ANRP and the DCM/PNA took place this quarter. One hundred samples were collected in six regions of Burkina Faso (Boucle du Mouhoun, Cascades, Centre, Centre-Sud, Est, Plateau Central) and screened using the Minilab™ thin-layer chromatography (TLC). Two samples failed screening tests. One sample failed disintegration, and one sample failed TLC. Three other samples were not screened and are undergoing more advanced testing. In total, the laboratory is conducting confirmatory testing on four samples using high-performance liquid chromatography (HPLC). The laboratory has not been able to run dissolution test on the sample that failed disintegration due to the fact that dissolution tester is currently out of service.

The results of PMS activities will be shared with stakeholders in workshop to be held in January 2019.

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

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Under this objective an activity relating to the development of PMS procedures was cancelled following a shift in the priorities of the Agence National de Régulation Pharmaceutique (National Pharmaceutical Regulatory Agency). USAID Mission was informed of the cancellation.

## **Ethiopia**

### **I. Quarter 1 Highlights**

In Q1, the medicine and medical devices registration directive, developed by the Ethiopian Food, Medicine and Health Care Administration and Control Authority (EFMHACA) with technical assistance from PQM, was reviewed and is currently awaiting further discussion with stakeholders and subsequent approval from EFMHACA management. This directive provides a legal backup to the registration guidelines, as there is no specific legal document that enforces requirements for registration of medicines and medical devices.

PQM provided technical assistance to EFMHACA to develop the pharmaceuticals traceability directive. Another workshop was organized to develop medical device registration strategy. The strategy is aimed at enhancing the registration system for medical devices and supplies in order to increase availability of medical devices and supplies in the country.

PQM provided technical assistance to inform system development modifications in order to optimize the registration process. These modifications, including additional system requirements, were made to enhance the software functionality. For instance, the purchase order approval system was optimized to approve the request using the system (self-paced) approval.

Training of trainers on audit-based inspection was provided by EFMHACA headquarters (in collaboration with PQM) to a total of 188 staff members from Ethiopia's regional regulatory authorities and EFMHACA. In the previous year, PQM had provided technical support for the development of an inspection manual that outlines appropriate steps for auditing medicine retail outlets and distributors with respect to good dispensing, good storage, and good distribution practices. This type of inspection has been referred to as "audit-based inspection," which requires inspectors to crosscheck whether establishments are authorized to handle the products found within their establishments and whether the products are obtained from legal sources. This rigorous process of auditing during inspection is expected to boost the capacity of EFMHACA and regional regulators to detect and prevent the circulation of poor-quality medicines, thereby helping to ensure the safety, quality, and effective use of medicines circulating in Ethiopia's market. The training was designed to help EFMHACA and regional regulatory bodies to effectively scale up implementation of audit-based inspections. USP/PQM provided technical support through the preparation of proposal and training materials for the training of trainers.

Following PQM's recommendations from the last supportive supervision, staff from the Diredawa and Mekele branches of EFMHACA laboratories received training in instrument calibration and qualification. The training was provided by EFMHACA central staff, while PQM covered the cost of the trainers. This is aimed to enhance building the intra-organizational training capabilities and practices in addition to building the capacity of branch laboratories in the specific area of training covered.

As part of the GMP roadmap implementation, a GMP compliance assessment was conducted in nine local pharmaceutical manufacturing facilities. PQM participated in the assessment of Addis Pharmaceuticals (APF) IV factory (November 6–8) and EPHARM Sh. Co. (November 25–28). The report is being prepared, and the Government's decision will be sought after submission of the official reports.

## **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.

PQM contributes to the achievement of 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 1 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***

In the last quarter of FY18 PQM provided technical assistance in the development of a medicine and medical devices registration directive, and a 5-day workshop was conducted to complete the first draft.

In Q1, the review of the directive has continued, and it is currently awaiting further discussion with stakeholders and approval by EFMHACA management. Despite the existence of a guideline for product registration, there is no specific legal document that requires the registration of medicines and medical devices. Hence, the development of a directive for medicine registration was found to be highly essential. The directive will be applicable for the marketing authorization of medicines and medical devices manufactured locally or imported. It is also in line with international best practices and is based on guidelines developed for medicines and medical devices registration in Ethiopia with technical support from PQM. The existence of such a directive will help enhance enforcement of the guidelines, as it establishes a legally binding framework.

PQM also participated in a workshop organized on medical device registration strategy at Bishoftu on November 21–25. The strategy is aimed to facilitate the registration system of medical devices and supplies, thereby helping to increase the availability of the medical devices and supplies in the country. PQM played a key role during the development of this strategy. The strategy has been finalized and submitted to EFMHACA management for approval.

In FY 2018, a pharmaceutical traceability strategy was developed, and PQM provided technical support through its participation as a member of technical working group. As a continuing effort, in Q1 the authority developed a draft directive on pharmaceutical traceability. Two workshops were conducted with technical working groups and relevant EFMHACA staff to enrich the document. In addition, a 2-day workshop was conducted on November 26–27 with various external stakeholders, including manufacturers, importers, wholesalers, retailers, and associations to gather feedback and establish consensus on the directive. Feedback from the workshop was incorporated, and a final draft was made ready for approval by EFMHACA management.

In the next quarter, PQM will continue to provide technical assistance for the completion of the two directives (pharmaceutical traceability directive, and medicine and medical devices registration directive) and the medical devices and supplies registration strategy. The successful completion and implementation of these directives will not only improve access to essential medicines through enforcing expedited registration schemes but also enhance the traceability of products, thereby improving the effectiveness of regulatory actions, such as product recall, in cases of

safety concerns on particular medicines. This will ultimately contribute toward improving the availability of quality-assured medicines in support of priority health programs including malaria, MNCH, tuberculosis, and HIV/AIDS.

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

In FY18, PQM supported EFMHACA in the development of guidelines for clinical trial authorization, GCP, training on GCP inspection, a revised guideline for medicine registration, vaccines, similar biotherapeutic products, and biotherapeutic protein products prepared by recombinant DNA technology. The capacity developed and systems established with support from PQM will help EFMHACA to improve the overarching goal of ensuring public safety through strengthening processes for medicine registration and review of clinical trial applications.

In Q1, in order to facilitate the implementation of developed guidelines, staff working on registration and customer service directorates were trained on the GCP inspection and registration of vaccines, similar biological products, and biotherapeutic protein products. Training was provided to a total of 22 EFMHACA staff on October 18–26. This training is expected to facilitate registration of biological products, including vaccines, biosimilar, and other biotherapeutic products, thereby helping to improve access to new and innovative products that have public health importance to the Ethiopian population.

As part of the *Expediting Medicine Market Authorization Strategy, 2017*, which was developed with PQM support, EFMHACA will use external human resources to reduce the backlog of dossier applications, which will help increase access to medicines for priority health programs including malaria and MNCH. In line with this, PQM supported EFMHACA in the training of 6 new EFMHACA staff and 42 external staff from the Addis Ababa Regulatory Authority School of Pharmacy (Addis Ababa University), St. Paul Hospital Millennium Medical College, and Menelik II Health Science College. This first-round training was conducted on December 10–14 at Bishoftu. These newly trained experts are expected to serve as additional workforce for EFMHACA to support dossier review in order to prevent similar backlogs from occurring in the future. The training was exclusively financed by EFMHACA itself, while PQM provided technical assistance through contributing trainers. The effort made to increase the engagement of EFMHACA through budget allocation for human resource capacity-building is expected to enhance sustainability and institution ownership post PQM.

In addition, PQM supported EFMHACA on the following activities:

- PQM participated in the selection of medicines and medical devices for speeding up registration under EFMHACA flagship activities that are considered of very high priority and are regularly monitored by higher management, including the Minister of Health. As part of this effort, the gap between the registered medicines and the planned procurement through PFSA (PFSA List) was evaluated/assessed. The unregistered products in the PFSA's procurement list were identified and submitted to management for registration under a speedy process. The management decided to use the fast-track designation registration procedure for registering those products. The identified lists were announced to all potential applicants using various communication mechanisms for them to use the fast-track opportunity to register their products.

PQM continued to provide ongoing technical assistance for improvements to the medicine registration information system. This system was developed and implemented over the last 3 years and continues to undergo improvements and modifications for additional system requirements and uses. In Q1, the purchase order approval system was optimized to approve the request using the system (self-paced) approval. This approval process enables applicants to generate purchase order approval letter online, using the system, without a need to visit EFMHACA. This will substantially reduce waiting time and improves transparency.

A regulatory information management system is critical for a national regulatory authority, as it improves decision-making, transparency, and accountability, thereby improving public confidence in the authority. EFMHACA is working toward the development of a web-based medical devices registration system. PQM provided technical assistance to EFMHACA through attending a workshop on Medical Device Information System (MDIS) development organized on September 18–19. PQM played a key role in chairing the technical working group and provided input in defining the requirements and mapping the processes for the development of MDIS.

Training of trainers (was provided to staff of Ethiopia's regional regulatory authorities and EFMHACA on audit inspection. In addition to contributing trainers, PQM provided technical support through the preparation of a proposal for the training-of-trainers training and training materials development. The training covers the role of different sectors in quality management of medicine at different level of the distribution chain; the auditing process; quality management in supply chain; management responsibility; premises and facilities; material management; resource management; validation, calibration, verification, and internal audits; products complaints; products recall; contract activities; documentation; and necessary legal documents and results of audit inspection. A total of 188 experts were trained. Presentation of these findings helped the audience to identify gaps in the overall inspection, including

inspection tool, for improvement during upcoming inspections. In the previous year, PQM had provided technical support for the development of an inspection manual that outlines appropriate steps to be followed for auditing medicine retail outlets and distributors with respect to good dispensing, good storage, and good distribution practices. This type of inspection has been referred to as audit-based inspection, which requires inspectors to crosscheck whether establishments are authorized to handle the products found within their establishments and whether the products are obtained from legal sources. This rigorous process of auditing during inspection is expected to boost the capacity of EFMHACA and regional regulators to detect and prevent the circulation of poor-quality medicines, thereby helping to ensure the safety, quality, and effective use of medicines circulating in Ethiopia's market. The training was designed to help EFMHACA and regional regulatory bodies to effectively scale up implementation of audit-based inspection. The training was financed by EFMHACA, which is a sign of ownership and sustainability of in-service training programs that used to be supported by PQM.

In addition, training was provided November 6–9 to one regional regulatory body (Tigray regional regulatory body) and EFMHACA North branch inspectors on conformity assessment, with respect to ISO 17020 requirements for conducting inspection. The training covered general requirements such as impartiality, independence, and confidentiality of inspection; structure requirements of inspection bodies; resource requirements; process requirements; management requirements; and required documents and formats; and monitoring and evaluation. USP/PQM provided technical assistance in developing training materials and participated as a trainer. This training is part of the effort to scale up implementation of good inspection practices to regions.

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

In FY18, PQM capacitated the National Metrology Institute (NMI) in Addis Ababa to help it provide calibration services to EFMHACA. Since then, the progressive changes at NMI have brought a successful result for enabling transitioning of laboratory equipment calibration.

In Q1, NMI was able to successfully calibrate all equipment of both the medicines and food QC EFMHACA laboratories. This is a remarkable achievement and showcases the path toward sustaining the laboratories' accreditation through securing the equipment calibration piece. EFMHACA has also formalized the relationship with NMI to ensure ongoing support for equipment calibration. In addition to EFMHACA, other similar institutions requiring calibration would also benefit from this capacity in the country.

In the past years, PQM has been building the capacity of the branch EFMHACA laboratories so that they will be able to test medicines for quality at their level. Based on recommendations of the last supportive supervision conducted at each EFMHACA laboratory branch, in Q1 PQM helped train laboratory branch technical staff on instrument calibration. The training was conducted on October 15–19 at EFMHACA's Diredawa and Mekele branches. A total of 16 staff were trained. Areas covered during the training included performance verification testing (PVT) for HPLC, ultraviolet visible (UV-Vis) spectrophotometer, pH meter, and analytical balance.

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

Planned activities were accomplished under this activity during previous quarters, and there is no update for Q1.

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

PMS of antimalarial medicines is one of the planned activities under FY19. Based on the plan, the PMS protocol was customized for the branch laboratories to be used in their PMS activities. Accordingly, samples of antimalarial medicines were collected by the five EFMHACA branch laboratories. In relation to this, list of laboratory supplies required for testing the PMS samples was identified and quantified, and procurement was started. The collected samples will be sent to each branch laboratory for testing. A generic PMS guideline has been drafted and shared with EFMHACA for further revision. The guideline adopts key principles for the implementation of risk-based PMS.

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

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As part of the GMP roadmap implementation, initial and mid-term assessments were conducted in 2012 and 2016. According to the GMP roadmap document, the grace period provided for local manufacturers to comply with GMP ends in 2018. Hence, the final GMP compliance assessment was conducted in nine local pharmaceutical manufacturing facilities. PQM participated in the assessment of APF IV factory on November 6–8 and EPHARM Sh. Co. on November 25–28. The report is being prepared, and the government's decision will be sought after submission of the official reports.

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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***

In Q1, PQM, represented by its Chief of party (COP) gave a presentation at a regional workshop organized for training on key enabling factors for successful local production and supply of quality-assured medicines. The presentation was entitled “Overview of Local Manufacturers’ Experiences: Lessons from PQM.” Stakeholders including WHO, NEPAD, and local manufactures participated in the workshop. The presentation addresses PQM background information, key challenges in the regulatory and manufacturing sectors, and PQM’s experience in helping the government of Ethiopia to overcome such challenges. This workshop was jointly organized by WHO and PQM in collaboration with NEPAD and benefits local manufacturers in Africa. In addition to the Ethiopia COP, two PQM technical experts, with funding from PQM core portfolios, also presented during the workshop.

As part of providing technical assistance to EFMHACA to strengthen and sustain its public health programs on its safety monitoring and pharmacovigilance system, PQM participated in the facilitation of a training of trainers organized at Bishoftu by the PROFORMA project and EFMHACA for 40 selected Wereda Expanded Program of Immunization (EPI) representatives and Ministry of Education representatives.

Based on a request from EFMHACA management, PQM staff was selected to serve on the committee organized to restructure the pharmacovigilance team and regulatory information development and communication team (which performs activities on antimicrobial resistance, narcotic and psychotropic substance control, tobacco control, customer service center for prescreening of medicines, and Health Regulatory Information Center). Accordingly, PQM has actively participated in the development of terms of reference for the committee and participated on assessment of the system.

PQM provided technical assistance in the recording of 95 adverse drug event reports into the pharmacovigilance data recording system, 12 of which were product defects. Twenty-eight adverse drug reaction reports were shared with WHO. A letter of further investigation on product quality defects was sent to the Facility Inspection directorate on 11 medicines, and a quarterly newsletter was also prepared.

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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. There are no additional updates for Q1.

## **IV. Key Challenges**

With the recent change in government in Ethiopia, the continuing replacement of high-level government officials requires additional efforts in the creation of awareness on PQM activities and support to EFMHACA. PQM has proactively worked to fill any information gap through ad hoc briefing and communications whenever needed.

# **Ghana**

## **I. Quarter 1 Highlights**

PQM Ghana activities from FY18 were extended into 2019. These activities continue to focus on the ongoing technical assistance to Entrance Pharmaceuticals Limited (EPL) to address the gaps identified during an assessment in FY18 Q1. With ongoing PQM technical assistance, the manufacturer has continued to take positive strides to improve its GMP compliance and progress toward submitting its artemether–lumefantrine product dossier to the WHO prequalification program. Based on the ongoing progress, the manufacturer is expected to submit its dossier for WHO prequalification sometime in March 2019. In addition to ongoing remote technical support, PQM provided onsite review of the corrective and preventive action (CAPA) plan and technical guidance on appropriate implementation of the plan. Based on the review, it is noted that EPL has rectified and implemented about 40 percent of its CAPAs and is expected to continue making progress with the remainder.

In continuation of the support to the local pharmaceutical sector in Ghana, PQM in collaboration with the Ghana FDA (GFDA) Drug Industrial Support Department (DISD) to provide training on select GMP topics to local pharmaceutical manufacturers. This is the first of a series of GMP-related trainings planned by FDA to build capacity for GMP compliance within the local industry. As a demonstration of country ownership and sustainability, the training was organized by GFDA and the Pharmaceutical Manufacturers Association in Ghana (PMAG). Both PQM and GFDA served as trainers.

Preliminary data from the PMS of uterotonics (oxytocin and ergometrine injections) conducted by GFDA in September 2018 indicated a large number (63%,  $n=105$ ) of unregistered oxytocin injection samples within the supply chain. This significant finding prompted, as an immediate regulatory action, a GFDA letter to the Minister of Health to trigger higher-level discussion, particularly because some of the unregistered products were found in public sector facilities under the control of the Ministry of Health. In addition, PQM also recommends the FDA work with public health facilities to ensure procurement manuals require approval of only registered products or request for a waiver, if this is not already the case. Testing of the samples is still ongoing, and the results will be available and published next quarter.

## 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 medicine 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.

Medicine quality surveillance is also a priority of the Ghana FDA. The authority continues to implement routine surveillance of priority medicines used in the treatment of malaria and those used for Maternal and Neo-natal child health programs.

## III. Quarter 1 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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#### ***Facilitate PMS of MCH products***

Implementation of activities for the surveillance of the quality of oxytocin and ergometrine injections began in Q1. Samples were collected from all 10 regions in Ghana and are currently undergoing analytical testing at the GFDA laboratory. Preliminary findings from the survey indicated that 62.9% ( $n=105$ ) of oxytocin injection samples collected were not registered or authorized for distribution or use in the country by GFDA. Most of the unregistered medicines were collected from public sector facilities, which prompted GFDA to immediately notify the Minister of Health to ensure proper procurement practices are followed and reiterate that only duly registered medicines should be procured. The results of the analytical test are still pending and will be disseminated once they are available in Q2.

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

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Activities under this objective were completed in Q3.

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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***

GFDA DISD continues to work closely with PQM GMP experts as technical assistance is provided to EPL. Recognizing the improvements achieved by EPL toward closing its GMP technical capacity gaps, GFDA DISD seeks to extend its support to the local pharmaceutical manufacturing sector to help bridge some of the human capacity gaps identified through the GMP roadmap. Some of these human capacity gaps were also observed during the PQM assessment of four local manufacturers in November 2017. The FDA DISD has thus partnered with PMAG to provide a series of GMP-related trainings to build capacity for GMP compliance within the country. This partnership demonstrates local ownership and strengthens the sustainability of the efforts to improve GMP compliance.

As a first in this series of GMP trainings, in collaboration with GFDA DISD, PQM provided training on select GMP topics to local pharmaceutical manufacturers in Ghana. Participants who benefited from the training included 64 people from 19 local manufacturing companies and GFDA staff (as training of trainers). The technical trainings were provided by both PQM and GFDA staff and covered the following five topics: pharmaceutical QMS; manufacturing premises design, installation, and qualification; development of a validation master plan and validation protocols; GMP in the QC laboratory and GMP in production; and quality risk management. PQM envisions that in addition to the benefit to local manufacturers, GFDA staff will continue to utilize the same materials to provide future trainings and refreshers, as needed. These materials can serve to train future staff at GFDA.

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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, in addition to ongoing remote technical assistance, PQM GMP experts also provided an onsite technical support. Key documents and processes were reviewed and technical advice provided for continued implementation of the CAPAs developed by EPL following the initial gap assessment in October–November 2017. Based on current reviews, EPL is deemed to have completed about 40 percent of its CAPA plan and continues to make progress on the others.

From a project timeline perspective, EPL continues to experience unplanned delays, mostly related to importation of equipment and materials to address its needs; however, EPL management continues to demonstrate commitment to the goals of the project toward the submission of its artemether–lumefantrine dossier for WHO prequalification. Following a technical review meeting held at EPL's facility on December 13, the project is deemed on course, and EPL is expected to have its dossier submitted for WHO prequalification by March 31, 2019.

## Guinea

### I. Quarter 1 Highlights

In the previous quarter, PQM reviewed the EU-funded laboratory renovation plan and provided amendments in compliance with international standards of good laboratory safety in the analytical/physical chemistry area. In Q1, the renovation and installations of security exits in the laboratory were completed. Additional separated areas for weighing and for receiving laboratory supplies were also added to the laboratory spaces, as recommended by PQM.

PQM trained laboratory staff on the proper use of Karl Fischer equipment and assisted the laboratory in developing laboratory technical and managerial documentation.

For National Directorate of Pharmacy and Medicine (DNPM) activities, the DNPM Director designated a focal person to work with PQM on the first review of the PMS protocol. The first review has been completed and submitted to DNPM director for his final review. The next step is to share this protocol version with all parties involved in the PMS program for their review and implementation. Any further amendments will have to be approved by the Director to finalize the protocol.

### 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 MRA 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 1 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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After the promulgation of the pharmaceutical law, DNPM is working on the elaboration of texts of enactment of the law. These texts will help DNPM to undertake a new function under its mandate, such as PMS. Having these texts elaborated by DNPM will also help PQM in the implementation phase of the PMS program and inspection of the pharmaceutical manufacturer facilities.

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

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At the request of the DNPM Director, PQM is planning to support strengthening the inspection and import control activities instead of the registration activities that were planned in the FY18 work plan. In Q1, PQM worked on hiring a consultant to support DNPM's request.

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

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To advance the validation of the PMS protocol, PQM requested the DNPM Director to designate a focal person for this activity. In Q1, PQM worked with the focal person and other DNPM staff and reviewed the first draft of the protocol. During the review process, PQM went over the content of the protocol and explained all the process of the PMS activities. This is the second time PQM is providing this type of assistance because the current DNPM PMS staff were newly recruited after the reorganization of the MOH. In addition to the PMS protocol, PQM prepared an agenda of PMS activities that includes designation of staff to be trained in sampling of medicines and testing collected samples using Minilab™ as a prescreening tool.

As next steps, the revised PMS protocol and agenda will be sent by DNPM to the heads of major health programs and to MOH stakeholders who are to be involved in this activity for review. Following this step, PQM will help DNPM in organizing a workshop for the final validation of the PMS protocol and the launch of the first official PMS round.

Following the validation of the protocol, PQM will provide the needed training(s) and support to DNPM for direct implementation of the PMS activities in Conakry, with samples collected from one sentinel site.

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

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In Q4, PQM followed up with the laboratory on implementation of the revised renovation plan and the safety measures recommended by the PQM consultant. PQM also shipped the necessary reagents and laboratory supplies to conduct analytical training as part of the FY 2018 work plan. In Q1, PQM trained five laboratory staff on the proper use of Karl Fischer and assisted laboratory in developing some laboratory technical standard operating procedures (SOPs) such as SOPs for the proper use of Karl Fischer and provided guidance on the establishment of its quality manual.

## IGAD

### I. Quarter 1 Highlights

PQM conducted a workshop with members of the IGAD Expert Working Group on PMS to implement the work plan programmed quality survey. The purpose of this survey was to determine the prevalence of substandard and falsified medicines within IGAD cross-border areas. The workshop was designed to build the capacity of IGAD-MRH member states on medicines quality surveillance and to facilitate planning for sample collection during the survey. The workshop was held in Entebbe, Uganda, on October 1–5, with a focus on training member states on risk-based PMS, finalizing the PMS protocol, and training sample collectors on the protocol. PQM's risk based PMS approach,

including the MedRS tool, was utilized for the development of the final protocol. The protocol was finalized and approved by participating member states, and sample collection is expected to commence next quarter.

The pharmacovigilance systems self-assessment of IGAD member countries' MRAs was completed in Q1. Preliminary result from the assessment showed several deficiencies in member states' pharmacovigilance systems, including absence of laws, guidelines, SOPs, and other documentation addressing pharmacovigilance activities. The result also showed that the status of pharmacovigilance systems among member countries varied from no existing pharmacovigilance center or designated full time, to those with no annual allocated government budget and no platform for coordination of activities.

Including this intervention on the PQM work plan allowed IGAD-MRH to efficiently use the same EWG to coordinate both safety and quality surveillance in the region. PQM helped facilitate the technical discussion, thus enabling member states to carry out self-assessments and identify gaps in the implementation of pharmacovigilance activities within their respective countries. The information from this preliminary self-assessment will be utilized by any future implementing partner with a pharmacovigilance mandate to strengthen safety monitoring in the region.

## II. IGAD Context

The IGAD region comprises eight countries in the horn of Africa region and includes Djibouti, Eritrea, Ethiopia, Kenya, Somalia, South Sudan, Sudan, and Uganda. The region experiences migration and cross-border mobility due to economic uncertainties and political conflicts. 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 tuberculosis 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 1 Progress by Objective

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### **Objective 1 – 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**

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In the previous quarter, PQM worked with the EWG to facilitate a gap assessment of pharmacovigilance/PMS documents and practices. However, the assessment was not completed by most member states. In Q1, PQM used the PMS sample collectors training workshop platform to solicit completion of a self-assessment checklist. Accordingly, six of the seven IGAD member states MRA representatives (except Djibouti) completed the checklist, and a preliminary assessment report of pharmacovigilance systems among the IGAD member states was drafted by PQM.

The assessment conducted focused on understanding the status of the pharmacovigilance system in IGAD member countries. Preliminary data indicate that almost half of the members have no functional pharmacovigilance system for monitoring medicines safety for any medicines. The preliminary assessment result showed several deficiencies, including absence of laws, guidelines, SOPs and other documentation addressing pharmacovigilance activities. The result also showed that the status of pharmacovigilance systems varied from no existing pharmacovigilance center

with no designated full time staff (South Sudan), to those with no annual allocated government budget (Somalia) and no platform for coordination of pharmacovigilance activities (Ethiopia, South Sudan, and Somalia). Djibouti did not respond to the checklist as there is no existing system for pharmacovigilance in the country. The draft pharmacovigilance assessment report will be shared for adoption by member states during the PMS result validation workshop, planned for next quarter.

Based on draft report results, PQM recommends providing technical assistance to help build a pharmacovigilance system in member states, which can then be harmonized through the regional IGAD MRH platform. Some of this includes technical assistance for development of legal frameworks, guidelines, SOPs, reporting forms, training of staff, improving the coordination of pharmacovigilance activities, creation of communication mechanisms, and other components necessary for the establishment and functioning of a proper pharmacovigilance center.

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**Objective 2 – 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**

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During the past fiscal year (FY18 Q4), a draft survey protocol to determine the prevalence of substandard and falsified MNCH-FP/TB/HIV medicines was prepared; IGAD cross-border areas were identified for medicine sample collection and a risk based PMS approach was introduced to participants in the kickoff workshop at Addis Ababa.

TA was also provided to Uganda NDA for the adoption of risk based PMS; this resulted in the development of the national PMS plan for 2018.

In this first quarter of FY19, in continuation of the support for PMS to determine prevalence of SF medicines within IGAD cross border areas, a workshop was held in Entebbe on October 1– 5, with a focus on finalizing the PMS protocol, training sample collectors on the protocol, and providing training on PQM's risk based PMS approach. Three PQM experts provided technical assistance during the workshop, and the MedRS tool to support risk-based PMS was introduced. The tool was used to identify the most susceptible medicines; determine the number of samples; and prioritize sampling at the most vulnerable locations of the IGAD cross-border sites (city and regions to collect samples). The final protocol developed collaboratively by all participants was signed by the member states. All IGAD member countries were represented at the workshop. A total of 35 people attended the workshop, including trainees from member states, the IGAD-MRH secretariat team, and USAID/East Africa representatives. Although Sudan and South Sudan representatives were present, their participation was not funded through USAID but through some other IGAD-MRH funding sources.

Outcomes from the workshop included:

- The protocol for PMS on oxytocin and amoxicillin DT was completed and signed by member states.
- 25 national MRA members completed training on PMS protocol development, the risk-based PMS approach, and MedRS.

In addition to the oxytocin injection selected during the June 2018 workshop, amoxicillin DT/suspension was added as a priority medicine for surveillance. The workshop also discussed the logistics for sample collection: shipping, testing, report writing, and result dissemination. Necessary sample collection materials were distributed to representatives from member states during the workshop.

Tentative timelines and budgets for sample collection by each country were developed, with a plan to commence sampling in late October 2018. This timeline has since been revised due to IGAD logistical challenges. Sample collection from the cross-border areas began in December 2018 and was expected to be completed by January 31, 2019. All collected samples will be shipped to the EFMHACA laboratory in Ethiopia for testing, and the results are expected next quarter. A result validation workshop will be conducted in February/March 2019, after which the results will be formally disseminated to all relevant stakeholder.

Following the workshop, PQM also provided USP amoxicillin and USP oxytocin reference standards required for the analytical testing of the samples to the EFMHACA laboratory in Ethiopia to facilitate analytical testing of the samples.

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

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No activity to report this quarter.

# Kenya

## I. Quarter 1 Highlights

The USAID Mission approved the FY18 work plan that was submitted in FY18 Q4. At the time of finalizing this report, PQM was informed that the suspension had been lifted, allowing the work to continue.

# Liberia

## I. Quarter 1 Highlights

As part of strengthening the capacities of the Liberia Medicines and Health Products Regulatory Authority (LMHRA), USAID awarded a fixed award (FAA) to the authority to conduct risk-based PMS. The Authority has made significant progress in the implementation of the FAA activities and completed three milestones that included sampling and testing of antimalarial medicines with Minilab™. However, the LMHRA QC laboratory was unable to conduct the confirmatory testing as part of milestone 4. This challenge pushed LMHRA to request a 3-month extension of the FAA. Q1 was also marked by capacity- and skills-building of five LMHRA inspectors on GMP inspection. The training incorporated actual hands-on experience at a distribution chain site in Monrovia and at a manufacturing site in Ghana, equipping the inspectors with skills they need to conduct current GMP inspections of foreign manufacturers that apply for marketing authorization of their products in Liberia.

## 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 partnerships to increase access to quality-assured antimalarial medicines.

Since 2011, PQM has provided technical assistance to strengthen PMS in Liberia through MQM for antimalarial medicines and has encouraged LMHRA to take the appropriate regulatory actions when poor-quality medicines are identified. As a result of these MQM activities, several antimalarial medicines, including quinine tablets and chloroquine, were removed from circulation. Monotherapies such as quinine tablets and chloroquine were once widely available but have been subsequently banned through a regulatory action by LMHRA and since then have become less prevalent. Although 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 and substandard medical products and increasing awareness about the quality of medicines.

As part of the approved FY 2018 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 1 Progress by Objective

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

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Previously in 2018, PQM had supported LMHRA's QC laboratory to transition to a temporary facility and provided guidance on laboratory security measures and partitioning of the physicochemistry area. PQM also assisted with the installation of selected laboratory equipment and training on preventive maintenance. Through USP, in Q1 PQM donated some laboratory equipment to LMHRA to enable it to continue its quality control functions. LMHRA is still

waiting to receive the remaining laboratory equipment ordered from a local vendor. The equipment donated by USP (valued at 19,480 USD) includes the following:

- Mettler Toledo analytical laboratory balance (a highly sensitive laboratory instrument designed to accurately measure mass).
- Waters HPLC (HPLC is an analytical technique used to separate, identify, and quantify each component in a mixture to assess whether medicine is substandard or not).
- HP laptop Model No. TPN-F102.

PQM plans to carry out the remaining FY18 laboratory activities, including training on compendial testing, review of PMS activities, and preparation of the dissemination meeting, next quarter.

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

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Liberia currently does not have an in-country manufacturing company, and LMHRA inspectors have no manufacturing sites to develop practical experience needed for manufacturing site audits prior to product registration. To build capacity for facility inspection and empower LMHRA inspectors to carry out this regulatory function, PQM conducted a series of GxP trainings incorporating theoretical as well as hands-on learning. The first 5 days of the GxP theoretical training included information on good regulatory practice, good distribution practices, and good storage practices, and hands-on inspection of a medicine distribution chain in Monrovia. This was followed by a 3-day hands-on manufacturing facility inspection training conducted at a manufacturer site in Ghana. The training provided the opportunity for LMHRA inspectors to apply theoretical knowledge gained for the first 5 days and practice in a real-world setting. The goal was to build their capabilities and confidence in future current GMP audits/inspections of manufacturing facilities to assure medicines quality in the Liberian market.

Five LMHRA inspectors benefited from this training. Next steps include for LMHRA to start conducting current GMP inspections of overseas manufacturers as part of its marketing authorization process to allow supply of medicines into the Liberian market.

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

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No new information to report on Q1.

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

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According to the approved Liberian FAA, LMHRA is supposed to complete all milestones by December 2018. However, due to the laboratory challenges in receiving the equipment needed to conduct QC testing (milestone 4), the Authority requested from PQM to extend the FAA until March 2019. The request was submitted to USAID HQ for approval.

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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 completing the confirmatory testing of collected antimalarial medicines under the extended FAA (milestone 4).

## **IV. Key Challenges**

- There has been slow progress in getting approval from the Global Fund to build the permanent laboratory. For this reason, activities under this section have been reprogrammed.
- Delays in receiving laboratory equipment, reagents, and consumables impeded the execution of the FAA milestone 4 (QC testing), which in return pushed LMHRA to request an extension of the PMS FAA until March 2019.

# Mali

## I. Quarter 1 Highlights

PQM continued to strengthen the LNS in building its quality management and monitoring the quality of antimalarial medicines. PQM assisted the laboratory in developing 27 QMS documents. To continue to support PMS activities, PQM convened a meeting with LNS, DPM, PNLP, and the Pharmacist Association to finalize a protocol for monitoring the quality of antimalarial medicines that incorporates taking immediate action at the site of sampling. The lack of regulatory actions following the finding of falsified antimalarial medicines has been a challenge. The falsified antimalarials found previously had the same lot numbers from supposedly the same claimed manufacturers. If the same products are found, there will be no need to test them and the DPM should be able to take them out. The Pharmacist Association is willing to support PMS activities in the future through direct participation using its own resources.

## 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 1 Progress by Objective

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

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PQM staff met with DPM management to inquire about its progress toward adopting a legal provision for establishing a national pharmaceutical regulatory agency. The provision was returned to the directorate for revision. PQM offered to review the revised provision and provide feedback to the DPM.

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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 continues to assist the laboratory in building its QMS by developing 27 QMS documents, including 14 SOPs. The finalization and adoption of developed documents have stalled at the laboratory management level. PQM revisited the SOP on document management and control that the LNS Director General modified to give him sole authority to sign off any QMS document. PQM provided guidance to revise the procedure and clarify the roles and responsibilities of the LNS Director General, his Deputy, the QA Manager and his Deputy, Laboratory Manager, and other personnel. To address the challenge in the documentation and review of laboratory work, PQM assist LNS in developing or revising a set of SOPs. Other SOPs were developed to align with the new ISO 17025-2017 standard.

The following high-level SOPs were drafted in Q1:

1. Quality management
2. Risk and change control
3. Trending of analytical data

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### Objective 3 – Strengthen sustainable local capacity to monitor the quality of medicines in the country

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Taking into consideration the lessons learned from previous PMS activities carried out in 2017 and 2018 and the lack or delay in action taking on noncompliant antimalarial medicines, PQM coordinated with LNS, DPM, and PNLP to develop a protocol for monitoring the quality of antimalarial medicines that will include withdrawal or quarantining of suspected products found at the time of sampling.

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

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Seasonal malaria chemoprevention (SMC) is being used in Mali to reduce the burden of malaria in children under 5. PQM is facilitating a study on resistance to sulfadoxine–pyrimethamine and amodiaquine, the combination used in SMC. The Laboratory of Applied Molecular Biology conducting the study completed the first milestone, which includes training of staff and the preparation of the site. Twenty participants attended the training, including medical staff members and personnel recruited to work on the project. The site preparation included purchase of reagents and supplies. The enrollment started in the site of Dioro.

### IV. Key Challenges

LNS progress to attain international standards level has been hampered by the ineffective leadership of the laboratory's management. Despite PQM efforts, LNS management has been slow in sharing quality control test results of samples collected as part of PMS activities with local stakeholders.

## Mozambique

### I. Quarter 1 Highlights

Strengthening the medicine regulatory systems of pharmaceuticals has been the primary goal of the PQM program in Mozambique. In Q1, the National Directorate of Pharmacy (DNF) received PQM support in different operational areas:

- Approval of LNCQM's preventive maintenance plan (PMP) by the laboratory management. The PMP will help the national medicine laboratory plan ahead to ensure equipment are qualified and validated, as required, to promote the accuracy and reliability of results.
- Development of a draft risk-based PMS protocol for the planned medicines surveillance exercise to assess the quality of selected medicines in the markets.
- Completed review and contribution to the technical content of the DNF's pharmaceutical inspection regulation for Mozambique.

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

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

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

With more than 90 percent of medicines circulating in Mozambique being imported, the authorities are aware of the country's vulnerability and exposure to poor-quality medicines. This new legislature, including Article 4 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 1 Progress by Objective

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

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To strengthen the capacity of Mozambique's national laboratory and ensure that all LNCQM laboratory equipment is qualified and functional, with PQM support LNCQM categorized the laboratory equipment using a risk-based analytical instrumentation qualification approach, USP <1058>. This integrated risk-based approach helps promote efficiency and cost savings for laboratories, utilizing a three-step categorization process for the identification of the equipment with the greatest need for qualification. Analytical instrument qualification helps ensure that equipment is fit for its purpose. LNCQM equipment was categorized into three groups based on this approach: group A (least complex standard equipment used without measurement capability, require no further qualification), group B (instruments that may provide a measurement; proper function requires routine calibration, maintenance and performance checks), and group C (equipment with a significant degree of computerization, all elements of qualification must be considered to ensure proper functioning). This was done using the equipment data gathered from the Instrument Master List. PQM collaborated with LNCQM to develop a detailed PMP based on the procedural gaps present in LNCQM's QMS and instrumentation categorization. This plan contains suggested performance verification intervals and defines which equipment may be verified or calibrated in house rather than externally.

Availability of supplies and reagents is pivotal to LNCQM's operation. PQM continues to support procurement of key reagents and supplies for LNCQM, while discussing with DNF the identification of sustainable ways to generate revenue to support LNCQM activities. In Q1, PQM worked on several procurement requests for reagents and supplies for LNCQM. While some supplies were received, efforts to get more reagents and other supplies have been intensified.

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

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To support and strengthen the PMS system in Mozambique, PQM had conducted a workshop during the previous quarter. In Q1, the committee shared with PQM a draft protocol for the planned PMS activity incorporating results from the MedRS tool used for the selection of high-risk provinces, cities, and facilities, as well as type of medicines to sample. PQM technical staff reviewed the draft and provided feedback to DNF, including the protocol development committee. This approach was utilized to let country staff gain experience in developing PMS protocols to build country capacity and self-reliance.

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

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To strengthen the medicine regulatory system in Mozambique, key regulations were identified for development; this was in line with the revised pharmaceutical law approved under the republic of Mozambique law no 12 of 2017, which was published in the gazette on September 8, 2017. For the operationalization of the law, DNF identified priority regulations to be developed first. In Q1, PQM reviewed and provided technical contributions to the pharmaceutical inspection regulation to ensure it meets the requirements of both local and international laws. PQM support included highlighting key contents of a well-written regulation and qualifications and functions of suitable inspectors, as well as identifying missing information to be added to meet local and international requirements.

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

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To increase DNF visibility and capacity through interaction and participation in international conferences, PQM supported the attendance of DNF staff at the medicines quality and public health conference in Oxford, London.

The conference provided a unique opportunity for DNF, as an interested party in this field, to participate and learn from the discussion on the problem and outlined necessary steps to tackle falsified and substandard medical products on a country and global scale. DNF staff also learned from the ideas and experiences shared by other regulatory authorities and stakeholders in this sector.

### IV. Key Challenges

Sustainability of medicines quality testing is a big concern after the PQM program closes in Mozambique, since the laboratory does not generate funds and receives inadequate financial support from the government.

# Nigeria

## I. Quarter 1 Highlights

Two NAFDAC laboratories (Yaba and Agulu) achieved ISO/IEC 17025:2005 reaccreditation. There is ongoing support for NAFDAC's National Control Laboratory for Vaccine and other Biologicals, which is at a very advanced stage. The ISO/IEC audit of this laboratory will take place next quarter. Final samples test results from the PMS conducted in FY18 for antimalarials became available in Q1. As a result of the audit, the laboratory will be able to test rapid diagnostic tests and support the National Malaria Elimination Program in Nigeria; this will be the first time a laboratory in Nigeria will be accredited to perform this test.

PQM continues to provide technical assistance to local manufacturers in Nigeria to support production of priority public health products of interest. In Q1, two product dossiers (chlorhexidine gel and magnesium sulfate injection) were submitted to WAHO for review and approval as part of the medicine registration harmonization initiative. Once approved, marketing authorization can be sought for the West African countries to market these products. A magnesium sulfate injection dossier was also submitted to the Tanzania FDA for review and approval. PQM is currently providing technical assistance to Juhel Pharmaceuticals for submission of magnesium sulfate injection for WHO prequalification. Also in Q1, a large quantity of chlorhexidine gel was procured for distribution across various countries in Africa.

## II. Country Context

Through PMI funding, USAID/Nigeria is focused on strengthening NAFDAC's regulatory capacity and increasing the availability of locally manufactured quality-assured antimalarial medicines to support PMI's overarching goal to reduce malaria-associated mortality 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, the National Institute for Pharmaceutical Research and Development (NIPRD), and the National Malaria Elimination Program. In addition, there are pharmaceutical and nutraceutical manufacturers and other stakeholders whose activities directly impact system strengthening of NAFDAC and PQM-supported local manufacturers.

## III. Quarter 1 Progress by Objective

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### Objective 1 – Strengthen the national quality assurance and regulatory system

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In line with the Nigeria's FY19 work plan activity, PQM Nigeria will focus on sustainable channels to support NAFDAC in adoption of risk-based PMS principles for its national PMS program. In FY18 Q2, PQM provided hands-on training to NAFDAC staff on the use of the MedRS tool. This tool is a complement to PQM's risk-based PMS guidelines. It allows MRAs to assess medicines risk when selecting those to be included in the national PMS plan. The tool helps MRAs make statistically sound decisions, so the number of samples to be collected is statistically representative, and it also allows the MRA to randomize the selection of outlets where the samples are collected based on risk. PQM's PMS guidelines also help NQCLs to prioritize analytical test for the samples collected during PMS.

Following the training in FY18 Q2, the NAFDAC PMS team will adopt elements of the risk-based PMS approach in the next round of PMS of antimalarials and prioritize the MCH products scheduled for next quarter. This will be the last collaborative PMS exercise for the PQM program in Nigeria.

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

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The ISO/IEC 17025 is an international accreditation standard for laboratories demonstrating technical proficiency and ability to produce reliable, precise, and accurate tests and calibration data for testing equipment. Three NAFDAC NQCLs initially achieved ISO/IEC 17025 accreditation: Yaba in FY16 and Agulu and Kaduna in FY17. To ensure that

accredited laboratories continue to perform at the same international standard, surveillance visits and biennial reaccreditations are required. In Q1, ISO/IEC 17025:2005 reaccreditation assessments of NAFDAC's Yaba and Agulu laboratories were conducted by ANAB, the third-party assessor. Both laboratories had three to four minor nonconformances. All identified nonconformances were resolved by NAFDAC staff without support from PQM, and reaccreditation certificates were awarded to both laboratories for all test methods, including microbiology. All associated costs for the reaccreditation of the laboratories, including logistics, were paid for by NAFDAC without financial support from PQM.

PQM conducted a mock audit of NAFDAC's National Control Laboratory for Vaccine and other Biologicals (NCLVB) using the ISO/IEC 17025:2005 audit checklist. NCLVB is the only laboratory in Nigeria responsible for the quality control of vaccines and biologics; when accredited, the laboratory will provide quality testing for vaccines developed and imported into the country. The laboratory audit was conducted by witnessing 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, and uniformity of dosage unit. Review of documents and key informant interviews were conducted to assess the laboratory's QMS. Key findings included 5 major and 10 minor nonconformances. Minimal technical assistance will be provided by PQM as the laboratory staff from the sister Yaba accredited laboratory will provide most of the technical assistance needed to resolve all identified nonconformances, ahead of the third-party audit by ANAB scheduled for next quarter.

Additionally, through PQM's support, NAFDAC is now linked to a local accreditation body, Nigeria National Accreditation Service (NiNAS). It is expected that the cost of accreditation will decrease as a result of utilizing this accreditation body. In Q1, in collaboration with NiNAS, PQM trained 13 NAFDAC and NIPRD laboratory staff and 10 NiNAS staff on requirements for the new ISO 17025:2017. The training was essential, as all accredited laboratories are expected to upgrade their status of accreditation to ISO/IEC 17025:2017. The training sessions compared clauses of the former ISO 17025:2005 and the new ISO 17025:2017 versions, including harmonization of laboratory documents to fit the new ISO 17025:2017 and a pragmatic approach to transition to the new version. The new ISO/IEC 17025:2017 specifies the general requirements for the competence, impartiality, and consistent operation of laboratories. It is applicable to all organizations performing laboratory activities, regardless of the number of personnel and will be used in confirming or recognizing the competence of laboratories by regulatory authorities, laboratory customers, and accreditation bodies.

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

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A continuous supply of quality-assured products—particularly for essential priority medicines for TB, NTDs, and MNCH—is necessary to address national health priorities and plans. PQM works with manufacturers to attain compliance with current GMP and 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 will decrease reliance on international donations and help establish a sustainable local supply with national resources.

In Q1, PQM provided technical assistance to a local manufacturer toward WHO prequalification of two products, oxytocin injection and magnesium sulfate. As part of building the capacity of local manufacturers, PQM provided technical support to nine local manufacturers interested in producing critical MNCH products, such as zinc sulfate tablet, oral rehydration salts (ORS), chlorhexidine, amoxicillin dispersible tablet (DT), artemether–lumefantrine, oxytocin injection, magnesium sulfate injection, and ready-to-use therapeutic food.

Last quarter, the management of Juhel Pharmaceuticals indicated their intention of prequalify oxytocin injection. The PQM GMP team developed a roadmap with timelines for WHO prequalification of oxytocin, including the reformulation process. The roadmap was shared with the management for their commitment and buy-in of the process. As part of the developed roadmap for technical assistance for WHO prequalification of oxytocin injection (10iu in 1ml), data for oxytocin dossier were updated in Q1. The PQM GMP team will continue to monitor the accelerated study for more data, in preparation for submission to the WHO prequalification dossier team.

In Q1, with technical assistance from PQM, Juhel Pharmaceuticals successfully submitted the magnesium sulfate injection dossier for approval to the Tanzania FDA and WAHO. Once marketing authorization is approved, this lifesaving medicine will be available in other West African countries and Tanzania. A GMP inspection of Juhel Pharmaceuticals was conducted by a team of QA experts sent by WAHO. The inspection findings had no critical observation. Also in Q1, the Medical Export Group, an international pharmaceutical wholesale organization, delivered 4,700 doses of oxytocin injection from Juhel Pharmaceuticals.

Other activities carried out this quarter include:

- In the last 2 years of implementation, PQM provided continuous technical assistance to Drugfield Pharmaceuticals for production of quality-assured chlorhexidine gel, a lifesaving medicine for newborns. This has improved the quality of production and increased procurement interest across Africa. The company submitted a dossier for chlorhexidine to WAHO. As part of the requirement for a submitted dossier, the WAHO QA team conducted a GMP inspection of the facility. The key findings had no critical observations. Drugfield Pharmaceuticals also received a procurement order for 100,000 tubes of chlorhexidine gel from the Government of Ghana. The Promoting Alternative Thinking Strategies Program (PATHS) made a procurement order for delivery in 3 countries: 27,000 tubes for Niger Republic, 16000 tubes for Ivory Coast, and 25,000 tubes for Benin republic. The gel tubes will be used for program interventions in the respective countries. Drugfield commenced the registration process for chlorhexidine gel in the Republic of South Africa, Eswatini (formally Swaziland), and Botswana. After completion of the registration process, there will be an increased supply of quality-assured chlorhexidine in southern Africa.
- In FY18, PQM held a series of meetings with the Director General of NAFDAC, Director and staff of the NAFDAC Drug Evaluation and Research directorate, and other key stakeholders in the health sector of the country. The primary objective of the meetings was to discuss further the modalities of executing the countrywide GMP roadmap. The GMP roadmap activity aims to evaluate the capacity of local pharmaceutical manufacturers in the country against international GMP requirements; the findings will inform pharmaceutical sector reform in Nigeria (the pharmaceutical sector reform will involve different stakeholders, including NIPRD, Ministry of Industry, Ministry of Finance, and the PMGMAN to address the systemic sector growth inhibition). Key outcomes of the meetings included that NAFDAC will take the lead and provide the human resources needed for a countrywide implementation of the GMP roadmap in Nigeria; the inspection of facilities will be conducted in phases. In preparation for the inspection of facilities, a 3-day workshop was organized for selected 37 NAFDAC staff with the Director, Drug Evaluation and Research in attendance. This was done to familiarize them with existing protocols and tools needed in the field during the inspection exercise.
- The first phase of the GMP inspection was concluded in Q1 with the inspection of 100 out of 123 companies. The last phase of inspections will be completed next quarter. The evaluation of results gathered during inspection and the risk-based categorization of companies based on their compliance with WHO GMP standard will commence next quarter.
- PQM has continued to provide guidance remotely to other companies (Swipha and May & Baker) as they make progress in their product development.

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

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Last quarter, PQM conducted a Pharmaceutical Monitoring and Evaluation (M&E) Plan workshop to develop performance monitoring indicators, clearly articulated goals, targets, and methods of data collection and management. This was to help improve the use data for evidence-based decision-making in the regulatory agency. As part of the next steps after the workshop, PQM continued to provide technical assistance to NAFDAC's M&E team to design and adopt an improved data reporting system and develop a pharmaceutical M&E plan. The first draft of the pharmaceutical M&E plan was concluded in Q1. Next steps include completing the review and editorial process of the first draft of the pharmaceutical M&E plan and providing technical assistance to set up an electronic database for data collection next quarter.

NAFDAC facilitated a dissemination meeting to discuss the PMS results of the antimalarial study this quarter. The meeting had in attendance NAFDAC's Director General; Director of Registration and Regulatory Affairs; PQM staff; representative of the Director of Food and Drug Services, Federal Ministry of Health; National Secretary of Pharmaceutical Society of Nigeria; representative of the Registrar, Pharmacists Council of Nigeria; Chairman of Association of Community Pharmacists of Nigeria; representatives of Pharmaceutical Manufacturing Group of Manufacturers Association of Nigeria; marketing authorization holders, including Sanofi Wintrop, Greenlife Pharmaceutical Ltd, ATSI Pharmaceuticals, Pfizer Plc, GSK Plc, Reals Pharmaceutical Ltd, Medik Pharmacy Limited, Geneith Pharmaceutical, Swipha Plc, Drug Field Pharmaceutical, EUROMED Limited, and Emzor Pharmaceutical Limited.

Key recommendations made at the meeting included:

- Marketing authorization holders should ensure that distributors, wholesalers, and retailers stockpile medicines under suitable conditions as indicated on the medicines' package, to ensure the quality of medicines is maintained along the distribution chain.
- NAFDAC's Pharmacovigilance/Post-Marketing Surveillance Directorate should sustain the mop-up of failed products to prevent continued exposure to the population of substandard, falsified and unregistered antimalarial medicines.
- In line with NAFDAC's sustainability plan, the cost associated with PMS should be included as part of medicines registration fees in the country.
- Drug Evaluation and Research Directorate should strengthen monitoring of GMP of manufacturers of antimalarial medicines, especially the manufacturers of failed samples.
- The Port Inspection Directorate should sustain the surveillance on imported antimalarial medicines to ensure only quality-assured antimalarial medicines are imported into the country.
- NAFDAC staff at the zonal and state offices should intensify the monitoring of distribution and retail outlets, especially in rural areas, to ensure that antimalarial medicines are stored under suitable conditions.

Updates on continuous regulatory actions will be made available next quarter.

## Senegal

### I. Quarter 1 Highlights

During FY 18 Q3 and Q4, PQM provided intensive technical assistance to LNCM for activities pertaining to qualification, calibration, and maintenance of laboratory equipment. However, in Q1 modest progress was made by the laboratory toward the implementation of the ISO 17025 action plan.

The accreditation of LNCM is unlikely to occur this year. Given this situation, PQM reprogrammed the remaining FY 18 activities to support DPM, the medicines regulatory department. The Mission agreed with the proposed PQM strategy for Senegal moving forward.

### 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 eradicated 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 prequalification or ISO 17025:2005 accreditation.

### III. Quarter 1 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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In FY18, PQM provided intensive technical support to LNCM that included maintenance and calibration of laboratory equipment and training on their proper use. PQM also provided a mock audit and followed up with the CAPA action plan. In FY19 Q1, PQM continued working with LNCM with the goal of advancing the process of ISO 17025 accreditation and helped the laboratory develop laboratory documents, including SOPs and forms. The SOPs will be used as guidance/instructions that needed to be followed by the laboratory analysts in performing the instrument performance calibration/verification activities. These forms will be used as a supporting document to the SOPs to fill in with the final results obtained from each test and showing the status of each test. These forms are a standardized documentation template, which can be used for recording results obtained from each test as a way of improving documentation and test traceability.

As next steps, the LNCM is working to:

- Update the SOPs of the equipment under the scope of accreditation (working on the comments, suggestions, and drafted SOPs provided during the PQM Q4 training).
- Follow/execute those SOPs to make sure all topics are covered (perform a dry run of the SOP).
- Conduct a final review of the developed SOPs before sending for approval.
- Train analysts on those SOPs (internally, by the one who wrote those SOPs).
- Put the instruments on the Instrument Master List and assign the calibration and next due calibration dates.

Despite the tremendous technical support provided to the laboratory, LNCM follow-up on the ISO 17025 plan in addressing the PQM audit findings was very slow and did not meet the deadlines. Therefore, due to the time limitation to close out the Senegal project, PQM will not be able to support the official audit by the accrediting body TUNAC. PQM has shared this challenge with the Mission and reprogrammed the FY18 remaining activities to support DPM activities.

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

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To ensure direct implementation and sustainability of the PMS activities, USAID granted LNCM its first FAA. Following the FAA approval process, with PQM guidance, LNCM is working to implement the first milestones of the FAA, which include meeting with key stakeholders to identify the samples to be tested and discuss the sampling strategy and QC testing using a risk-based PMS protocol.

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

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In Senegal, the DPM database is hosted and secured through a nongovernmental organization called GAINDE 2000.<sup>1</sup> In August 2018, PQM provided technical support to DPM to improve the registration and import control database. As part of this assistance, PQM has provided recommendations to DPM and GAINDE 2000 staff on ways to improve the services provided by GAINDE 2000 to DPM.

In Q1, GAINDE 2000 Manager's submitted a letter to the DPM Director to inform him that his organization has taken into account the improvement of services recommended by PQM during the August meetings. As a next step, GAINDE 2000 invited DPM staff to process the import files through the ORBUS platform to verify the effectiveness of these improvements.

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<sup>1</sup> GAINDE 2000 is a Senegalese company leader in the field of ICT, which specializes in the facilitation of trade, the modernization of customs activities and the dematerialization of public formalities. It is a public-private partnership that was created in 2002 with the mission of developing and operating the ORBUS platform, a one-stop shop to facilitate foreign trade formalities.

The other PQM recommendations pertaining to data security, ease of use, and user friendliness of the interfaces with the addition of new modules will be taken into account in the next ORBUS version, which is scheduled to be operational during the first quarter of the year 2019.

## IV. Key Challenges

Despite the tremendous technical support provided to the laboratory, the follow-up by LNCM on the ISO 17025 plan in addressing the PQM audit findings was very slow and did not meet the deadlines. Therefore, due to the time limitation to close out the Senegal project, PQM will not be able to support the official audit by TUNAC. PQM has shared this challenge with the Mission and reprogrammed the FY18 remaining activities to support DPM activities.

# West Bank and Gaza

## I. Quarter 1 Highlights

To support the local pharmaceutical manufacturers expand their sales outside of the Palestinian territories, PQM in 2015–2016 conducted a baseline GMP assessment followed by full assessment of each manufacturer product line. In Q1, PQM conducted a follow-up audit focused on CAPAs taken in response to findings of the full GMP audit performed in 2016.

Also in FY 18, PQM conducted a 2-week assessment of the QA/QC of the regulatory authority, General Directorate of Pharmacy (GDP), and the national quality control laboratory (CPHL). Based on the assessment outcomes, PQM supported CPHL to address identified gaps. In Q1, however, PQM worked with GDP toward addressing identified gaps in the legal policy framework and to improve the registration processes.

## 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 1 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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During the assessment of GDP using the WHO Global Benchmarking Tool (GBT), PQM provided recommendations and guidance on how to address gaps in the current legal framework. As part of the technical assistance provided to GDP, PQM provided technical support to the authority for the review of 12 sections of the national pharmaceutical policy (NPP). The revised NPP was submitted to GDP to share with the key stakeholders for review and approval before its adoption by the Minister of Health's Cabinet.

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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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One of the key findings of the GBT assessment of GDP is the need to assist GDP in establishing the required policies and improving critical functions such as registration, inspection, and clinical trials.

During this quarter, PQM conducted a follow-up assessment to address key findings, to provide recommendations and identify training needs to improve the main functions of GDP, including registration.

The main activities conducted during this quarter included:

- Provided technical assistance to develop and revise the dossier assessment tools, guidelines, and SOPs for registration/ marketing authorization, renewal and variation/amendments.

- Built the capacity and skills of GDP registration staff on Good Review Practices based on WHO guidelines.
- Built the capacity and skills of the same registration staff on the common technical document format (CTD) dossier evaluation/compilation.
- Provided technical assistance to develop the standards for an integrated Regulatory Information Management System (RIMS) to improve efficiency in handling the regulatory functions and monitoring the GMP status of the manufacturers and their applications for market authorization.

The next steps include:

- GDP staff of the registration department will confirm the list of SOPs to be developed, timelines, and staff responsible.
- Registration department staff will draft relevant SOPs.
- The MOH Director General of Health Policies and Planning will assist GDP in setting up the QMS for the Registration Department, local area network connectivity, and acquisition of a server.
- The PQM program will provide technical assistance to review draft SOPs.

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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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CPHL is a member of USP's MENA Network of Official Medicines Quality Control Laboratories (NOMCoL). In Q1, PQM supported one staff from CPHL to attend a workshop in Jordan. The workshop activities included building capacity and skills on:

- Good Documentation Practices , Good Laboratory Practices and Data Integrity
- General Chapter <1029> Good Documentation Guidelines
- High Pressure Liquid Chromatography
- General Chapter <621>Chromatography
- Theory and Best Practices
- Troubleshooting

The training provided during the workshop will help CPHL to conduct ILT equivalent to proficiency testing, one of the requirements of the ISO 17025 standards. This training aimed to strengthen the capacity of CPHL and improve analytical skills of staff to meet international standards.

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

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In Q1, PQM conducted follow-up audits of three pharmaceutical manufacturers (Beit Jala Pharmaceuticals Company, Jerusalem Pharmaceutical Company, and Birzeit Pharmaceuticals Company) to evaluate implementation of CAPA from the initial GMP audit conducted by PQM. The audit revealed that the three companies implemented 90 percent of the CAPAs, resolving findings from the full GMP assessment. The remaining deficiencies (10%) were broadly discussed with the QA directors of the companies. Overall, all manufacturers demonstrated very good understanding of GMP requirements (e.g., concerning change control, quality risk management, and handling of deviations and out-of-specification results). All manufacturers have expanded their portfolio of manufactured medicinal products and expanded their markets outside of Palestine. Part of the audit was dedicated to explanation of new GMP requirements, especially concerning cleaning validation and implementation of risk based approach following toxicological assessment of handled substances.

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

- Limited direct communications with the key stakeholders.
- The procurement process is tedious and requires several layers of communications and clearance.
- Travel logistics require a lengthy process to get a travel visa to the West Bank.

# Asia



# Bangladesh

## I. Quarter 1 Highlights

PQM's activities during FY 2019 Q1 were focused on the implementation of objectives 1, 2, 3, and 4 in the approved FY19 work plan and remaining activities from the last quarter of FY18 work plan. The National Control Laboratory (NCL) was assessed by the ANSI-ASQ National Accreditation Board (ANAB) and was found to comply with the requirements of international standard ISO/IEC 17025:2017 in the field of testing. The laboratory received the accreditation certificate, demonstrating its technical competence for defined scopes and operations of laboratory QMS. It would provide a conduit for regulators and industries to ensure reliable products and services to meet their specific needs. Q1 highlights include the following:

- In October, two experts from PQM headquarters conducted an advanced GMP inspection training for Directorate General of Drug Administration (DGDA) inspectors on principles, process, and procedures for regulatory inspection and conducted a mock inspection demonstration in a manufacturing plant. Through this training, DGDA inspectors understood well the advanced topics and the practical approach for a regulatory inspection. This training would help DGDA inspectors to better guide the manufacturers to implement and comply with international GMP standards to ensure quality-assured medical products are released for public consumption.
- In December, the GMP specialist of Bangladesh PQM joined the DGDA officers in conducting GMP inspection of a pharmaceutical company (Optonin Pharmaceuticals Ltd. Barisal) as part of the hands-on activities after the advanced GMP training held in October 2018. The joint inspection enabled the participants to apply the knowledge gained from the GMP training and translated into practical audit technique and documentation review at the actual manufacturing facilities.
- On October 20–26, PQM experts from headquarters conducted an M&E training for DGDA and NCL staff to enhance their capacity to monitor the progress of DGDA's 5-year Strategic Plan and WHO Institutional Development Plan (IDP). Fifteen DGDA and NCL staff and five Bangladesh PQM staff participated in the training. Among the training objectives, most of the participants reported they felt more knowledgeable about identifying why M&E is important, identifying key elements of an M&E plan, and identifying components of an M&E system. Thirteen participants strongly agreed/agreed that the training would be useful in their work by identifying key elements of M&E and implementing them. Moreover, this training will be helpful for them to select and identify precise parameters for M&E and incorporate those into M&E planning for next year as well as help them to monitor and report generation for the annual performance agreement. In addition, M&E activities will apply to NCL's routine program and strengthen the database information.
- To strengthen DGDA's MQM, PQM continued supporting DGDA's PMS committee to implement risk-based PMS. Between November 26 and December 20, Bangladesh PQM visited five Minilab™ sentinel sites—Barisal, Chittagong, Khulna, Rangpur, Rajshahi—where Minilab™ were deployed. A total of 18 DGDA inspectors were trained on risk-based PMS in those 5 field visits. During the training session, the PQM experts conducted hands-on demonstration on the risk-based PMS strategy, principle, process, and procedure. The participants practically carried out the full process by themselves and successfully performed all steps. Field inspectors sent suspicious samples screened with Minilab™ to NCL for compendial (L3) tests and then for corresponding regulatory actions in case of failure. The Director General recognized the importance of the risk-based approach to strengthen PMS function of the MRA.
- PQM continued to support NCL after the recent ISO/IEC 17025:2017 accreditation. With guidance from PQM Rockville experts, Bangladesh PQM assisted NCL to develop the Laboratory Information File (LIF) for applying for WHO prequalification, covering the scope on physicochemical and microbiology laboratory. On November 11, NCL submitted its expression of interest (EOI) and LIF to participate in the system of mutual audits within the network of QC laboratories involved in WHO prequalification.
- PQM continued to support NCL in performing proficiency testing and ILT. In Q1, NCL performed one proficiency test on loss on drying (LOD) and two ILTs on assay and LOD and successfully passed with a result provided by Sigma Aldrich, Germany, and USP-Ghana respectively. Through this program, NCL analysts showed their competency, which ultimately helped NCL toward sustaining the ISO 17025 standard as well as moving forward to the WHO prequalification process.
- As part of technical training, Bangladesh PQM continued to conduct refresher training for DGDA and NCL staff on various technical areas, including M&E training. In Q1, a total of 85 (62 male and 23 female) DGDA and NCL staff were trained on key operation areas (listed below) through nine hands-on and theoretical trainings.
- PQM staff assisted DGDA and NCL in developing SOPs, key documents, and CAPA implementation. In Q1, one new SOP was developed and implemented at NCL. In addition, PQM assisted follow with-up on 65

CAPAs that were generated by the observation of the WHO interim benchmarking assessment held on September 16–20, 2018.

- On December 18–19, the NCL management team conducted an NCL management review meeting. DGDA's Senior Director and PQM technical staff attended the meeting. The QA Head from the management team reviewed the previous meeting action items and discussed current improvement opportunities. PQM staff provided guidance and input on sustaining the existing standard (ISO/IEC 17025:2017) and achieving WHO prequalification. Some key improvement opportunities were identified, and NCL management agreed to work on these for improvement of NCL operations.

## II. Country Context

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

## III. Quarter 1 Progress by Objective

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

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In terms of laboratory capacity-building, PQM has been providing technical guidance/input to NCL to strengthen its QMS toward attaining compliance with international standard. Recently, NCL successfully achieved ISO/IEC 17025:2017 accreditation by ANAB.

PQM worked alongside NCL management and technical staff to follow up on its progress in the CAPA plan developed based on the findings from an internal audit and a PQM audit. In Q1, CAPAs were addressed and ongoing support was being provided to close some of them.

With the assistance of PQM technical staff in Bangladesh, NCL staff developed SOPs to improve internal processes toward achieving compliance with international standards. PQM also provided support to review out-of-specification, deviation, and change control reports around investigation, root cause analysis, risk assessment, and action plans. Logbooks were reviewed accordingly. The following are some key accomplishments during this quarter:

- PQM continued to support NCL for sustaining the standards of recent ISO/IEC 17025:2017 accreditation. Through the guidance from PQM HQ experts, Bangladesh PQM assisted NCL to develop the LIF for submission toward WHO prequalification for its physicochemical and microbiology laboratory. On November 11, NCL submitted its EOI and LIF to participate in the system of mutual audits within the network of QC laboratories involved in WHO prequalification.
- PQM continued to support NCL in performing proficiency testing and ILT. In Q1, NCL performed one proficiency test on LOD and two ILTs on assay and LOD and successfully passed. Results were provided by Sigma Aldrich, Germany, and USP-Ghana, respectively. Through this program NCL analysts demonstrated their competency, which ultimately helped NCL toward obtaining the ISO/IEC 17025:2017 standard as well as to move forward with the WHO prequalification process.
- PQM continued to provide guidance and support to evaluate equipment specifications of government procurement. In Q1, PQM experts assisted NCL to review the specifications of various equipment (e.g., auto pipette filler, conductivity meter, dissolution tester, disintegration tester, pH meter, HPLC column, thermo-hygrometer, and HPLC) based on the necessary configuration toward complying with international standards such as ISO/IEC 17025:2017 or WHO prequalification.
- PQM supported NCL to procure HPLC columns. NCL received 18 out of 33 HPLC columns, and the rest are in the process of being delivered. A performance check of the three columns was completed by the laboratory analysts and found to satisfactorily meet manufacturing and compendia specification.
- PQM staff assisted in developing SOPs, reviewing key documents, following up on CAPA implementation, and calibrating equipment.

### Summary of Laboratory Progress from October to December 2018

Items	Number of Items completed
Approved and implemented SOP through PQM review	1
<b>CAPA status in Q1 FY19:</b>	
An internal audit was conducted on October 28-30, 2018	CAPA development under process
<b>Total remaining CAPA up to December-2018:</b>	
CAPA from NCL Internal Audit – March 2017 (28) (CAPA No.: CAPA/MB/003/17)	Completed: 26 (0 in Q1) Under follow-up: 2
CAPA from PQM assessment on November 2017 (13) (CAPA No.: CAPA/CD/ (001-013) /FEB/18)	Completed: 11 (0 in Q1) Pending: 2 to be followed up
Calibration performed by NCL	1. Mettler Toledo pH Meter (2) 2. Electronic Balance (3)

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

On September 27, 2018, a progression update meeting was conducted with ACI Limited at their corporate office Gulshan 2. In the meeting PQM Asia Program Manager Mr. Cheng Tiang Ng along with COP and the Bangladesh PQM staff were present. During this meeting ACI provided an update on Chlorhexidine Di-gluconate 7.1% solution manufacturing and their progress towards participating UNICEF procurement process. ACI informed PQM that they have already submitted their EOI in the UNICEF procurement process along with the answers to questionnaire. ACI requested PQM to review the responses to questionnaire and dossier of CHX. Bangladesh PQM staff have started review and set target to finish it by February 2019. The review of the questionnaire and dossier will help ACI to fulfil the requirement of national GMP standard of DGDA as well as help them to move forward to participate in UNICEF procurement process.

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

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

- On October 13–17, two experts from PQM headquarters conducted an advanced GMP inspection training for DGDA inspectors on principles, processes, and procedures for regulatory inspection and conducted a mock inspection in a manufacturing plant. In the first part (theory session), 23 DGDA staff and 3 Bangladesh PQM staff attended at the Hotel Lake Breeze, Gulshan1, Dhaka. For the second part (practical session), 15 DGDA inspectors attended the mock inspection on October 17 with the HQ experts at Incepta Pharmaceuticals Limited, Jirabo, Savar, Bangladesh plant. Overall, 14 DGDA staff completed both parts of this training. Through this training, DGDA inspectors were well-trained on advanced topics such as QMS, quality risk management, change control, CAPA, investigation and root cause analysis, validation, qualification, HVAC systems, and the practical approach for an inspection. This training will help DGDA inspectors better guide and regulate manufacturers to implement and adhere to international GMP regulations/guidelines, thus eventually leading to availability of better quality-assured medical products to the Bangladeshi public.
- On December 21–22, a GMP specialist from Bangladesh PQM attended the inspection of a pharmaceutical company (Opsonin Pharmaceuticals Ltd. Barisal) with the DGDA inspection team. The purpose of the



PQM QH GMP experts Teferi Bedane and Fasika Mekete conducted GMP training with DGDA and NCL staff on October 13-17 at Hotel Lake Breeze, Gulshan 1, Dhaka. Photo credit: Md. Azad

participation was to follow up on the application of the audit technique and documentation review by DGDA inspectors who received the 5-day advance GMP training by PQM experts from headquarters.

- On October 20–26, PQM experts conducted an M&E training for DGDA staff to enhance their capacity to monitor the progress of its 5-year Strategic Plan and WHO IDP. Fifteen DGDA staff and five Bangladesh PQM staff participated in the training. Nine DGDA staff completed the training post-test questionnaire, and results indicate that all showed improved understanding of M&E. Among the training objectives, most of the participants reported they felt more knowledgeable about identifying why M&E is important; identifying key elements of an M&E plan; and identifying components of an M&E system. Thirteen participants strongly agreed/agreed that the training would be useful in their work and knowledge gained would aid in identifying key elements of M&E for implementation to strengthen DGDA's performance. M&E parameters identified could be incorporated into M&E planning for the next fiscal year to promote use of data-informed reports for effective decision-making. In addition, routine M&E information will strengthen NCL's database and improve performance monitoring of its activities.
- To strengthen DGDA's medicines quality management, PQM continued to support the risk-based PMS guidelines committee to implement risk-based PMS. PQM aimed at supporting DGDA in developing a comprehensive and cost-effective guideline in a resource-scarce setting. On November 6, the Director General requested PQM staff to visit the five sentinel sites to follow on and demonstrate risk-based sampling and Minilab™ screening with the field inspectors. On November 13, a risk-based PMS guideline review meeting was held at DGDA at which most DGDA officials were present. The recommendations from that meeting were incorporated in the guidelines. Between November 26 and December 20, Bangladesh PQM staff visited five sentinel sites (Barisal, Chittagong, Khulna, Rangpur, and Rajshahi) where Minilab™ was established. The purpose of these visits was to conduct field-based hands-on training on multilevel screening techniques for identifying suspicious medicines. During the training session, the PQM experts conducted hands-on demonstration on the risk-based PMS strategy, principle, processes, and procedure. Under PQM guidance, staff were practically trained on risk-based sampling from the market, performed visual inspection of the collected samples (L1), and conducted Minilab™ screening tests (L2) of the collected samples. The participants carried out the full process independently and successfully performed all the steps for risk-based PMS. For the next step, field inspectors sent suspicious samples to NCL for compendial (L3) tests. The Director General recognized the importance of the risk-based approach and decided to form a risk-based PMS committee involving stakeholders (TB/MNCH/FP programs) to implement risk-based PMS functions according to the guidance document.
- On September 16–20, a WHO global team from Geneva assessed the DGDA functions as per the GBT and shared their observations and recommendations toward achieving Maturity Level III. PQM staff assisted DGDA in addressing those CAPAs raised from these observations and recommendations by the WHO assessor. In relation to the observations of 5 functions (regulatory inspection, marketing authorization, clinical trial oversight, laboratory access and testing, and lot release), 65 CAPAs have been raised, and PQM has been providing technical assistance to address the CAPAs. The CAPA implementation strengthened DGDA's regulatory functions progressively and helped them toward WHO Maturity Level III. The CAPA items and their status are listed below.

#### Summary of DGDA Progress from October to December 2018

PQM staff assisted to following up on CAPAs implementation

Items	Number of Items completed
<b>CAPA status in Q1 FY19:</b>	
CAPA generated during Q1 (Oct to Dec-2018) based on the observations by WHO interim benchmarking assessment using GBT held on October 16-20,2018	65
Marketing Authorization (MA): 11	All CAPAs are under review by DGDA staff with PQM staff providing oversight
Laboratory Access and Testing (LAT): 12	
Clinical Trial Oversight (CTO): 13	
Lot Release (LR): 14	
Regulatory Inspection (RI): 15	

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

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PQM continued to facilitate the development of National Quality Assurance Guidelines for medical products. In Q1, Bangladesh PQM staff conducted three consecutive meetings internally on October 29, December 4, and December 24 to address the recommendations of the first meeting of the core committee on August 30. The draft document prepared would be shared with the stakeholders and the core committee.

**Summary of Trainings conducted in Q1 FY19**

SL/ No.	Training	Date	Laboratory Designation	Gender	Total Trained	Technical Areas	Training conducted by
01	Good practices (GxP) in pharmaceuticals: Advanced (theoretical and practical)	October 13–17	DGDA, NCL	13M, 1F	14	GMP	HQ staff
02	M&E training for DGDA	October 24–25	DGDA, NCL	14M, 6F	20	M&E	HQ staff
03	Refresher training on implementation of RB-PMS through Minilab™ and others field-based techniques	November 26–28	Chittagong field inspectors	3M, 2F	05	RB-PMS	Local staff
04	Refresher training on implementation of RB-PMS through Minilab™ and other field-based techniques	November 26–28	Khulna field inspectors	4M, 1F	05	RB-PMS	Local staff
05	Refresher training on implementation of RB-PMS through Minilab™ and other field-based techniques	December 3–5	Barisal field inspectors	2M, 1F	03	RB-PMS	Local staff
06	Refresher training on QMS – CAPA, OOS, deviation management	November 27	NCL	10 M, 05 F	15	QMS	Local staff
07	Refresher training on calibration management system of NCL	December 11	NCL	12 M, 06 F	18	ALS	Local staff
08	Refresher training on implementation of RB-PMS through using Minilab™ and other field-based techniques	December 10–12	Rangpur field inspectors	2M, 1F	03	RB-PMS	Local staff
09	Refresher training on implementation of RB-PMS through using Minilab™ and other field-based techniques	December 18–20	Rajshahi field inspectors	02 M	02	RB-PMS	Local staff
	Total in Q1 FY19			M=62 F= 23	85	GMP=14 ALS= 18 QMS=15 M&E=20 RB-PMS=18	

## IV. Key Challenges

- Utilization of Bangladesh government resources along with the support provided by USAID is important. If government resources do not materialize as anticipated, it could hamper the achievement of overall program objectives.
- Customs clearance of donated items remains a challenge for DGDA to manage, which continues to impact the program in Bangladesh.
- Safety and security remain a concern in Bangladesh. Since June 2018, 1.2 million Rohingya refugees have arrived in the southeast region of Bangladesh, near the border with Myanmar. The current Rohingya refugee crisis is a global concern. The PQM country focal person is closely working with the global security director to monitor the security situation.

## V. Lessons Learned

Motivated leadership in key positions is critical for decision-making and for ensuring an environment that leads to optimal performance. The availability of motivated and skilled personnel is also a key ingredient for success. The motivation of existing NCL and Chittagong Drug Testing Laboratory (DTL) staff emerged as a concern in different observations. Special attention needs to be provided in identifying and resolving potential negative situations and behaviors, especially in NCL.

## VI. Sustainability, Partner Contributions, and Ownership

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

# Indonesia

## I. Quarter 1 Highlights

Q1 activities primarily focused on finishing out the approved FY18 USAID work plan activities, continuing and initiating FY19 activities, and preparing for the PQM closeout vis-à-vis program operations. Activities for FY19 focus on achieving project targets, including WHO prequalification, policy work, and assistance to the government disease control programs through manufacturing and quality control support.

## 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 prequalification status. Beginning in 2013, PQM expanded its activities to build the capacity of the country's MRA, the National Agency for Drug and Food Control (Badan POM; (BPOM)), as well as 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 1 Progress by Objective

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#### **Objective 1 – To strengthen Indonesia's medicines quality assurance system by supporting BPOM and MOH to achieve international standards for medicines quality control (sampling, testing, data dissemination) capacity**

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##### **FY 18 carryover activities:**

PQM continued to support the PPOMN central/national laboratories (BPOM) during the annual national workshop on selected quality control topics provided to BBPOM provincial laboratory supervisors and staff (with a PTBB pool of training experts). A second training workshop was convened at the PTBB national laboratory for 16 provincial BPOM laboratory officers with a focus on analytical instrument testing of impurities in medicines to combat HIV/AIDS, tuberculosis, and malaria. This training utilized the PQM-supported pool of experts that was previously trained in the training-of-trainers workshop. This activity is focused on sustainability through transfer of technical knowledge and skill-building in training on relevant analytical topics that can be carried forward in the future.

The PQM program continued its program of intensive training and technical assistance to the provincial BBPOM Denpasar QC laboratory on the WHO prequalification implementation plan. In Q1, activities focused primarily on official adoption of drafted laboratory procedures and the continued compilation of the LIF, which is the document the laboratory will submit to WHO for consideration for prequalification. An internal BPOM audit according to WHO Technical Report Series (TRS) 957, Annex 1, 2010 and ISO/IEC 17025:2017 was conducted in Q1 in preparation for the anticipated WHO audit. PQM will assist in the CAPA implementation and general improvements to complete the WHO prequalification implementation plan on time. In addition, the following activities were conducted onsite:

- Facilitated and presented on implementation progress toward WHO prequalification during the BPOM Internal Management Review on December 11, with 30 BBPOM Denpasar personnel participating.
- PQM conducted a training for the laboratory on WHO TRS No. 961, Annex 13, 2011, WHO TRS 1003, Annex 3, 2017, and on the difference between WHO TRS 957, Annex 1 and ISO/IEC 17025 requirements on December 10–11 for 21 participants.
- Provided instrument calibration service for the Shimadzu and Waters equipment to comply with standard requirements (including three Shimadzu HPLCs, two spectrophotometer UV-Vis, one Fourier transform infrared, one gas chromatography instrument, and 1 Waters HPLC).
- Upgraded the overall laboratory facilities to fulfill WHO requirements for safety, security, and working environment, begun in November with anticipated completion in early January 2019. The upgrades include installation of restricted access security for the Terana Laboratory, installation of new ceramic standard sinks, provision and installation of new A/C, and relocation of the weighing room, Reference Standards storage room, and washing room.

PQM supported BBPOM Denpasar to participate in the Asia-Pacific NOMCoL ILT quality assurance program. The albendazole sample and reference standard were received and analysis was begun in Q1, with testing results to be submitted to USP in early January 2019.

##### **FY19 activities:**

As part of the WHO prequalification implementation plan for the BPOM Bidang Kimia Obat NAPPZA national quality control laboratory, PQM provided technical assistance to complete the CAPA plan from the May 2018 WHO inspection. This was completed, and documentation was submitted to WHO on December 2. WHO's reinspection of the laboratory for prequalification is planned for February 18–20, 2019, and will be supported by PQM.

During Q1, PQM supported the PTBB national and selected BBPOM provincial QC Labs for testing antiretroviral (ARV) and anti-TB medicines from the National AIDS Program as part of QA for ARV medicines national PMS and special investigations. This included procurement of 38 primary chemical reference standards for ARV and anti-TB medicines to be provided to BPOM for quality control testing purposes. These reference standards will be used to test demonstration samples during the upcoming WHO reinspection for prequalification in February.

PQM worked with the Pharmaceutical Chemistry QC Laboratory of the Faculty of Pharmacy, University of Indonesia, toward its goal to achieve ISO/IEC 17025:2017 accreditation. PQM donated key laboratory equipment (e.g., analytical balance, microbalance, HPLC, oven vacuum, and Water determination equipment–Karl Fischer) to the Pharmacy Faculty of University of Indonesia laboratory, as well as procured and facilitated installation of the HPLC software.

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**Objective 2 – Increase the local supply of quality-assured TB medicines in Indonesia**

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**FY 18 carryover activity:**

PQM provided technical assistance to pharmaceutical manufacturer Sanbe Farma/Caprifarmindo to finalize the levofloxacin 500 mg product dossier for submission to WHO for prequalification during FY19 and conducted a final product dossier assessment and facility, documentation, and practices mock audit. The product dossier evaluation took place over a period of 1 month during November and December. Sanbe Farma/Caprifarmindo is currently finalizing the contents of the dossier and will target submission to WHO for early January 2019. In Q1, PQM also conducted a training on quality risk management and good storage practices for the Sanbe Farma/Caprifarmindo QC laboratory for 33 staff.

**FY19 activity:**

PQM provided technical assistance to two local manufacturers (one private, one public/BUMN) and to the National Tuberculosis Program (NTP) in support of increasing access to quality-assured drug-sensitive and drug-resistant medicines for use by the government disease control program, including the daily dose 2 fixed-dose combination (FDC) rifampicin 150 mg/isoniazid 75 mg and moxifloxacin for use in the short-course treatment for drug-resistant TB adopted by NTP. In Q1, PQM followed up the progress of product development for the 2FDC (RH 150/75) with PT Imedco Djaja and submitted the final GMP audit report assistance on drafting a post-audit CAPA plan. PQM provided training on good storage practices and data integrity on November 16, with 37 internal staff participating. PQM also supported the drafting of new and revised SOPs, supplied USP NF reference documents, and provided moxifloxacin reference standards for product development and comparative dissolution study for moxifloxacin 400 mg. Discussions have already begun with NTP regarding procurement via e-catalog for these new products, and a fast-track registration process is underway with BPOM.

PQM worked with the public BUMN manufacturer PT Phapros to assist in its 2FDC RH product development for NTP, including conducting a training on good storage practices on November 12, with 18 internal staff participating.

PQM supported the national Bioavailability/Bioequivalence Forum through verification of the CRO PT Pharma Metric Laboratories CAPA plan following PQM's initial audit during FY18 and provided two additional USP 40 NF 35 flash disks for QC testing.

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**Objective 3 – Policy, advocacy, and collaboration by enhancing the technical capacity of the government of Indonesia to develop and implement inter-agency (MOH, BPOM, donors, professional associations, academia) policies and procedures for medicines quality assurance**

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**FY18 carryover activity:**

PQM finalized the draft of the Technical Guidelines for PMK 75/2018 Implementation in the Field with input from BPOM (Directorate KMEI) and the Ministry of Health (Directorate of Public Medicines). The draft was submitted to the Directorate General of Pharmaceuticals and Medical Devices (Farmalkes) on November 30 for adoption. PQM plans to continue to facilitate interagency meetings (National TB Program, National AIDS Program, Directorate KMEI, Directorate of Public Medicines) regarding the operationalization of the PMK 75/2016 Technical Guidelines following adoption in 2019.

PQM supported the Indonesian Pharmacists' Association and the Federation of ASEAN Pharmaceutical Associations (FAPA) on finalization and rollout of the MOH regulation PMK 72/2016 Good Pharmacy Practices in hospital pharmacy installations/dispensaries, including drafting SOPs and rolling out dissemination/socialization, memoranda of understanding, and scientific symposiums, in response to the falsified vaccine scandal of 2016 during Q1.

In Q1, PQM participated in the National Seminar for Reducing Stunting and the Strategy for TB Elimination, convened by the National Institute for Health Research and Development on November 22. PQM discussed the role of the pharmaceutical manufacturers as key actors in supporting the reduction of stunting and the elimination of TB in Indonesia, and that quality-assured medicines must be supplied to the TB and MCH programs for success to be achieved in reaching these targets.

Also in Q1, PQM held discussions with Chemonics PSM regarding convening the ARV medicines registration workshop, tentatively set for February 2019. PQM also participated in ARV supply chain management guidelines meetings, convened by Chemonics PSM in support of Subdit HIV/AIDS. Discussions were held with the Director of Public Medicine at Farmalkes to initiate planning communication and coordination for logistics for ARVs, TB, and other program medicines.

PQM, together with BPOM, finalized the draft official goods and services handover document (referred to as a BAST document) for the period of January–December 2018, which was submitted to the Biro of KSLN for review on November 30. The draft BAST handover document for 2018 was submitted to BPOM in November 2018, and PQM followed up with an additional request letter for BPOM to assign a signatory person during that time.

PQM participated in USAID's Supply Chain Management Implementing Partners meeting at the US Embassy. This was a coordination and communication meeting for IPs and USAID, and to encourage collaboration among partners, such as facilitating PQM to assist PSM/Chemonics to convene the ARV registration workshop for manufacturers and enabling PQM to work with KNCV/CTB to provide a guest lecture at FF-UI, along with the NTP.

#### **FY19 activity:**

PQM participated in the international workshop on “AMR Control: Raising Awareness and Understanding on AMR through the One Health Approach for Health Professional,” co-convened by WHO Indonesia and the Director General of Health Services, on November 28–29. There is still a need in the professional community for increased awareness of the relationship between poor-quality medicines and the emergence of antimicrobial resistance, and a clear role for PQM to continue advocating to health professionals for this purpose.

PQM conducted an onsite training on good storage practices for PT Kimia Farma with 36 participants from the Kimia Farma plant in Jakarta on October 30. PQM also provided a training presentation for 103 manufacturers on data integrity at the Pharma Series Seminar for 2018. Additionally, a GSP training was conducted for Hisfarin Jawa Tengah and attended by 111 pharmacists on November 11, demonstrating the eagerness of pharmacists working within manufacturing industry to improve their knowledge on good storage practices.

PQM also convened a professional seminar on TB for the Faculty of Pharmacy at the University of Indonesia, including the following topics:

- National Guidelines for TB Treatment, delivered by the Director of the national MOH CDC/P2PML.
- Sharing Experiences on the Role of Pharmacists in the TB Program, delivered by KNCV/Challenge TB program, under the Public-Private Mix program.
- Good Quality TB Medicines: Sharing Experiences in Achieving WHO prequalification, delivered by USP-PQM.

Following this lecture seminar, Challenge TB made connections with the Faculty of Pharmacy to further discuss engagement with the program on the Public-Private Mix project to work with community pharmacies and with the nearby local puskesmas in support of the TB program.

## **IV. Key Challenges**

PQM faces additional constraints as this is the final year of project implementation, and timelines must be adhered to in order to meet overall project targets. The considerable technical challenges and logistical challenges in achieving WHO prequalification, as well as ensuring long-term sustainability, are challenging as the adoption and control lies primarily with the government partners. Having sufficient government buy-in and momentum to carry forward these initiatives to ensure that the programs and institutional changes remain in place and continue post-PQM will be the main focus for the remainder of the program.

## **V. Lessons Learned**

PQM continues to learn how to engage with government partners, which can be a daunting task at times due to rigid bureaucratic regulations, shifting timelines, and unmet schedules. Considerable resources must be committed to ensure that international donor-driven projects achieve success, including substantial groundwork with planning and cooperation bureaus in addition to government technical counterparts.

# **Myanmar**

## **I. Quarter 1 Highlights**

With PQM's technical assistant, in Q1 the Department of Food and Drug Administration's (DFDA) Pharmaceutical Chemistry (PC) Laboratory achieved ISO 17025: 2017 reaccreditation. This new version of the standard was recently published in 2017; the 2005 to 2017 standard would no longer be accepted after December 31, 2018. All reaccreditations and new accreditations are required to follow the 2017 standard.

On November 9, PQM was invited to take part in a consultative meeting on Myanmar National Medicine Policy organized by WHO. Several key partners working on the QA/QC of medicines and supply chain management such as UNOPS, UNICEF, JSI, CHAI, GHSC-PSM/Chemonics, PSI and Myanmar Pharmaceutical Association, were present and participated actively. The draft National Medicine Policy prepared by MOHS required some work, so the implementing partners spent a significant amount of time on rewriting and rewording the document incorporating language around quality medicines availability, affordability, and procurement/supply chain management of essential medicines. PQM's contributions focused on strategies to enhance QA/QC of medicines in Myanmar.

The second meeting was held on November 20. WHO, PQM, and the other partners worked on rewriting and rewording the policies encompassing QA/QC and pharmacovigilance systems in the country.

With PQM's support, in Q1 DFDA has finalized the first draft of the PMS baseline survey protocol document for TB. An anti-TB medicines quality survey is planned in Q2 in seven geographical regions in the country.

## **II. Country Context**

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

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

To modernize DFDA and develop strong QA systems for Myanmar, alongside with developing laboratory capacity, other key functions—such as product evaluation and registration, licensing, supply chain inspection, and PMS systems—need to be strengthened. Pharmaceutical legislation, such as the National Drug Policy and National Drug Law, 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.

In addition to PQM's work on malaria, DFDA and PQM are planning to strengthen the QA systems of anti-TB medicines in both the public and private sectors. Since there are very few data available on the quality of anti-TB medicines in the country, PQM and DFDA are conducting a baseline survey on the quality, availability, and sources of anti-TB medicines in Myanmar. The data from the study will be used to provide valuable inputs for national TB programs and partners on programmatic decision-making as well as to provide recommendations for strengthening of DFDA PMS and inspection systems.

## **III. Quarter 1 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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All activities under Objective 1 have been completed.

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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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With technical assistance and supervision from PQM, DFDA's PC laboratory has successfully established the sampling technique and conducted the chemical residue testing of deltamethrin in long-lasting insecticidal nets (LLINs). Sixty LLINs from the 24-month assessment of the "LLIN Efficacy Monitoring Study" conducted by VectorWorks/PSI and funded by PMI were tested at the PC laboratory.

The dissemination workshop on the findings from 24-month assessment was held on November 8. During the workshop, PMI expressed appreciation for PQM's technical assistance to build in-country technical capacity to perform chemical residue testing of deltamethrin in LLINs.

DFDA's PC laboratory has successfully accomplished ISO 17025 reaccreditation by a third-party assessor (ANAB) with support and technical assistance from PQM. On October 1–3, ANAB conducted a 3-day onsite assessment on 10 test scopes in line with the new ISO 17025:2017 standards. Six nonconformities were found during the assessment. The laboratory performed the corrective actions and risk management procedures for the six nonconformities, and documents were submitted to ANAB within the allocated time. ANAB accepted the corrective actions and officially announced the ISO 17025:2017 reaccreditation of DFDA PC laboratory on November 14.

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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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Nothing to report this quarter. Mandalay lab construction was delayed. At this moment, there is no information on the completion date of the construction as all constructions at DFDA are halted.

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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. Mandalay laboratory construction is delayed, and the current laboratory is not suitable for ISO 17025 requirements.

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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. Both laboratory constructions in Yangon and Mandalay are delayed. The activity can begin only after the constructions are finished.

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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 is on hold by DFDA. The procurement of Raman devices is on hold by DFDA.

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

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The baseline survey of the TB protocol document (first draft version) for PMS was drafted in consultation with DFDA. After close consultation and alignment with DFDA, seven geographical regions (Yangon Region, Mandalay Region, Bago Region, Kayin State, Kayah State, Mon State, and Southern Shan State) were selected for samples collection based on the following criteria: TB incidence, accessibility, and security situations. As there are no reliable data on the availability of anti-TB medicines in Myanmar, PQM and DFDA will try to collect every kind of anti-TB medicine found on the market. The quality testing of the collected medicines will be performed at the DFDA PC laboratory.

The draft protocol was submitted to PQM headquarters for editorial review. PQM and DFDA will begin the implementation of the baseline survey in the Q2.



*The assessor from ANAB, conducting the ISO 17025 re-accreditation with the DFDA QA team.*

# Pakistan

## I. Quarter 1 Highlights

This Q1 report highlights key success and challenges and measures progress on intermediate results in the PQM program Results Framework that are in line with the new USAID Pakistan Country Development Cooperation strategy (CDCS) 2018–2023 under Development Objective (DO) 2 (Strengthened Capacity to Prevent Violent Extremism in Key Areas) and DO 3 (Increased Private Sector-Led Inclusive Economic Growth).

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

In consultation with the USAID Mission in Pakistan, in FY 2017, PQM identified the need to provide support for essential maternal and child health medicines. Focus is placed on products that are either not produced in country or are in short supply; have issues of quality, safety, and efficacy; and for which there is a dire need in the country. During Q1, technical assistance continued to manufacturers focusing on four products:

- **Amoxicillin DT:** Macter International completed 73 percent of the CAPA plan based on PQM audit observations and is expected to achieve 100 percent during Q2. Another project manufacturer, CSH Pharmaceuticals, is working on closure of all nonconformances, and a detailed plan is expected in Q2.
- **Zinc DT and zinc DT/ORS co-pack:** Of three manufacturers receiving technical assistance from PQM for zinc DT production, M/s Pharvevo was inspected by WHO for prequalification in Q4. The audit report by the WHO prequalification team is awaited, and PQM will follow up with further technical assistance, if required. Atco Laboratories has invested in a dedicated section for zinc DT manufacturing. This new section was inspected by the Drug Regulatory Authority of Pakistan (DRAP) and recommended for approval. Aspin Pharma, another project manufacturer, has initiated palatability studies that are likely to be completed by the end of Q2.
- **Chlorhexidine gel:** With PQM support, four manufacturers (Atco Laboratories, Aspin Pharmaceuticals, Zafa Pharma, and Akhai Pharmaceuticals) had successfully launched chlorhexidine 7.1% gel in the local market. In Q1, PQM randomly collected samples of CHX produced by these manufacturers and had them tested at the Pakistan Drugs Testing and Research Center (PDTRC), an ISO 17025 accredited laboratory. Testing results confirm that the products are of standard quality.

In Q1, 4 days of hands-on training on CTD format was conducted in Karachi. This training was attended by 111 participants from pharmaceutical industry and regulators from federal and provincial governments. This enhanced the participants' knowledge of CTD requirements with the overall objective of implementing CTD as the official format for registration application.

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

PQM continued its technical assistance to selected laboratories toward attaining internationally recognized certifications such as ISO 17025 and/or WHO prequalification. With PQM support, in Q1 another regulatory laboratory (DTL Bahawalpur) attained ISO 17025 certification by the Pakistan National Accreditation Council (PNAC). Moreover, with PQM support, DTL Faisalabad and DTL Multan LIFs are ready for submission for WHO prequalification.

In Q1, PQM conducted a 2-week-long hands-on capacity- and skills-building training at DTL Lahore and the Provincial Quality Control Board (PQCB). This hands-on experience was attended by 32 analysts and gave them the opportunity to enhance their skills on different quality-testing techniques and improve the laboratory's ability to test medicines and comply with international standards.

### IR 1.1 Quality assurance policies, legislation, guidelines and procedures improved and IR 1.2 Registration, inspection and licensing functions of medicine regulatory agencies

To facilitate DRAP's achievement of Global Benchmarking Maturity Level III, in Q1 PQM technical support continued to focus on improving product quality assessment and registration processes. This included conducting a detailed gap assessment of DRAP with respect to ISO 9001 certification for all 13 divisions, which was followed by training on ISO 9001:2015 implementation for DRAP divisional coordinators as well as revision of policies and guidelines in line with institutional development plans. This includes revision of DRAP's GMP checklist based on WHO and Pharmaceutical Inspection Co-operation Scheme (PIC/S) guidelines, risk-based guidelines for vendor qualification, recall guidelines (role of DRAP), and risk-based inspection practices.

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

In collaboration with PQM, DRAP is preparing the document on a regulatory framework for an effective PMS system, which will be presented at the stakeholders (DRAP and provincial health authorities) meeting for debate and approval by the respective authority for implementation. In Q1, PQM continued consultations with authorities for a consultative workshop on a PMS regulatory framework, to be conducted during Q2.

## 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 1 Progress by Objective

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**Objective 1 – (Corresponding to PQM IR 2.1 & (CDCS) 2.3.2: Continue to provide technical assistance to selected manufacturers that receive registration of CHX and to other potential MCH product manufacturers to improve their cGMP standards to qualify for WHO PQ, ERP, and local registration**

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### Activity 1.1: Technical assistance to manufacturers of priority products

In consultation with the USAID Mission in Pakistan, in FY 2019, PQM continued to provide support for the manufacturers of essential MNCH medicines. Focus remained on the products that are either not produced in country or are in short supply; have issues of quality, safety, and efficacy; and for which there is a dire need in the country. Technical assistance to manufacturers in FY 2019 Q1 remained focused on four products. Below is a detailed report on the selected products and targeted manufacturers:

- **Amoxicillin DT:** In FY 2018 PQM selected two potential manufacturers of amoxicillin dispersible tablets (DT), based on the availability of the manufacturing facility and the manufacturers' willingness to produce products for the national market and achieve WHO prequalification. Macter International (a pharmaceutical manufacturer in Karachi with a penicillin manufacturing facility) and CSH Pharma (a pharmaceutical manufacturer with its manufacturing facility in Lahore) were the two selected manufacturers.
- **Macter International:** PQM conducted a detailed audit of the facility in Q1. The report was shared with Macter, which developed a CAPA plan. PQM supported the manufacturer in implementation of the CAPA plan and in development of a stable formulation that was put on stability testing. The manufacturer showed steady progress. Macter will complete the CAPA, achieved 73 percent of the CAPA plan, and is on target to achieve 100 percent closure of nonconformances by the first month of Q2. With PQM's support, in FY 18, Macter developed a stable formulation of amoxicillin DT. In November (Q1), Macter produced two laboratory scale and one pilot batches for stability testing. The 6-month stability testing of the three batches will be complete in May 2019. Macter has invested in new production equipment for exclusive production of pilot/commercial batches of amoxicillin DT and is in the process of conducting palatability studies through a CRO. Macter is working to get itself registered with UNICEF by Q2. The dossier is also under development, and PQM will assist Macter in completing it by Q3.
- **CSH Pharmaceuticals:** PQM audited M/s CSH Pharmaceuticals, the other potential amoxicillin DT manufacturer, in September and shared the report with CSH in Q1. CSH is expected to respond to all observations and, for each, include a description of the corrective action implemented or planned to be implemented, as well as the date of completion or target date for completion. In addition, CSH should submit supporting documentation with the response as objective evidence of completion of corrective actions. The acceptability of corrective actions will be assessed through evaluation of the response to each observation

and will be followed up during the next assessment. If necessary, an onsite follow-up assessment may be conducted to verify effective implementation of corrective actions.

- **Zinc DT and Zinc DT/ORS co-pack:** PQM has been working with three manufacturers for zinc DT development and one manufacturer for zinc DT/ORS co-packaging development. A detailed report of Q1 activities is provided below.
  - **Pharmevo Pharmaceuticals:** Pharmevo is one of the three manufacturers receiving technical assistance from PQM for zinc DT production. In FY18 Q4, WHO inspected Pharmevo for prequalification. PQM assisted the manufacturer to respond to observations and questions from the auditors. The audit report by the WHO prequalification team is awaited by the manufacturer. Once the audit report is received, PQM will follow up with technical assistance if required.
  - **Atco Laboratories:** PQM has been supporting Atco Laboratories for zinc DT, zinc oral solution, and zinc DT/ORS co-packaging. M/s Atco is already registered with UNICEF and has been allotted a registration number.
    - **Zinc oral solution:** With PQM support, Atco corrected its formulation of zinc oral solution as per the USP monograph, and the stability study performed on development batches has shown satisfactory results. The 6-month accelerated stability study will be complete in February 2019. The manufacturer will produce one laboratory scale batch of 100 liters and one pilot batch of 1,000 liters in January 2019 to conduct long-term stability testing.
    - **Zinc DT:** For production of zinc DT, Atco developed a new manufacturing section that has been inspected by the DRAP panel of inspectors and is recommended for licensing. The meeting of the Central Licensing Board is expected in January 2019, when Atco is likely to get approval for production in the new facility. Atco will manufacture 1 laboratory scale batch of 25,000 tabs and 1 commercial batch of 220,000 tablets in new facility, tentatively in February 2019. Atco also intends to conduct palatability studies after it has prepared the pilot batches at the new facility.
    - **Co-packaging:** PQM will assist Atco in getting approval of the co-packaging from DRAP.
  - **Aspin Laboratories:** PQM has been supporting M/s Aspin for zinc DT since FY18. PQM assisted Aspin in developing the formulation of zinc DT that was successfully developed. In July 2018, 1 pilot batch (100,000 tablets) and 2 laboratory scale batches (each of 25,000 tablets) were manufactured. The zinc DT batches have undergone a 5-month stability study. The results complied with the compendial specification. Aspin initiated palatability studies that are likely to be completed by the end of Q2. The manufacturer is registered with UNICEF and the registration number was also allotted to M/s Aspin. The dossier is being developed and is likely to be available by Q2 for review by PQM before it is submitted to UNICEF.
  - **Chlorhexidine gel:** PQM supported four manufacturers for development of chlorhexidine 7.1% gel. The product is being marketed by four manufacturers (Atco Laboratories, Aspin Pharmaceuticals, Zafa Pharma, and Akhai Pharma) M/s Akhai and Zafa have not shown the interest in UNICEF Expert Review Panel (ERP), so technical assistance to these manufacturers ended. However, PQM will continue to support the medicines quality control laboratory to monitor the quality of CHX gel produced by these manufacturers through testing of random sampling in order to ensure high-quality products remain available in the market. The products are available in all provinces and regions of Pakistan as over-the-counter medicines readily accessible by the general public and are also available for procurement by provincial governments (where they are already included in the list of essential medicines for lady health workers under the Prime Minister's Program for Family Planning and Primary Health Care). M/s Atco and Zafa had supplied some batches to government hospitals. Atco Laboratories and Aspin Pharmaceuticals are waiting for the procurement tender by UNICEF for the ERP. UNICEF has informed both manufacturers that the ERP will be conducted once the tender for procurement issued and their bid is received.

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

As discussed under Activity 1.1, to monitor the quality of the products by the four manufacturers who got their products registered as a result of technical assistance they received from PQM is randomly collecting samples of CHX produced by the manufacturers and getting these tested at PDTRC, an ISO 17025 accredited laboratory. Testing results confirm that the products are of standard quality, as seen below.

Manufacturer	Product Name	Batch Number	Results
Akhai Pharma	Loxidin Gel 10 gm	777101	Complies with USP 41
Aspin Pharma	Sepidyl Topical Gel	K0048	Complies with USP 41
Aspin Pharma	Sepidyl Topical Gel	K0053	Complies with USP 41
Atco Pharma	Umbelica Gel 10 gm	17001	Complies with USP 41

PQM will continue to facilitate testing priority products by manufacturers who received technical assistance since the PQM program started in Pakistan in order to ensure their quality.

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

With advocacy from PQM, DRAP decided to shift to the CTD template for registration application of all medicines. In FY18, DRAP officially declared the CTD would be the only format for submitting medicine registration applications as of January 2019. At the request of DRAP and the industry, PQM conducted three trainings for the industry and one training for DRAP in FY 2017. The objective of trainings was to sensitize the industry on the CTD requirements and prepare their technical personnel for adopting the document and be able to develop the dossier.

At the request of PPMA, a series of two trainings were planned, one for the industry situated in the north of the country and other for the industry situated in south. DRAP was taken on board on the trainings by updating the CEO about the objectives of the training and expected outcomes. At the first training, conducted at Lahore in FY18, PPMA arranged for logistics and PQM provided technical expertise. This is a good example of how effectively the message of PQM was taken positively by the industry regarding CTD adoption. The training at Lahore was attended by manufacturers from the north of the country, from Peshawar to Lahore and surroundings, with participation from 120 (80 male and 40 female) technical personnel from industry.



*Hands-on training on CTD in Karachi, November 2018*

PQM conducted one hands-on training in Q1 in Karachi for the pharmaceutical industry based in the south. The training was very well-attended by technical personnel from the industry in Karachi and Baluchistan. The training was again held with active support of PPMA, which paid the cost of logistics, while PQM provided technical expertise. The 4-day training was attended by 111 (59 male and 52 female) technical personnel of the top-line pharmaceutical industry. It was a 4-day interactive session in which the participation of attendees was overwhelming, and the participants' interest was evident from their involvement in technical discussions. The closing ceremony was attended by the DRAP CEO, who expressed great appreciation for the support provided by USAID and PQM in conducting such training activities. He also showed his confidence that USAID and USP will continue to support both the industry and the DRAP in best interest of the patients.

The PPMA Chairman and senior members of the pharmaceutical industry were also highly appreciative of the contribution made by USAID and PQM toward betterment of the industry in the areas of GMP and implementation of the CTD. The Chairman showed his interest in arranging more such training sessions and requested PQM to support future activities also by providing technical assistance.

Assumptions and risks for activities under Objective 1 include:

- Change in stakeholders' priorities.
- Security situation may affect the visits of international certification bodies (WHO, UNICEF) and expatriates technical experts' visits (USP).
- Change of government/change in tax and duties.
- Limited resources for sustainability of the interventions and progress made so far.
- Absence of follow-up technical support like PQM to DRAP and the industry.

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## **Objective 2 – (Corresponding to PQM IR 1.3 & (CDCS) 2.2.2 and 2.3.1: Strengthen the capacity of quality control laboratories to meet international standards**

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Substandard and falsified medicines cause treatment failure and adverse reactions, increase morbidity and mortality, and contribute to drug resistance development. Poor-quality medicines also increase healthcare costs to both patients and the health system as a whole, wasting resources that could otherwise be used to benefit public health. PQM's laboratory support program is contributing to systems strengthening and industry stability with healthy competition for safe and quality-assured medicines in Pakistan. Reliable quality testing utilizing a risk-based PMS approach to detect substandard and falsified medicines is now being implemented.

PQM's technical support to quality control laboratories is centered along three processes as follows:

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



*ISO 17025 Certificate of Accreditation*

### **Activity 2.1 Conduct a comprehensive assessment laboratories**

#### ***DTL Bahawalpur***

DTL Bahawalpur (situated in south Punjab, an underserved region) is a provincial regulatory laboratory that was established under the Drug Act of 1976 (now DRAP Act 2012). In FY18 Q4, PQM performed an audit of DTL Bahawalpur to assess its QMS and assist the laboratory in achieving ISO/IEC 17025 accreditation and subsequently WHO prequalification. In FY19 Q1, with PQM support based on the above-mentioned approach, DTL Bahawalpur

attained ISO 17025:2005 accreditation by PNAC. (The accreditation certificate number is LAB 165; it was granted on December 12, 2018, and is valid until December 10, 2021). Using processes described above, five PQM-supported laboratories have now achieved ISO certification.

PQM is providing subsequent support to DTL Bahawalpur to prepare its LIF for WHO prequalification. This involves a QMS assessment of the laboratory and identification of key interventions before preparation and submission of the LIF to WHO. The key intervention included review and update of documents related to QMS, control of documentation and records, personnel training, analyst authorization, equipment qualification, materials handling, safety plans, handling of samples, validation of analytical procedures, and investigation of out-of-specification results.

It is expected that prequalification will not only help DTL Bahawalpur to meet internationally recognized standards but will also ensure the accuracy of results and reliability of the laboratory in surveillance of medicines quality after market authorization.

#### ***DTL Rawalpindi***

In FY18 Q4, PQM performed an audit of DTL Rawalpindi, which was established under the Drug Act of 1976/DRAP Act of 2012. The objective was to conduct a gap assessment of DTL Rawalpindi with respect to the QMS and assist the laboratory in achieving ISO/IEC 17025 accreditation and subsequently WHO prequalification.

**Current Updates:** DTL Rawalpindi is working to address nonconformances. After addressing nonconformances, PQM will re-evaluate the laboratory's QMS before the ISO audit, which is expected in Q2. PQM will then assist DTL Rawalpindi in preparing and submitting its LIF for WHO prequalification.

#### ***Federal Government Appellate Laboratory, NIH Islamabad***

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

**Current Updates:** All newly procured equipment under the Global Fund grant has arrived at the appellate laboratory and is undergoing calibration and qualification. In Q1, PQM completed a rapid assessment of laboratory for ISO 17025, and a detailed gap assessment report will be shared with the laboratory at the start of Q2. Based on the report, PQM will continue to provide technical support via the three steps mentioned above, including preparation of a CAPA plan and review/update of QMS SOPs such as operational SOPs related to equipment.



*Examples of newly procured equipment*

### **Activity 2.2 Support quality management system (QMS) staff of government quality control laboratories for QMS development**

#### ***Capacity-Building Activities at the Drug Testing Laboratories located in Punjab during Q1***

In Q1, PQM provided a 1-week workshop to DTL Lahore and another 1-week workshop to the other DTLs in Punjab and PDTRC, Lahore on chromatography, dissolution, and performance verification testing for dissolution instruments. The topics were selected based on PQM assessment findings and areas identified by the laboratories that require additional technical support. The two sets of training were attended by 32 participants (13 male and 19 female), including laboratory managers and analysts. This training provided additional technical support in areas identified by the laboratory.

#### ***First Week Narrative Activity***

The first set of trainings was held at DTL Lahore. This training focused on review of current USP General Chapters for quality control of medicines using titration, atomic absorption, water determination, loss on drying, loss on ignition, gas chromatography, and mass spectroscopy, as well as an introduction to revisions to ISO 17025:2017: General Requirements for the competency of testing and calibration laboratories. For better learning outcomes, hands-on

sessions were conducted on evaluating medicines quality using chromatographic techniques, electronic instrumentation such as polarimeters and electronic balances, and sample preparation in compliance with USP General Chapters. Another focus of this training was to train the selected analysts as master trainers for specific topics so they can serve as resource persons for future trainings and promote the sustainability of PQM efforts. The training program's effectiveness was measured by pre- and post-training knowledge evaluations.

### **Second Week Narrative Activity**

The second set of training began at the Provincial Quality Control Board (PQCB), Lahore Regional Headquarters of Punjab. PQCB controls all Punjab DTLs, and its major role is to scrutinize the reports and cases of inspectors and government analysts, take appropriate actions on these reports (including prosecution and warning), and advise government and field staff on ways to ensure medicines quality. Participants from other regional laboratories were trained in the second week. To promote sustainability, selected DTL Lahore staff who participated in the workshop on the first week led the activities. In response to requests from laboratory personnel for more training, additional topics were added to the training agenda and presented on the third day. For the first 2 days of the second week, the selected DTL staff gave the presentations (sustainability through self-sufficiency), led participants through the group exercises, responded to questions from their colleagues, and performed in a very professional manner. The PQM team participated by providing technical assistance as needed. On the third day, the training venue moved to PDTRC in Lahore for additional training topics and hands-on training in the laboratory facilities. As PQM is supporting DTL Faisalabad and DTL Multan in preparing their LIFs for WHO prequalification, a PQM Regulatory Affairs specialist discussed and reviewed initial drafts prepared by both DTLs. This provided participants from other DTLs the opportunity to learn about WHO requirements for preparing a LIF.

### **Additional topic related to WHO Prequalification**

PQM also presented on change control, deviation handling, vendor qualification, and risk management to assist the laboratories to reach their goal of becoming WHO prequalified.

The participants completed the activities on the agenda through Wednesday of the second week. However, due to a nationwide protest that included blockage of transportation routes, the workshop had to end at that point. The PQM team continues to work with DTL management and looks forward to further activities.

It is expected these skill development training sessions will enable participants to comprehend and apply the USP general chapters on titration, atomic absorption, LOD, loss on ignition, water determination, and gas chromatography to their laboratory work to evaluate the quality of medicines. Participants should also be able to understand updates to the international standard for testing and calibration laboratories.

Furthermore, it is expected that the trained participants from this training will organize similar trainings for all the other employees (from DTLs of Punjab and PDTRC) using same training material.



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

### **CDL Karachi**

**Introduction:** The Central Drug Laboratory (CDL) in Karachi is working under the DRAP Act 2012 (Drugs Act 1976), and falls under the ambit of the DRAP. Its principal role and function is to perform analysis of samples taken during inspections (PMS) by Federal Inspectors of Drugs and certification of export medicines. CDL Karachi is also offering service for the provinces that do not have their own laboratory or lack certain analytical techniques or capacity. Furthermore, this laboratory is expected to provide premarket testing of medicines, as well as reference standards for test analysis as per pharmacopeia specification.

**Brief from Previous Quarter:** Based on PQM's advocacy, DRAP invested \$4 million in CDL infrastructural work and equipment. PQM reviewed CDL's QMS and shared results with laboratory management. The laboratory is preparing the final QMS document, including the LIF to be submitted for WHO prequalification.

**Current Updates:** All new expected equipment has arrived at CDL, and their calibration and qualification are underway. PQM completed review of QMS SOPs and is now supporting the laboratory in developing SOPs related to equipment. Support to this laboratory to meet international standards will promote accurate and reliable premarket testing of generics and new medicines applying for market authorization.

#### **PDTRC Lahore**

**Introduction:** PDTRC is a project of the Punjab Industrial Estates Development and Management Company, which is owned by the Government of Punjab. Initially, PDTRC was called Pharma Lab. A Board appointed a committee called the Pharma Lab Advisory Committee (PLAC), which consisted of eight members, to closely monitor building construction, equipment procurement, and hiring. PLAC also decided to change Pharma Lab's name to the Pakistan Drugs Testing and Research Center (PDTRC). The pharmaceutical laboratory has been accredited by the Government of Punjab Health Department's PQCB under the Drugs Act 1976/DRAP Act 2012 for testing and analysis of medicines. It has also been approved by DRAP to conduct bioequivalence studies.

**Brief from Previous Quarters:** PQM has been working with PDTRC toward WHO prequalification since 2018 and has supported the laboratory in preparing its QMS documents and improving its working standards. PQM also helped PDTRC develop its LIF for WHO, which was accepted and followed by the WHO peer audit in December 2017. PQM supported PDTRC in developing a CAPA plan based on the peer audit report. PQM supported the closure of various observations mentioned in the CAPA and arranged for a final review of PDTRC preparedness before the WHO inspection visit in July 2018. The WHO audit assessment report was received at the end of FY18 Q4 with no critical observations (the detailed report was shared in the FY18 annual report).

**Current Updates:** PQM is assisting PDTRC in preparation of the CAPA plan, and technical assistance is being extended for closure of all 14 observations made by the WHO prequalification team. PQM has also arranged for a microbalance for the laboratory, which is one of the observations by the WHO prequalification team.

This will be the first public-private partnership regulatory laboratory expected to acquire WHO prequalification status. Prequalification of the laboratory will provide testing facilities for the prequalification of locally manufactured medicines, especially for integrated disease programs, as well as for testing of medicines to be exported to comply with the requirements of certain importing countries. This laboratory will also be used for pre- and post-marketing of pharmaceuticals as required. Furthermore, it is expected that this laboratory will provide quality control services for pharmaceutical products to UN agencies and their partners, procurement agencies serving national authorities, and UN agencies and/or national authorities of WHO Regional Member States. This will lead to saving the high cost of foreign testing by the local pharmaceutical manufacturers as well as revenue generation.

#### **DTL Lahore**

**Introduction:** DTL Lahore is a government regulatory laboratory in the Province of Punjab. It is one of the oldest quality control testing laboratories for the provincial government of Punjab. Provincial governments are responsible for the supply chain and distribution networks in the province that deliver medicines to the point of use. Key elements of this are as follows:

- Wholesale distribution of medicines.
- Procurement by public sector hospitals.
- Sale and supply by pharmacy outlets to the public.
- Post-marketing quality surveillance.

To meet these obligations, provincial inspectors from an area of specified jurisdiction visit wholesale dealers and pharmacy outlets. During these inspections, they take samples that are sent to the respective DTLs. The procedure for these analyses is provided for in the Drugs Act, which defines the responsibilities of the laboratory, the Laboratory Director, and the Government Analyst together with the report format and the specifications to be used.

**Brief from Previous Quarter:** In FY18 Q4, through PQM's continuous support, DTL Lahore attained ISO 17025:2005 accreditation by PNAC. (The accreditation certificate number is LAB 162; it was granted on August 31, 2018, and is valid until August 30, 2021).

**Current Updates:** Through PQM technical assistance, DTL Lahore has prepared its LIF for WHO prequalification. The LIF is under final review by PQM and will be followed by preparation and submission of an EOI for



LABORATORY  
INFORMATION FILE



Drug Testing Laboratory Faisalabad

LABORATORY INFORMATION FILE



**DTL Faisalabad Laboratory  
Information File for WHO PQ**

WHO prequalification in FY19 Q2. It is expected that this will not only help DTL Lahore meet internationally recognized standards but will also ensure the accuracy of results and reliability of the laboratory in surveillance of medicines quality aftermarket authorization.

### **DTL Faisalabad**

**Introduction:** DTL Faisalabad is a regulatory laboratory that was established under section 15 of the Drugs Act of 1976. It provides services in pharmaceutical testing of medicines samples to the Drug Control Wing, Government of the Punjab, and Primary & Secondary Healthcare Department through assigned medicines inspectors that cover a specific jurisdiction. PQCB (the internal customer of the laboratory) is the designated body in the Drug Control Wing of the Department that has the technical capabilities and legal function to scrutinize test reports, audit, and suggest improvements in the DTLs.

**Brief from Previous Quarter:** In FY18 Q4, PQM conducted a gap assessment of DTL Faisalabad to verify the level of compliance with WHO Good Practices for pharmaceutical quality control laboratories (WHO TRS, No. 957, 2010). The assessment focused on compliance of the laboratory's QMS implementation status to WHO prequalification guidelines and to determine areas for improvement. The gap assessment identified deficiencies and areas of improvement (details were shared in the last quarter) that need to be addressed before submitting the EOI and LIF to WHO (e.g., key SOPs, SOPs that require revision, and areas that require improvement and need to be addressed, such as documentation, training on QMS system, and other laboratory trainings).

**Current Updates:** With PQM continuous support, DTL Faisalabad has removed 10 of 21 major observations that were required for submission of its LIF to WHO. PQM also completed a detailed review of the LIF and assisted DTL Faisalabad in preparing its EOI application for WHO prequalification. With PQM support, DTL Faisalabad's EOI application and LIF for WHO prequalification are ready and expected to be submitted at the beginning of FY19 Q2. PQM will provide technical assistance to DTL Faisalabad for addressing any query from the WHO prequalification team for successful acceptance of the LIF. In the meantime, PQM will continue to provide technical support to DTL Faisalabad to remove nonconformances and further prepare for the WHO peer audit visit.

Prequalification of this laboratory will provide reliable testing services for surveillance of medicines quality to three divisions of Punjab (Faisalabad, Gujranwala, and Sargodha), benefiting 38 million people who are more vulnerable to substandard and falsified medicines.



### **DTL Multan**

**Introduction:** DTL Multan (situated and serving south Punjab is one of the under served region) is a regulatory laboratory that was established under section 15 of the Drugs Act of 1976 (now DRAP ACT 2012). It provides services in pharmaceutical testing of medicines samples to the Drug Control Wing, Government of the Punjab, and Primary & Secondary Healthcare Department, through assigned drug inspectors that cover a specific jurisdiction. The PQCB (internal customer of the laboratory) is the designated body in the Drug Control Wing of the Department that has the technical capabilities and legal function to scrutinize test reports, audit, and suggest improvements in the DTLs.

**Brief from Previous Quarter:** In FY18 Q4, PQM performed an audit of DTL Multan to assess the laboratory's compliance with WHO Good Practices for pharmaceutical quality control laboratories (WHO TRS, No. 957, 2010). The gap assessment identified deficiencies and areas of improvement (details were shared in the FY18 annual report) that must be addressed before submitting the EOI and LIF to WHO. DTL Multan has removed the nonconformances based on PQM's assessment findings on areas that require improvement, such as documentation, QMS training, and laboratory training and practices, including data integrity, risk management, change control, deviation, and validation/verification of methods.

**Current Updates:** With PQM support, DTL Multan has addressed the gaps identified and removed 12 of 21 major nonconformances that were required for the EOI application to the WHO prequalification team. PQM extended its technical assistance to develop the LIF in accordance with WHO requirements. DTL Multan's EOI application and LIF for WHO prequalification are ready and expected to be submitted at the start of Q2. PQM will continue to provide technical assistance to laboratory staff to address any query from the WHO prequalification team for successful acceptance of the LIF and further preparation for the WHO peer audit visit.

Prequalification of this laboratory will provide reliable testing services for surveillance of medicines quality to 2 divisions of Punjab (Multan and Dera Ghazi Khan), benefiting a population of 15.7 million people, which is less

*DTL Multan Laboratory  
Information File for WHO PQ*

developed and more vulnerable to substandard and falsified medicines. The DTL Multan catchment area (administrative division of cities where laboratories provide testing services) is in the southern part of Punjab, which has the highest vulnerable population due to poverty, poor health facilities, and ongoing conflict and violence.

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

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

PQM is providing technical assistance to selected laboratories for participation in this scheme. In FY 2018, 10 laboratories (DTL Rawalpindi, DTL Faisalabad, DTL Multan, DTL Bahawalpur, DTL Lahore, PDTRC Lahore, CDL Karachi, DTL Quetta, Pakistan Army Laboratory Lahore, LNCM Morocco) participated in second round of ILC-T for four-fixed-dose combination (4FDC) anti-tuberculosis (TB) formulation. PQM provided the test material to each laboratory along with USP standards for the analysis. The results from the Morocco laboratory are awaited and expected to be received at the beginning of Q2. Once received, the reports from each laboratory will be reviewed, and individual feedback will be shared directly with the laboratory.

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

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

Assumptions and risks for activities under objective 2 include the following:

- A new political government and reforms in Punjab's health department are being carried out, which may affect progress and implementation of planned interventions.
- There is a delay in WHO's response on the EOI submitted application.
- The capital expenditure required for CAPA, including electronic system interfaces, may not be compatible.
- Access to market authorization data and unreliable manufacturers' methods of testing.
- Resources are limited for sustainability of the interventions and progress made so far.
- Absence of future technical assistance to maintain standards achieved and adopting new technology with support of PQM.

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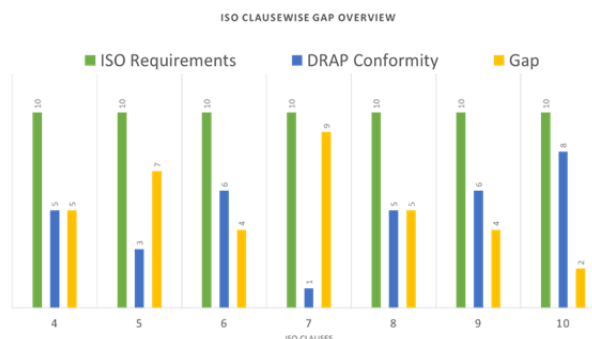
**Objective 3 – (Corresponding to PQM IR 1.1 and 1.2 & (CDCS) 2.2.2 and 2.3.1): Capacity building of DRAP Pharmaceutical Evaluations and Registration Division (PE&R) to improve its registration system to effectively evaluate all essential medicine products quality**

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

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

In Q1, a detailed gap assessment of DRAP was conducted to ascertain the gap between the desired and current state of ISO 9001 certification was performed. A formal gap analysis questionnaire was circulated among 13 divisional coordinators for



provision of their responses about the existence of division-specific organization charts, functions, SOPs, and job descriptions. Information gathered for the gap assessment included the information provided by the divisional QMS coordinators, desk review of DRAP documents, interviews of DRAP staff, and visits to different areas of the DRAP headquarters office building. Examination of available documentation (e.g., SOPs, job descriptions, functions, flowcharts provided by the divisional QMS coordinators) was carried out to identify gaps between the prevailing procedures and processes and the requirements of ISO 9001:2015 standard and to assess where DRAP stands now (current state vis-à-vis QMS) and where it should be (desired state vis-à-vis QMS). The difference between the two states provided recommendations with a clear road map for DRAP to meet its ultimate objective of implementing the QMS.

The gap analysis study discloses clause wise gap analysis vis-à-vis DRAP conformity to the requirements of ISO 9001:2015. In addition to the standardization of content and format, the presence of documentation is also considered a conformity. The bar chart shows the clause wise gaps and DRAP conformity.

**Training on QMS-ISO 9001:2015 implementation for DRAP QMS divisional coordinators:** A 3-day training on “QMS-ISO 9001:2015 implementation” was held on October 16–18 for QMS coordinators at DRAP HQ Islamabad. The specific objectives of this 3-day training were to enable participants to understand QMS procedures and requirements and to learn risk-based thinking. It was activity-based training, and all 17 QMS coordinators participated in the training exercises. The participants learned all the clauses of ISO 9001:2015 and practiced techniques to develop documentation in light of QMS requirements.



*Inaugural session: Training on QMS-ISO 9001 for DRAP Divisional Coordinators at DRAP Islamabad.*

### **Activity 3.3 Support development and/or revision of policies/strategies, adoption of guideline and regulations**

To help strengthen regulatory systems, PQM is supporting DRAP to improve product quality assessment and the registration process, as well as to build the capacity of dossier evaluators and the inspectorate to perform surveillance of medicines quality for both federal and provincial authorities. This will significantly reduce the backlog of registration applications. In addition, switching to CTD facilitates good review practices for safety, quality, and efficacy data by applicants. Timely and efficient review and approval of essential medicines will ensure that quality-assured medicines are readily available for public health treatment programs in Pakistan.

**Technical Assistance to Drug Regulatory Authority of Pakistan for achieving WHO GBT Level III compliance:** DRAP requested PQM support to achieve WHO Maturity Level III based on the GBT. Level III is the minimum acceptable level for a stable, well-functioning, and integrated regulatory system. By achieving Maturity Level III, DRAP would attain WHO Listed Authority status. This would help DRAP perform functions using systematic regulatory approaches; enabling good quality, safety, and efficacy assessment; safeguarding patients from substandard and falsified medicines; ensuring consistency and transparency in decisions; and achieving worldwide recognition of its regulatory decisions. A fully functional DRAP is a prerequisite for WHO prequalification of vaccines, and it is expected this condition will be extended to medicines in near future.

### **WHO Maturity Levels Scale**



**Brief from Previous Quarter:** In FY18 Q4, PQM supported DRAP for self-assessment of all nine regulatory functions using GBT indicators. Based on gaps identified during the self-assessment, PQM is supporting DRAP in developing IDPs. One major gap identified was lack of a QMS, an integral part of the ISO 9001:2015 standard. PQM hired a consultant firm to support DRAP in achieving ISO 9001:2005 standards (as per WHO recommendations).

**Current Updates: Institutional Developmental Plans (IDPs):** In Q1, PQM continued to support DRAP to address gaps identified in IDPs. The following guidelines/documents were reviewed, adapted, and/or prepared:

- Revision of GMP checklist of DRAP based on WHO and Pharmaceutical Inspection Co-operation Scheme (PIC/S) guidelines:
- Draft prepared for risk-based guidelines for vendor qualification.
- Recall guidelines (role of DRAP).
- Risk-based inspection practices.
- Template for writing assessment reports (dossiers/product specific inspections/GMP/ reviewer comments).

**DRAP Progress on Attainment of Level III**

Function assessed	Number of Sub Indicators achieved/Expected to be achieved	% of Sub Indicators achieved/Expected to be achieved	Status of Maturity level
01-NATIONAL REGULATORY SYSTEM	34 out of 62	55%	1
02-REGISTRATION AND MARKETING AUTHORIZATION	21 out of 33	64%	2
03-VIGILANCE	9 out of 25	36%	1
04-MARKET SURVEILLANCE AND CONTROL	17.5 out of 26	67%	2
05-LICENSING PREMISES	15.5 out of 20	78%	2
06-REGULATORY INSPECTION	19 out of 29	66%	2
07-LABORATORY ACCESS AND TESTING	19 out of 34	56%	1
08-CLINICAL TRIAL'S OVERSIGHT	17 out of 31	55%	1
09-NRA LOT RELEASE	15 out of 23	65%	1
Total	167 out of 283	Average 60%	Overall 2

Furthermore, meetings were held with the DRAP core committee to develop documents/guidelines/SOPs on the following gaps:

- DRAP on communication strategy with external and internal stakeholders.
- DRAP framework on core competencies for all technical positions.
- HR performance-based monitoring system (including development of key performance indicators).
- Development of a database for inspections and dashboard for SOP storage and retrieval.
- Independent quality assurance board to monitor implementation of regulatory decisions and handle complaints.
- Premarket testing of all applied products.

Assumptions and risks for activities under objective 3 include the following:

- Ground conditions may not remain suitable (change in political government).
- Overly optimistic schedule of IDP implementation by DRAP.
- Lack of a change management process in DRAP.
- Limited funds for capacity-building activities/guidelines development.
- Limited funds to support DRAP for implementation of new mandatory functions required for Level III compliance (pharmacovigilance, clinical trial, risk-based PMS).
- Limited resources for sustainability of the interventions and progress made so far.

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**Objective 4 – (Corresponding to PQM IR 1.5 & (CDCS) 2.2.2 and 2.3.1): Capacity building of inspectorates at federal and provincial levels to perform their role effectively in pharmaceutical establishments licensing, post-marketing surveillance of medicines quality, and enforcement action**

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Under the Drug Act of 1976, DRAP and provincial health authorities are responsible for PMS such that surveillance at the manufacturing stage is DRAP's responsibility, whereas surveillance of the supply chain rests with provincial authorities. The samples collected by inspectorates are tested by the designated laboratories, and the reports are submitted to DRAP for compilation. This indicator is reported annually, but PQM liaisons closely with DRAP to ensure the data received from provinces and gathered by DRAP are maintained in DRAP's database. PMS is being conducted by provinces and DRAP. The Drugs Act 1976 empowers the provinces to prepare and implement rules for PMS, so all provinces are conducting PMS as per their own set of rules made under the provisions of Drugs Act 1976. However, the rules prepared by each province differ somewhat from each other. These differences create the burden of repeat testing of the same product at different laboratories, and a targeted, coordinated surveillance is not possible for follow-up.

PQM is working with DRAP to prepare a regulatory framework for an effective PMS system. Once developed, this will enhance both DRAP and provincial government inspectorates' collaboration and capacity. The new regulations will not only increase the strength of enforcement against substandard and falsified products in the supply chain but also enhance the relationship among the regulatory functions divided between DRAP and provincial health authorities. In collaboration with PQM, DRAP is preparing the document, which will be presented at the stakeholders (DRAP and provincial health authorities) meeting for debate and approval by the respective authority for implementation. PQM will conduct a training of inspectors from DRAP and provincial health authorities once the new regulations are approved and implemented by the respective governments.

## IV. Key Challenges

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

Another challenge that PQM faces is that medicines regulation is part of a complex system. Effective regulation can ascertain more issues. On the other hand, PQM is advocating for risk-based PMS, which is cost effective in contrast to sporadic surveillance without any plan or risk consideration. This is not an issue unique to PQM—it is common to all health system interventions. PQM can measure how its work contributes to systems strengthening only with an in-depth understanding of how systems behave (complex system theory) and how the health systems in which it works function.

PQM has been working collaboratively and maintaining open communication with key regulatory stakeholders in Pakistan (e.g., DRAP, Ministry of National Health Services Regulations and Coordination, provincial governments, WHO). Past experience has shown that provincial governments are less inclined toward strengthening quality assurance and control systems, which negatively impacts the performance of many quality control laboratories. Punjab is an exception: with PQM support, four more laboratories achieved ISO 17025 accreditation in Q1, raising the total number of ISO certified laboratories in the country to five.

## V. Lessons Learned

PQM works closely with DRAP to strengthen its regulatory capacity. However, a review of provincial health authorities revealed that they require more technical assistance, especially in the smaller provinces. This support in the smaller provinces is necessary to protect public health by promoting the standardization of processes and actions countrywide. The technical assistance that the provinces require is in the areas of risk-based PMS and strengthening of the provincial quality control laboratories. Continued technical assistance is needed to sustain the interventions and progress made so far, as well as to implement new mandatory functions required for attaining Level III compliance based on WHO GBT (pharmacovigilance, clinical trial, risk-based PMS).

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

## VI. Cross-Cutting Issues

**Bioequivalence studies center and bioequivalence regulations:** Recent changes in international support mechanisms (e.g., the Global Fund to Fight AIDS, Tuberculosis and Malaria is reducing its support for supplies) are likely to affect Pakistan. Pakistan has one of the highest TB burdens in the region, and the National TB Control Program depends on Global Fund supply of WHO-prequalified anti-TB medicines to treat TB patients. PQM is supporting two Pakistani manufacturers that are producing first-line fixed-dose combinations, none of which has achieved WHO prequalification. Through USAID financial assistance, these manufactures will acquire their bioequivalence studies abroad. Pakistan has a handful of bioequivalence testing facilities that are in a poor state of operation. Bioequivalence studies are important to ascertain the equivalence of two proprietary preparations of a medicine. These bioequivalence centers require technical assistance to acquire international certifications, and bioequivalence regulations need to be strengthened.

**Laboratory Quality Management System for Public Health Laboratories:** PQM support to develop QMS for medicines quality testing laboratories has also emerged the need to support the public health laboratories in order to strengthen the quality of care and surveillance. Communicable diseases still remain a major public health concern and are the prime cause of morbidity and mortality in Pakistan. Pakistan bears a significant portion of the regional burden of many communicable diseases, including HIV/AIDS, hepatitis B and C, tuberculosis, and the burden of multidrug-resistant tuberculosis also pose a significant public health threat. Moreover, a recent outbreak of XDR typhoid and increasing trends of antimicrobial resistance have also put more emphasis on the role of public health laboratories. Both sets of laboratories (medicines quality testing and public health laboratories) are critical components of a health care system. The fundamental principle of QMS for both sets of laboratories are the same, and PQM can play a vital role in strengthening the network of public health laboratories in order to strengthen the quality of care and surveillance with the overall objective to promote the global health security agenda.

# Eastern Europe & Central Asia



# Kazakhstan

## I. Quarter 1 Highlights

In Q1, PQM continued technical assistance to the 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 prequalification. PQM also continued to work with Nobel Almaty Pharmaceutical Factory, a manufacturer of second-line anti-TB medicines.

In Q1, as a follow-up of PQM participation in the WHO prequalification team (PQT) peer review conducted in Q4 FY18, PQM developed a confidential assessment report and provided recommendations addressing observations by the WHO PQT. In December 2018, WHO PQT provided the report of the peer review audit, and PQM commenced technical assistance to the laboratory to prepare a CAPA plan addressing all observations of WHO PQT for submission within the timeframe directed by WHO PQT. Submission and acceptance of CAPA by WHO PQT will result in full WHO prequalification of the Karganda laboratory. This is an important milestone for the country toward ensuring the quality of medicines in the Kazakhstan market.

As part of technical assistance to Nobel Almaty Pharmaceutical Factory for its anti-TB product, in Q1 PQM provided technical assistance to finalize a development of CAPA based on PQM's GMP assessment visit in FY18. PQM developed and submitted to the manufacturer a confidential assessment report on risk mitigation of cross-contamination between the products manufactured at its new site and the products manufactured at the adjacent facilities. A CAPA plan on cross-contamination is being developed.

## 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 prequalification.

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 1 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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In Q1, PQM continued remote technical assistance to the Karaganda NQCL. As a follow-up to WHO PQT's peer review audit, PQM provided recommendations to the laboratory staff on how to address the observations made by WHO PQT. In December 2018, WHO PQT provided a report of the peer audit. There were no critical observations by WHO PQT. According to the report, "if the CAPAs are implemented, it could be considered that the Physicochemical Analysis Department of Testing Laboratory of NCEMMD Karaganda is ready for prequalification." Currently, PQM is providing technical assistance to the Karaganda laboratory to develop a CAPA plan based on WHO PQT observations, in addition to addressing observations. The CAPA plan, along with evidence of its implementation, will be submitted in mid-February 2019. WHO will evaluate the CAPA plan received from the laboratory and make a decision if a follow-up WHO PQT audit for prequalification is required.

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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 Q1, PQM continued support to Nobel Almaty Pharmaceutical Factory for its anti-TB product, levofloxacin. In FY18 PQM made two visits to the manufacturer: a GMP assessment of the new site where levofloxacin would be manufactured; and a specialized technical assistance visit to assess risk and identify risk mitigation measure to prevent cross-contamination between the products manufactured at its new site and the products manufactured at the adjacent facilities. In Q1 PQM provided technical assistance to finalize development of CAPA developed by the manufacturer after the GMP assessment visit. In addition, PQM developed a confidential assessment report on risk management of cross-contamination. Development of a CAPA plan on prevention of cross-contamination is underway by the manufacturer. PQM will continue remote assistance to the manufacturer and will provide further recommendations on mitigation of risks for cross-contamination between the products and support preparation of appropriate documentation to comply with international GMP standards.

## Uzbekistan

### I. Quarter 1 Highlights

In Q1, as a follow-up of the PQM's GMP assessment of the new manufacturing site of Nobel Pharmsanoat, PQM provided technical assistance to finalize the CAPA plan. As a follow-up to PQM's technical assistance for cross-contamination risk management, PQM developed a confidential assessment report for the manufacturer. This report recommends risk mitigation measures to prevent cross-contamination risk between the products manufactured at the new site and the products manufactured at the adjacent facility to promote product quality. A CAPA plan for cross-contamination risk mitigation is under development by the manufacturer.

In Q1, PQM conducted a 3-day training on Data Integrity and Documentation Management for the staff of the State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment under the Agency for Development of Pharmaceutical Industry, Ministry of Health of the Republic of Uzbekistan. The training was followed up by group discussions related to implementation of a CAPA plan, developed by the medicines QC laboratory as a result of the ISO 17025:2017 assessment by PQM in Q3.

PQM continues to support medicines QC laboratory activities; in Q1, three pieces of laboratory equipment were purchased to broaden the medicines quality testing scope and strengthen laboratory activities.

### 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 1 Progress by Objective

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

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In Q1, PQM continued to provide technical support to Nobel Pharmsanoat for its anti-TB product, levofloxacin. In this quarter, PQM’s technical assistance was focused on finalization of the CAPA plan developed by the manufacturer as a result of PQM’s GMP assessment visit in Q3 FY18 and, implementation of the CAPA plan. Also, in Q1, PQM developed and submitted to the manufacturer a confidential report on the assessment of the cross-contamination risk conducted in Q4 FY18. Based on the assessment, the manufacturer started development of CAPA plan for risk mitigation of product cross-contamination with PQM’s technical assistance.

PQM will continue technical support to the manufacturer for the CAPA plans implementation to promote compliance with international GMP standards. PQM will also discuss potential trainings needs for the staff of Nobel Pharmsanoat to support successful implementation of CAPA.

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

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In Q1 PQM continued technical assistance to State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment under the Agency for Development of Pharmaceutical Industry, Ministry of Health of the Republic of Uzbekistan in strengthening of their medicines quality control capabilities: PQM provided training to 23 representatives from various departments within the State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment on the fundamental principles of data integrity and practical applications as it relates to medicines quality control laboratories. The training focused on providing participants with an overview of the underlying principles of data integrity, illustrating activities that could pose risks to the quality of the data generated by the laboratory, and providing recommendations for preventative measures as well as corrective measures. The training provided a forum for participants to interact and share ideas to promote a quality-centered environment with key focus on generation of accurate, complete, and consistent data. The training activities provided participants with an opportunity to improve their understanding of data integrity in both theory and application. The training aimed to enhance the participants’ ability to identify data integrity issues through practical examples and case studies; participants also performed self-assessment of the laboratory’s quality and technical operations. Discussions throughout the sessions provided participants opportunities to ask questions and share experiences.

The training was followed up by a discussion of a CAPA plan prepared by the laboratory based on the observations made by PQM during the assessment of the physicochemical laboratory for compliance with ISO/IEC 17025:2017

requirements in Q3. The laboratory made some improvements of its QMS, but there are many activities listed in the plan that are still in progress with issues to be resolved.

PQM will continue technical assistance to the medicines QC laboratory. At the beginning of 2019, the medicines QC laboratory will renovate the laboratory area to improve its compliance with the ISO 17025 standard and good laboratory practices. After the renovation, PQM will provide training on good pharmaceutical quality control laboratory practices and continue technical assistance toward international ISO/IEC 17025 accreditation by an international laboratory accreditation cooperation (ILAC) MRA signatory agency or WHO prequalification. PQM will prepare an implementation plan for international accreditation or WHO prequalification.

In Q1, PQM purchased three instruments for the medicines QC laboratory under the Agency for Development of the Pharmaceutical Industry within MOH. The equipment has been delivered to the country and is currently going through custom clearance. After the equipment is received by the laboratory, the equipment vendor will install and train staff to use it appropriately.

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### **Objective 3 – Strengthen GMP inspection system**

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In Q1, there was no progress by the Agency for Development of the Pharmaceutical industry for the establishment of the working group for the PIC/S self-assessment questionnaire, as was previously agreed upon. PQM is following up with the Agency for Development of the Pharmaceutical industry to reconfirm their commitment towards PIC/S membership. PIC/S is an international mechanism leading the development and implementation of harmonized GMP standards and quality systems of Inspectorates in the field of medicinal products.

# Core Portfolio



# Core MNCH

## I. Quarter 1 Highlights

The PQM-supported Ukrainian manufacturer was visited by the WHO prequalification team for an inspection of its facility for magnesium sulfate injection in December 2018. There was no critical observation outcome from the inspection. A formal report is yet to be received from the WHO inspection team.

The dossiers of oxytocin and magnesium sulfate of the Nigerian manufacturer, Juhel Pharmaceuticals, were considered on the 9th East Africa Community (EAC) joint assessment meeting held December 3–7 in Entebbe, Uganda. If the products are approved, it would contribute to improving access to quality-assured priority MNCH products on the African market in the sustainable way.

## II. Health Element Context

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

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

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

## III. Quarter 1 Progress by Objective

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

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In Q1 PQM provided technical assistance to manufacturers of the following MNCH products:

- Magnesium sulfate FPP:
  - PQM continued technical assistance to the manufacturer in China. In Q1, the manufacturer produced three process validation batches, and stability studies were initiated. The manufacturer also started working on compiling the production dossier to submit to PQM for review.
  - The Ukrainian manufacturer’s dossier for magnesium sulfate was formally accepted for review by WHO PQT in July 2018; response to the first round of query is almost complete and will be sent to PQM for review prior to submission. In December 2018, WHO PQT conducted GMP audit of the manufacturing site. There were no critical observations during audit. After WHO PQT submits the audit report to the manufacturer, PQM will provide assistance in preparation and implementation of the CAPA plan.
- Amoxicillin FPP:
  - PQM staff visited the amoxicillin manufacturer (Ghana) in December 2018. The production line was assessed, and PQM will continue to provide assistance to compile and finalize dossier for submission to the EAC medicine registration harmonization mechanism. The EAC platform provides the opportunity for manufacturers to obtain blanket approval that facilitates in country product registration in member countries.
  - PQM is continuing to provide technical assistance at various stages to ensure that the manufacturers are making progress towards WHO PQ or for global procurement eligibility. This assistance will include providing feedback on the CAPAs as a result of the WHO inspection for the Ukrainian manufacturer.

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

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In order to support access to quality-assured priority MNCH products on the African market in the sustainable way, PQM encourages the manufacturers to apply for approval of their products through the EAC MRH mechanism. In Q1, PQM engaged two manufacturers to submit their dossiers for oxytocin and magnesium sulfate for EAC review. One Indonesian company, Sanbe, submitted its dossier for oxytocin; one Nigerian manufacturer, Juhel Pharmaceuticals, submitted its dossiers for oxytocin and magnesium sulfate to EAC.

The 9th EAC joint assessment meeting was held December 3–7 in Entebbe. During this meeting, six new applications were reviewed. Among them were two of Juhel's products: oxytocin and magnesium sulfate. The EAC joint assessment meeting requested additional information from the manufacturer. A final decision about approval of the product will be made after the manufacturer submits the requested information. The dossier for Sanbe's oxytocin was not reviewed, as the manufacturer did not pay GMP assessment fee prior to the meeting as requested.

In Q1, PQM worked with Sanbe to register oxytocin injection, a high-priority MNCH medicine using the WHO Collaborative Registration Procedure (CRP) mechanism. PQM has initiated a kickoff meeting with the PQM Pakistan colleagues and PQM Indonesia office to discuss the engagement of an Indonesian manufacturer to submit its oxytocin dossier to Pakistan—which recently became a WHO CRP member country. Through this mechanism, PQM will be working with the Pakistani regulatory authority to address gaps in the review of the dossier under WHO's requirements.

In Q2, PQM will continue to work with Juhel to respond to the EAC on the queries to manufacturer. PQM will work to engage additional manufacturers for submission of their dossiers for approval through the EAC MRH mechanism. PQM will work with Sanbe and the Pakistani field office staff to submit to DRAP for CRP.

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

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PQM finalized the agreement with GSK to transfer the product and manufacturing know-how pertaining to Umbipro (chlorhexidine gel) to PQM, such that PQM can subsequently build capacity of several local manufacturers through technology transfer to manufacturer chlorhexidine gel. In Q1, PQM staff visited the GSK site in the United Kingdom to obtain the manufacturing, laboratory, and regulatory information (dossier and tech transfer reports) for Umbipro. The PQM team was able to observe the equipment and manufacturing facilities for chlorhexidine.

Next steps include organizing a workshop in Africa where GSK and PQM will share the information with the interested manufacturers. This technology transfer initiative will help the local generic manufacturers to develop or improve their current manufacturing process to ensure availability of quality-assured and effective chlorhexidine in the local markets.

PQM also contributed to the "Training workshop on key enabling factors for successful local production and supply of quality-assured medicines" coordinated by NEPAD/PQM/WHO on December 17–19 in Addis Ababa, Ethiopia. PQM delivered two presentations on "Good products development practices" and "Elements of Sound Technology Transfer" during this workshop. PQM also participated in discussions and side-bar meetings, including discussions on the CHX technology transfer project. More details on the workshop are provided in the Cross Bureau section.

# **Core NTD**

## **I. Quarter 1 Highlights**

With PQM's technical assistance, Jiangsu Chengxin Pharma received GMP approval and full WHO prequalification for micronized and non-micronized praziquantel API in October 2018. This new source of quality-assured praziquantel API will contribute to the availability of quality-assured praziquantel FPP on the global market. Praziquantel is the only medicine recommended by WHO for the treatment of schistosomiasis, an NTD caused by parasitic worms.

## **II. Health Element Context**

NTDs have been a global concern for decades and a major cause of morbidity and mortality worldwide. More than a billion people—one-sixth of the world's population—suffer from one or more NTDs. These diseases affect the world's most vulnerable populations, almost exclusively impoverished populations living in rural areas and urban

slums of low-income countries. The impact of NTDs on individuals and communities is devastating. Many of them cause severe disfigurement and disabilities.

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

As PQM continues support for manufacturers to achieve prequalification of anti-NTD medicines, PQM also provides assistance to manufacturers in terms of 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 prequalification 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 1 Progress by Objective

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

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During Q1, 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 prequalification dossier queries for praziquantel API. As a result, one manufacturer, Jiangsu Chengxin Pharma, received WHO GMP approval and full WHO prequalification in October 2018 for micronized and non-micronized praziquantel API.
- The second Chinese manufacturer continued to prepare its responses for WHO prequalification assessment in Q1.

##### **Praziquantel FPP:**

- One of the two Indian manufacturers initiated GMP manufacturing of optimization batches in November 2018. The first batch analysis resulted in out-of-trend data for friability (tendency of a tablet to chip, break, or crumble when compressed). Upon completion of the investigation, a second batch was manufactured in December, which met all quality requirements.
- The second Indian manufacturer submitted the BE protocol to the ethics committee and local regulatory agency for approval. It is expected to be received in early Q2. BE study is tentatively scheduled to start in February 2019. The manufacturer continued working on implementation of cross-contamination risk mitigation measures based on PQM's assessment in Q4. In January 2019, PQM will visit the manufacturer to review CAPA compliance and provide technical support for pending issues and dossier preparedness.
- PQM is working with a third manufacturer (China). The BE study began in October 2018; once it is complete, PQM will reinitiate technical assistance to help compile the dossier for submission to WHO prequalification.

##### **Albendazole FPP:**

- Utilizing a thorough competitive process, PQM selected a manufacturer to receive financial and technical support for BE study of albendazole. The subaward package was submitted to USAID for approval. PQM has scheduled a visit to the facility in January 2019 to perform GMP assessment, conduct document verification, review dossier, and finalize project timeline.
- PQM is continuing to provide technical assistance at various stages to ensure that the manufacturers are making progress toward WHO prequalification.

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## Objective 2 – Technical support for bioequivalence study

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In Q1, PQM continued technical assistance to two manufacturers of praziquantel FPP in support of s BE studies preparations:

- The praziquantel BE study protocol of one manufacturer received approval from the local regulatory and ethics bodies. BE study will commence once the BE batch for the test product has been manufactured and analyzed. This is tentatively scheduled for Q2 in 2019. The second manufacturer has submitted its protocol to the local regulatory and ethics committee for approval. This approval is expected to be received in mid-January. The BE study is tentatively scheduled to be initiated in February 2019.

The candidate for financial and technical support to an albendazole manufacturer has been confirmed. A visit to the facility is scheduled for January 2019.

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

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No activity to report this quarter.

# Core TB

## I. Quarter 1 Highlights

PQM visited the clofazimine FPP facility to provide hands-on assistance to draft and submit the response to ERP queries. The team worked with the regulatory and research and development (R&D) teams to review the additional data requested and finalize the write-up response to the ERP. The two teams worked diligently and ensured that responses to the ERP queries were submitted in the timely manner.

Additionally, PQM was able to complete and publish a technical paper on mitigating cross-contamination in a multiproduct facility using risk-based cleaning validation methods. This paper, publicly available on the PQM website, provides an essential overview of the evolution of the regulatory expectations and industry advances in cleaning validation approaches, including recent risk assessment considerations. This report contains a case study and examples for manufacturers to understand and apply the strategies for maintaining a robust cleaning validation program and conducting risk mitigation for minimizing cross-contamination.

## 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 1 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 Q1, PQM provided technical assistance to manufacturers of the following TB products:

- **Clofazimine FPP:** Upon review of the dossier submitted to the ERP of the Global Fund in Q4, the ERP sent a request for additional technical information on the finished product prior to approval. PQM staff visited the manufacturer to work on additional data related to the stability, testing, and manufacturing of the finished product to be submitted to the Global Fund for further review and approval. PQM staff worked with the manufacturer's regulatory affairs and R&D teams for 1 week to gather and review the data and also help draft the response for submission to the Global Fund. The response was submitted to the Global Fund in late November 2018. PQM provided further assistance to respond to the questions and queries from the Global Fund ERP and in January 2019 the product received ERP's positive opinion after quality risk review that determined no objection for clofazimine 100 mg soft capsules manufactured by Dong-A.
- **Clofazimine API:** PQM also worked with the regulatory affairs team of the manufacturer to initiate the draft response for WHO prequalification assessment queries.
- **Rifapentine API:** One manufacturer (China) is continuing to implement PQM's comments to revise the API Master File (APIMF). Tentatively, the manufacturer is planning to submit the APIMF to WHO PQT by the end of March 2019.
- **Rifapentine FPP:** PQM is working with the FPP manufacturer (China) to implement the CAPAs as a result of PQM's assessment. The manufacturer is continuing to work on sourcing of the API for product development.
- **Kanamycin FPP:** PQM and the manufacturer are awaiting WHO PQT's final approval and issuance of WHO Public Assessment Report (WHO PAR). This report provides key outputs of WHO PQT for medicines providing insight and transparency regarding processes followed to prequalify the FPP of concern. There has been a significant delay in the publication of the WHO PAR so the manufacturer has reached out to WHO PQT for clarification.
- **Linezolid FPP:** The manufacturer is still awaiting final approval from US FDA. The API manufacturer had submitted an update to its drug master file, a document that details confidential information about facilities, processes, or articles used in manufacturing, processing, packaging and storing human drugs, and the finished product manufacturer is awaiting the analysis from the API manufacturer to submit to US FDA.
- **Rifampicin/isoniazid/ethambutol/pyrazinamide (4 FDC):**
  - One of the two Pakistani manufacturers received approval on the BE protocol from the local regulatory and ethics committee. It manufactured two 250,000 tablet batches in November 2018 and placed them on stability. A PQM visit is planned for early January 2019 to provide hands-on assistance in dossier compilation and final GMP assessment of the facility.
  - The second manufacturer received BE protocol approval from the local regulatory authority and ethics committee. Three batches of 30,000 tablets were placed on stability and yielded satisfactory results for 3 months accelerated time point. One batch of 300,000 tablets was placed on stability in October 2018. A draft dossier was received for review. A PQM visit is planned for early January 2019 to provide hands-on assistance in dossier compilation and final GMP assessment of the facility.

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

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PQM participated in the 49th UNION World Conference on Lung Health held in The Hague on October 24–27. PQM participated and contributed to different conference sessions. PQM uses this opportunity to stay up-to-date about the evolving approaches to TB treatment and control. This is crucial for making informed decisions that define future PQM priorities. PQM also met different partners and stakeholders including WHO, the Global Drug Facility, and manufacturers.

PQM identified the vendor for development of the GMP online module through a competitive process. Preparations for the subaward package for USAID approval is underway and will be submitted in early January, 2019. This activity will be cost-shared with Core NTD.

PQM completed and published a technical report on mitigating cross-contamination in a multiproduct facility using risk-based cleaning validation methods. This paper, publicly available on the PQM website, provides an essential overview of the evolution of the regulatory expectations and industry advances in cleaning validation approaches, including recent risk assessment considerations.

# Cross Bureau

## I. Quarter 1 Highlights

A NEPAD/PQM/WHO coordinated “Training workshop on key enabling factors for successful local production and supply of quality-assured medicines” was held on December 17–19 in Addis Ababa. Attendants included multiple international, regional, and NGO representatives, as well as more than 80 participants from African manufacturers. PQM personnel delivered five presentations at the workshop

The MedRS tool is available for field testing. The first field testing is scheduled to be conducted in Myanmar in Q2. After feedback from the field tests, the tool will be transferred to the PQM website in Q2, where it will be available to MRAs interested in using the tool during planning and implementation of risk-based PMS.

An e-course proposal on “Strengthening Quality Assurance Systems for Medical Products as an Essential Component of Health Systems” was submitted to and approved by the Global Health eLearning Center. The kickoff meeting with USAID’s partner in charge of online courses took place, and currently all nine course sessions are under development.

A regulatory system country profile for Bangladesh has been approved by country’s MRA. Malawi and Nigeria are still under review. Draft profiles for Ghana, Ethiopia, Mozambique, Myanmar, and Pakistan finalized by PQM will be submitted during Q2 to countries’ MRAs for completion of missing information and final review.

## 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 1 Progress by Objective

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

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#### **Activity 1.1: Attend and present at international meetings/panel discussions**

A NEPAD/PQM/WHO coordinated workshop to present and discuss key enabling factors for successful local production and supply of quality-assured medicines was held on December 17–19 in Addis Ababa. The objectives of the workshop were to provide training and guidance to African manufacturers on key issues for local production of

essential medicines, share experiences and lessons learned in achieving local production of quality-assured products, and understand the gaps and need in capacity-building for pharmaceutical manufacturers and regulators toward local production. Participants at the workshop included delegates from AfDB, EFMHACA, Global Fund, ICGB, IFC, Medicines Patent Pool, NAFDAC, NEPAD, PQM, UNAIDS, UNCTAD, UNICEF, SAPHRA, and WHO, as well as more than 80 participants representing local manufacturers from countries including Ethiopia, Ghana, Kenya, Nigeria, South Africa, Uganda, Tanzania, and Zimbabwe. PQM's attendance was partially funded through the Core MNCH portfolio, and the three PQM representatives made presentations on "PQM Overview of Local Manufacturers' Experience," "Good Products Development Practices," "Elements of Sound Technology Transfer," "Achieving Facility Compliance with WHO/International GXP Standards," and "Understanding Guidelines and Regulations on Post Approval Variations and Product Lifecycle Management"; they also participated in a number of side meetings and delivered closing remarks. WHO and other partners also made presentations based on relevant technical expertise.

The trip report and the "Points to Consider" document will be disseminated in Q2.

#### **Activity 1.2: Develop customized media reports from EPCMD countries to advocate the need for effective medicine quality assurance systems**

This activity was completed during FY18 Q4.

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

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No updates this quarter.

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

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##### **Activity 3.2: Finalize Online RB-PMS tool (MedRS)**

MedRS is a risk assessment tool that can be used to support planning and implementation of risk-based PMS.

For the most part, development of the tool had been completed during FY18, and in Q1 all remaining MedRS development issues identified have been addressed; the tool is now available for field testing. The first field testing is scheduled to be conducted in Myanmar in Q2. Feedback from the field tests will be incorporated into the tool, and the tool will be transferred to the PQM website in Q2.

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

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Following the revision of the scope and module content suggested by the AOR team, the e-course proposal on "Strengthening Quality Assurance Systems for Medical Products as an Essential Component of Health Systems" was completed and submitted to the Global Health eLearning Center. The proposal was accepted and the PQM team had a kickoff meeting with USAID's partner in charge of online courses (Knowledge for Health, K4H). Sessions development is under way, and a consultant to support development has been hired.

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#### **Objective 5 – Establish regulatory system country profiles**

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Information gathered by PQM for 2017 regulatory system country profiles for Bangladesh has been reviewed and approved by the MRA. Malawi's and Nigeria's reports are still under review by MRAs. All MRA-approved profiles will be uploaded in PQM website and disseminated

PQM drafts of FY18 profiles for Ghana, Ethiopia, Mozambique, Myanmar, and Pakistan have been completed with publicly available data and information from PQM's countries personnel and consultants. Missing information and final review will be countries' MRAs.

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

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The selection process of a consultant has been completed. Development of a contract with the hosting institution is under way.

# Management Overview

In Q1, PQM worked with the USAID Missions and core health element teams to obtain outstanding approvals for FY 2019 work plans. By the end of Q1, five out of six work plans (83%) had been approved. This includes the countries of Nigeria, Uzbekistan, Ethiopia, Indonesia, and Rwanda. The only outstanding work plan to be approved is Cross Bureau.

Also in Q1, PQM finalized one technical document "[Mitigating Cross-Contamination in Shared Production Facilities Using Risk-Based Cleaning Validation Methods: Considerations and Case Study](#)." This document provides an overview of the evolution of the regulatory expectations and industry advances in cleaning validation approaches. Cleaning validation is a requirement for preventing potential cross-contamination of products during manufacturing that can cause harm to the product consumers if not prevented. PQM also published its "[Technical Resource Inventory](#)" that provides easy access to technical materials through a regularly updated document. Five new success stories were also developed in Q1:

- [Increasing the Sustainability of Ethiopia's Medicines Quality Assurance System by Building Local Service Capacity](#)
- [Bangladesh Implements Updated Standards for Medicines Testing](#)
- [Guinea Updates its Pharmaceutical Regulatory Law \(French version\)](#)
- [Pakistan Acts Quickly to Recall Contaminated Medicines](#)
- [Using Mobile Technologies to Detect Poor-Quality Medicines in Benin \(French Version\)](#)

PQM's Technical Deputy Director participated in a technology transfer training workshop in November 2018. This event followed the press release in September 2018 by GSK, USAID, and USP on collaboration to help increase availability of quality-assured chlorhexidine—a life-saving antiseptic to prevent umbilical cord infections in newborns—in developing countries. The workshop served to initiate the knowledge transfer from GSK to USP for Umbipro®; and for USP to observe equipment and manufacturing facilities to supplement documentation already provided for the technology transfer. PQM will utilize the information gained to provide technical assistance in the form of training and technology transfer to interested local manufacturers in order to sustainably increase the supply and sources of quality-assured chlorhexidine in low-and middle-income countries.