

FY2016

**ANNUAL
PERFORMANCE REPORT
OCTOBER 1, 2015 – SEPTEMBER 30, 2016**



**PROMOTING THE
QUALITY
OF MEDICINES**

TABLE OF CONTENTS

NOTE FROM THE DIRECTOR	1
ACRONYMS	4
CHAPTER 1: BACKGROUND	5
Technical Approach	6
Measuring Our Results	7
CHAPTER 2: PROGRESS BY RESULT AREA	9
IR 1: National Regulatory Systems Strengthened	9
IR 2: Availability of Quality Medicines Increased	19
IR 3: Capacity to Detect Poor Medical Products Increased	25
IR 4: Use of Information for Decision Making Increased	29
CHAPTER 3: CHALLENGES, SUSTAINABILITY AND LESSONS LEARNED	37
Challenges	37
Lessons Learned	39
Sustainability, Partner Contributions and Ownership	39

NOTE FROM THE DIRECTOR



The Promoting the Quality of Medicines (PQM) program is funded by the United States Agency for International Development (USAID) and implemented by The U.S. Pharmacopeial Convention. This year we celebrate the seventh anniversary of this program and are deeply proud of the progress made by the countries and institutions with the support of the PQM program.

The PQM program provides technical assistance globally and currently operates in 34 countries to achieve its four main objectives. I am pleased to present our 2016 Annual Performance Report, which documents the major accomplishments this year and ongoing progress toward meeting our goal of strengthening quality assurance systems to sustainably ensure quality and safety of medical products and protect public health. These accomplishments are measured and organized around our four intermediate result areas.

Of the many highlights in each result area, I'd like to share just a few to illustrate our work throughout the year. Our teams in Nigeria and Indonesia provided advocacy and technical assistance to develop national-level regulations that will have lasting effects on quality assurance of medicines. In an effort to advance the availability of essential medicines, our team working on good manufacturing practices supported the prequalification of four active pharmaceutical ingredients as well as kanamycin finished pharmaceutical product, an important medicine for the treatment of multidrug-resistant tuberculosis. Our work to increase the capacity of countries to detect falsified, substandard and unapproved medical products resulted in 40 regulatory actions against substandard samples in

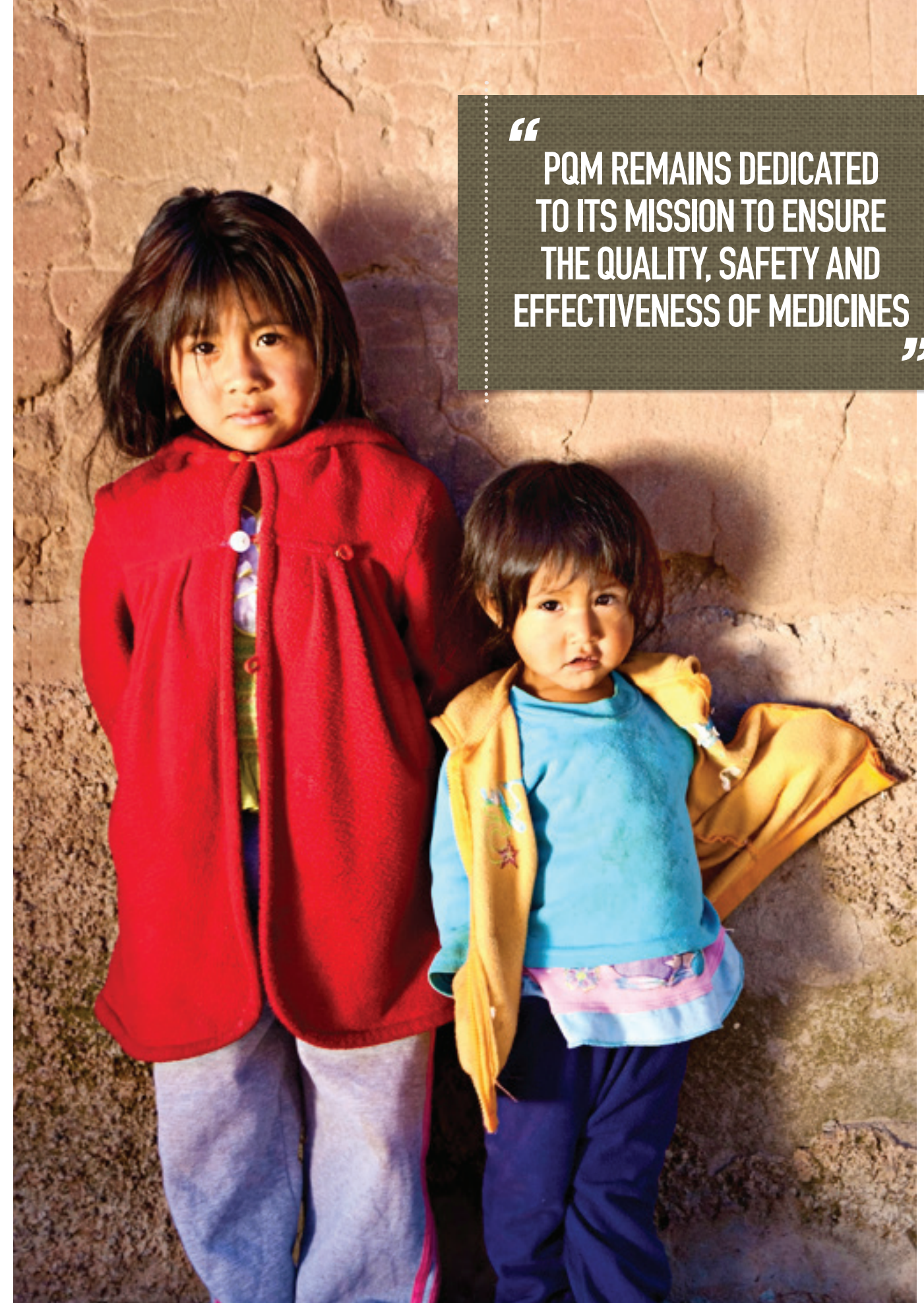
Liberia. In an effort to increase the use of evidence-based information for decision making, PQM launched the Poor-Quality Medicines ALERT to provide rapid access to information about poor-quality medicines. Finally, in an ongoing effort to promote local ownership and sustainability of efforts, PQM collaborated with a number of academic institutions to strengthen medicines quality assurance education curricula to prepare the next generation of pharmaceutical professionals.

As we transition to FY17, PQM remains dedicated to its mission to ensure the quality, safety and effectiveness of medicines essential to USAID priority diseases—namely HIV/AIDS, tuberculosis, malaria, neglected tropical diseases and diseases affecting maternal and child health—by providing a unique set of technical assistance to stakeholders that manufacture, test and regulate medicines. While there is still much more work to be done to tackle poor-quality medicines around the world, we look forward to building on this year's successes and doing even more to strengthen local health systems in the upcoming year.

It is a great honor to do the work we do, and to have the opportunity to collaborate with outstanding partners at the global, regional and local levels. Please continue to follow our progress toward ensuring that the best quality medicines are available to those who need them most around the world.

Jude I. Nwokike
Director, PQM Program

“
PQM REMAINS DEDICATED
TO ITS MISSION TO ENSURE
THE QUALITY, SAFETY AND
EFFECTIVENESS OF MEDICINES
”



ABOUT THE PROMOTING THE QUALITY OF MEDICINES PROGRAM

USAID Funding Sources	Global Health Bureau; Office of Health Systems; Office of Health, Infectious Diseases and Nutrition; USAID Country Missions
Name of Implementing Partner	Promoting the Quality of Medicines Implemented by the U.S. Pharmacopeial Convention
Cooperative Agreement Number	GHS-A-00-09-00003-00
Period of Performance	September 18, 2009, to September 17, 2019
Agreement Officer's Representative Team	Mr. Anthony Boni, Pharmaceutical Management Specialist Ms. Elisabeth Ludeman, Pharmaceutical Management Advisor Ms. Tobey Busch, Senior Pharmaceutical Management Advisor
PQM Responsible Staff	Mr. Jude Nwokike, Director

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

As of September 2016, USAID supports PQM's work in 34 countries, through 20 country missions, two regional missions, one cross bureau program and four core health programs.

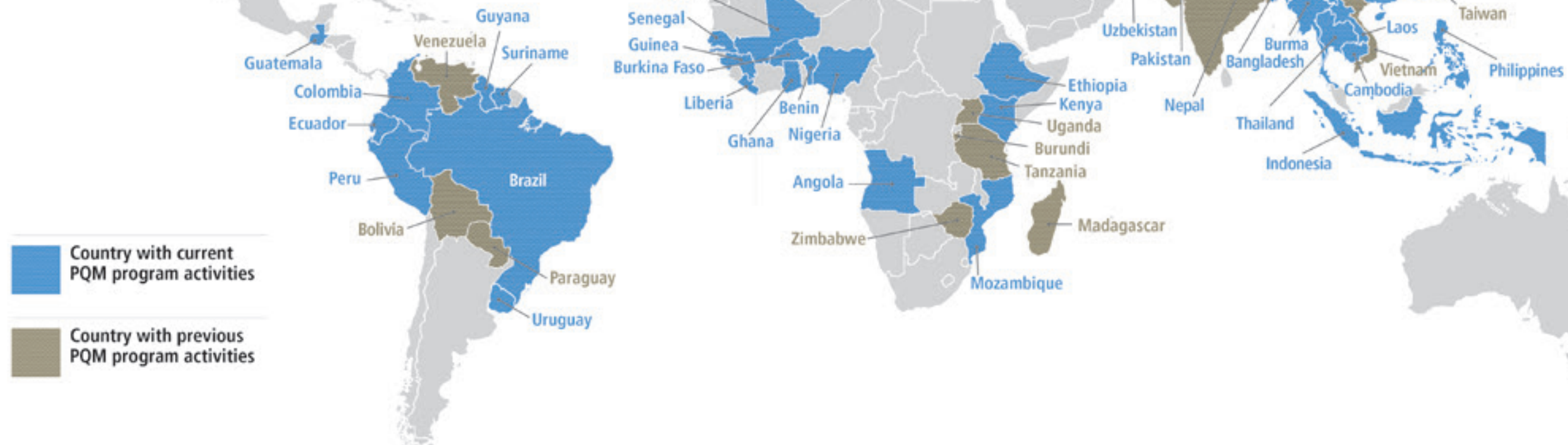
This report may be reproduced if credit is given to the PQM program. Please use the following citation:

Promoting the Quality of Medicines. 2016. *Promoting the Quality of Medicines Program Annual Performance Report: Project Year 2016, October 1, 2015 – September 30, 2016*. Submitted to the U.S. Agency for International Development by the Promoting the Quality of Medicines Program. Rockville, MD: United States Pharmacopeial Convention.

This document is made possible by the generous support of the American people through the United States Agency for International Development. The contents are the responsibility of the Promoting the Quality of Medicines program and do not necessarily reflect the views of USAID or the United States government.

AMI	Amazon Malaria Initiative	NTD	Neglected Tropical Disease
API	Active Pharmaceutical Ingredient	ORS	Oral Rehydration Solution
ARV	Antiretroviral	PIC/S	Pharmaceutical Inspection Co-operation Scheme
ASEAN	Association of Southeast Asian Nations	PMI	President's Malaria Initiative
CAPA	Corrective And Preventive Action	PMS	Post-Marketing Surveillance
CHX	Chlorhexidine	PQM	Promoting the Quality of Medicines
CNCC	National Center for Quality Control	PTB	Physikalisch-Technische Bundesanstalt
CRO	Contract Research Organization	QA	Quality Assurance
EAC	East African Community	QC	Quality Control
ERP	Expert Review Panel	QMS	Quality Management System
FDA	Food and Drug Administration or Authority	RDMA	Regional Development Mission for Asia
FDC	Fixed-Dose Combination	SOP	Standard Operating Procedure
FDD	Fixed-Dose Combination	SSFFC	Substandard/Spurious/Falsified/ Falsely-Labelled/Substandard
FPP	Finished Pharmaceutical Product	TA	Technical Assistance
GDP	Good Documentation Practices	TB	Tuberculosis
GF	Global Fund	USAID	United States Agency for International Development
GLP	Good Laboratory Practices	USP	United States Pharmacopeial Convention
GMP	Good Manufacturing Practices	UV	Ultraviolet
GPHF	Global Pharma Health Fund	WHO	World Health Organization
HPLC	High-Performance Liquid Chromatography	WHO PQ	World Health Organization Prequalification
HVAC	Heating, Ventilation and Air-Conditioning		
IEC	International Electrotechnical Commission		
ILT	Inter-Laboratory Testing		
IR	Intermediate Result		
ISO	International Standardization Organization		
JPR	Joint National Tuberculosis Program Review		
LMICs	Low- and Middle Income Countries		
M&E	Monitoring and Evaluation		
MDR-TB	Multidrug-Resistant TB		
MNCH	Maternal, Newborn and Child Health		
MOH	Ministry of Health		
MOI	Ministry of Industry		
MQDB	Medicines Quality Database		
MQM	Medicines Quality Monitoring		
MRA	Medicines Regulatory Authority		
NHQC	National Health Products Quality Control Center		
NQCL	National Quality Control Laboratory		
NTD	Neglected Tropical Disease		

BACKGROUND



The Promoting the Quality of Medicines (PQM) program is a cooperative agreement between the United States Agency for International Development (USAID) and The United States Pharmacopeial Convention (USP). Since 1992, USP has worked cooperatively with USAID to support developing countries in addressing critical issues related to medicines information and quality. The PQM program provides technical assistance to build capacity of medicines regulatory authorities

and quality assurance systems in countries with weak health systems. PQM also provides technical support to manufacturers of quality assured priority essential medicines for malaria, HIV/AIDS, tuberculosis, neglected tropical diseases and maternal and child health. There is increasing recognition of the burden of poor-quality medicines and their threat to public health, especially in low- and middle-income countries. Falsified and substandard medicines can cause treatment failure and adverse reactions,

can increase morbidity and mortality, and may contribute to antimicrobial resistance. These medicines represent not only a waste of scarce resources but also a substantial risk to public health. Further, they risk undermining decades of health investments, including those made by USAID. During FY16, PQM implemented projects in 34 countries and had four field offices in Ethiopia, Indonesia, Nigeria and the Philippines.

TECHNICAL APPROACH

Using a systems-based approach, PQM provides technical assistance in several areas to achieve the cooperative agreement's strategic objectives. PQM's approach includes risk management that is pragmatic, proportionate and by priority. PQM provides hands-on and follow-up support; this support is informed by current regulatory quality assurance (QA)/quality control (QC) best practices. Moreover, PQM's approach fosters sustainability by linking to regional

and national health and pharmaceutical strategies, attaining partner buy-in and commitment, leveraging regional harmonization initiatives, addressing financing and human resources constraints, and advocating for accountability and transparency. Many of these approaches are applied globally, but tailored to fit the needs of individual countries or regions. PQM strengthens the ability of medicines regulatory authorities (MRAs) and national quality control laboratories

(NQCLs) to test the quality of medicines entering and produced within their borders. Capacity is built through the development of policies necessary to properly regulate medicines and to inspect medicines manufacturers. NQCLs receive technical assistance to carry out the actual testing and monitoring of medicines, both imported into and manufactured within the country, through postmarketing surveillance (PMS), which applies risk-based testing of medicines at various points along the supply chain. PQM

4

PQM'S WORK RESTS ON OBJECTIVES

2009–2019

- 1 BUILD CAPACITY AND STRENGTHEN QA SYSTEMS
- 2 HELP INCREASE SUPPLY OF QA MEDICINES
- 3 COMBAT FALSIFIED, SUBSTANDARD AND UNAPPROVED MEDICINES
- 4 PROVIDE TECHNICAL LEADERSHIP

further supports NQCLs through hands-on training and technical assistance to improve laboratory standards and help them attain compliance with internationally recognized standards, such as International Standardization Organization (ISO) accreditation and/or World Health Organization Prequalification (WHO PQ), which demonstrate laboratory proficiency to produce consistently valid results.

PQM's systems-based approach also extends to medicines manufacturers. PQM experts support manufacturers in improving Good Manufacturing Practices (GMP) compliance and developing dossiers to submit to local MRAs, the WHO PQ program and/or other stringent regulatory authorities, thereby promoting security in the supply and availability of essential priority medicines for public health.

PQM also serves as a technical leader and advocate for medicines quality. PQM contributes to advocacy efforts

to eradicate falsified and substandard products through the dissemination of information for decision making and collaboration with diverse partners at local, national and international levels. Advocacy aims to advance the pharmaceutical quality agenda and to support enforcement actions against cases of falsified and substandard medicines.

MEASURING OUR RESULTS

PQM is able to achieve its strategic objectives by providing technical assistance in the four key Intermediate Result (IR) areas using a systems-based approach. The systems-based approach is tailored to fit the needs of individual countries or regions and includes all related stakeholders throughout the health system. Activities include building the capacity of countries' MRAs to review and approve quality assured essential medicines and strengthen their ability to protect their own population from poor-quality medicines. PQM works with national and regional regulatory authorities

to build sustainable capacity for medicines evaluation, manufacturing inspection and surveillance. PQM supports NQCLs through hands-on training and technical assistance to improve laboratory standards, to ensure that they produce consistently valid results by attaining compliance with internationally recognized certifications such as ISO accreditation and/or WHO PQ.

PQM also helps MRAs in key regulatory functions, including PMS, in which PQM assistance strengthens capabilities for programming, development and implementation. A particular area of focus in PMS has been assistance for medicines quality monitoring (MQM), which involves collecting medicines samples at sentinel sites or other venues specifically designed in the protocol and their

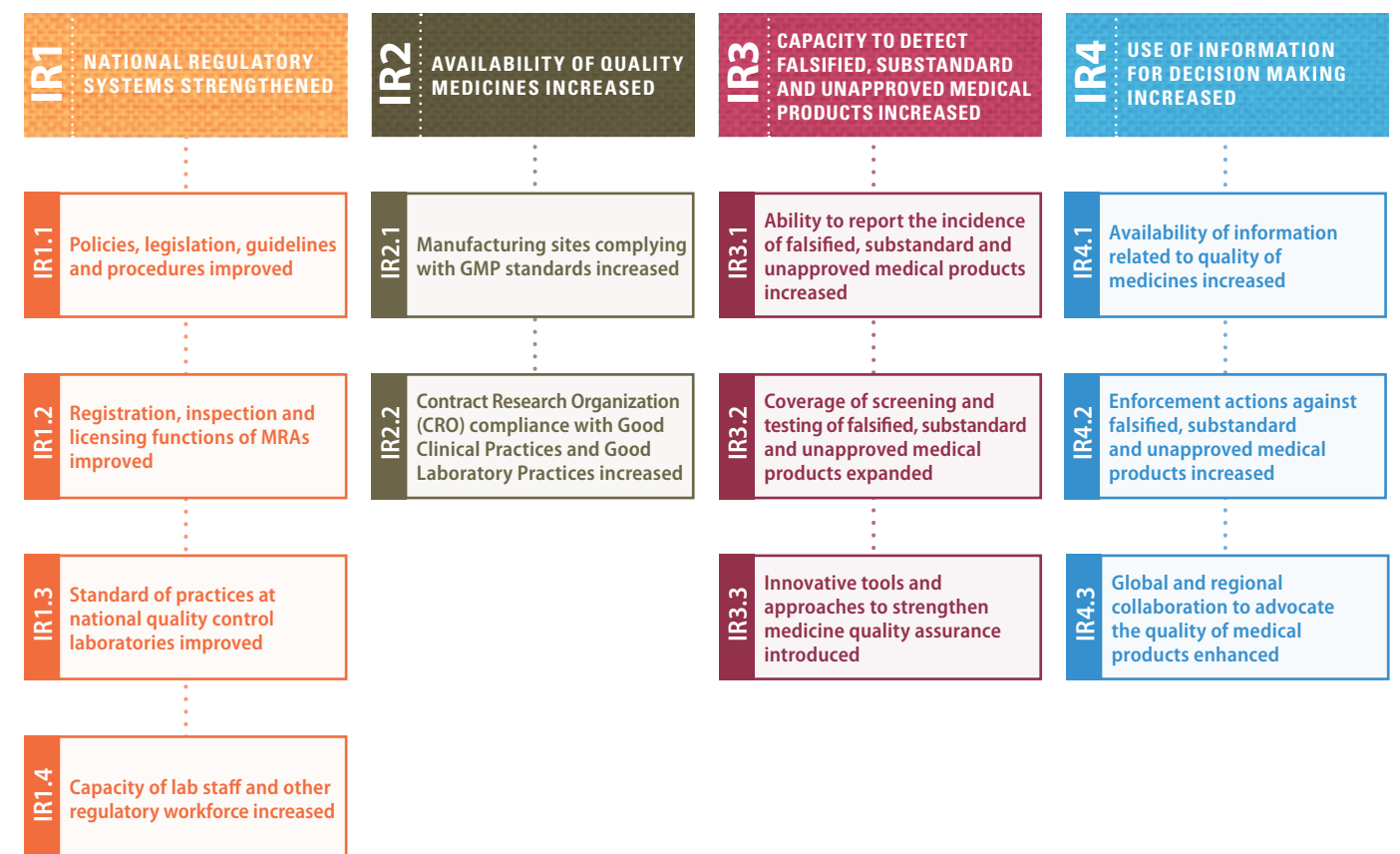
subsequent analysis. In most cases, these samples are initially screened in the field using a Global Pharma Health Fund (GPHF)-Minilab™ and afterward some of them (failing and a subset of passing samples) undergo confirmatory testing in the laboratory utilizing compendial methods.

PQM's systems-based approach also extends to medicines manufacturers. PQM experts in GMP travel to manufacturing sites to help companies improve their GMP compliance and support the development of dossiers for submission to the WHO PQ program.

This report presents highlights of PQM activities organized by Intermediate Result area for the FY16 period.

PQM GOAL

PHARMACEUTICAL QUALITY SYSTEMS ADVANCED TO SUSTAINABLY SUPPLY QUALITY MEDICINES AND PROTECT PUBLIC HEALTH IN DEVELOPING COUNTRIES



PROGRESS BY RESULT AREA



IR1 NATIONAL REGULATORY SYSTEMS STRENGTHENED

Strong MRAs are able to protect a country's population from poor-quality medicines and conversely provide the public access to quality assured medicines. PQM strengthens the capacity of MRAs to ensure the quality of medicines both produced and imported into a country. PQM works with MRAs to build strong internal structures, supports MRAs to register and license medicines to the market and builds the competency of the MRA and supporting NQCL to detect substandard medicines.

1.1 POLICIES, LEGISLATION, GUIDELINES AND PROCEDURES IMPROVED

Comprehensive and effective policies are fundamental to ensuring a well-functioning MRA, a vital part of a country's overall health system. PQM offers technical assistance to countries to develop effective and appropriate policies and regulations, from a national pharmaceutical law that outlines the mandate of the MRA to supporting the MRA in developing regulations and guidelines and adopting

accepted international standards of good regulatory practices. In FY16, PQM supported MRAs to develop 528 new procedures/guidelines, which establish basic laboratory standards in 16 countries (see Figure 1).

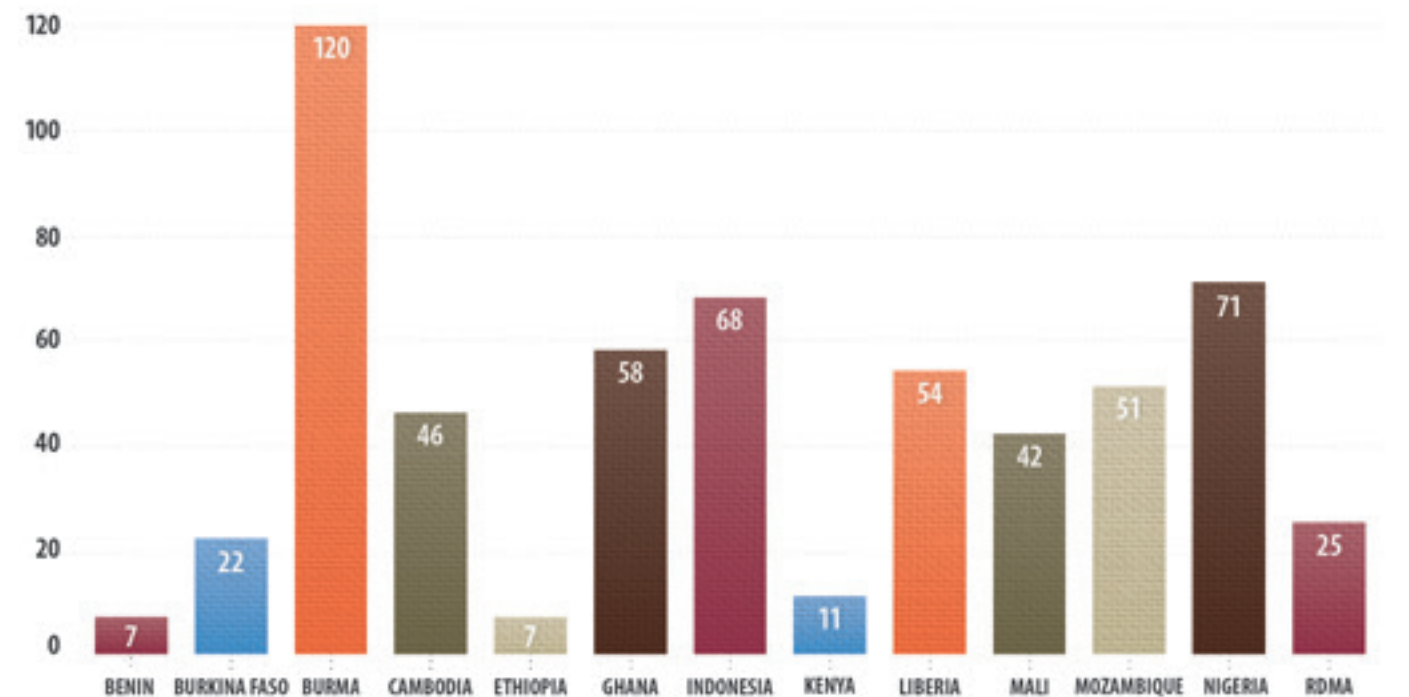
In Nigeria and Indonesia, PQM supported national-level quality assurance policies. Following PQM's technical assistance and advocacy efforts to develop Nigeria's Quality Assurance Policy, it was officially adopted by the Nigerian government in FY16. PQM is now working on supporting its implementation. The national-level policy establishes quality assurance and quality control regulations for all medical products along various points of the supply chain. Similarly, in Indonesia, a national-level regulation (called Menkes 33/2016) was adopted this year. During the third quarter, PQM conducted two seminational workshops convening officials from the Ministry of Health (MOH) and MRA for extensive discussion on additional provisions to strengthen quality assurance and PMS components of the regulation. Based on the outcome of these two workshops, during the fourth quarter, Menkes 2/2016 was revised to Menkes 33/2016, which now includes the additional quality assurance provisions.

In Mozambique and Guinea, PQM provided technical assistance in the form of reviewing and making suggestions to revise the national pharmaceutical law to be both comprehensive and actionable. In Mozambique, with PQM support the government established a technical working group with key stakeholders to develop appropriate and practical regulations that detail roles and responsibilities. In Guinea, PQM conducted two workshops in collaboration with the MOH to incorporate key provisions related to medicine and product registration, inspection, clinical trials and conflicts of interest.

In Bangladesh, the Philippines, Senegal and Ethiopia, PQM assisted respective regulatory authorities to establish, define, redefine and execute their regulatory mandate to competently regulate pharmaceutical products from pre- to postmarket. PQM began its first in-country activity in Bangladesh by conducting a gap analysis to determine the needs for capacity strengthening of the country's medicines

regulatory capacity. The findings of the gap assessment, as described in a technical report, are the basis for the Directorate's Annual Strategic Plan and the National Health Sector Plan (2016–2020). PQM provided technical assistance to the Philippine Food and Drug Administration to develop its five-year strategic plan (2017–2021) through the creation of terms of reference with specific competencies. The strategic priorities for strengthening the administration include reducing the time of processing registration applications and attaining a zero backlog, as well as strengthening administrative and regulatory actions. PQM worked with the Senegalese Directorate of Pharmacy and Drugs to incorporate critical elements into a draft five-year strategic plan, recommending the creation of an inspection department, the recruitment of qualified personnel, a list of training needs (GMP, dossier evaluation) and the creation of an efficient medicine registration system. PQM Ethiopia supported the MOI and MOH in the integration of the GMP roadmap into the National Plan of Action for Pharmaceutical

FIGURE 1: NUMBER OF PROCEDURES/GUIDELINES DEVELOPED OR UPDATED AND SUBMITTED FOR ADOPTION



ENSURING MEDICINE QUALITY AT THE HIGHEST LEVELS—PQM'S CONTRIBUTION TO NATIONAL-LEVEL PHARMACEUTICAL POLICY IN INDONESIA AND NIGERIA

MENKES 33/2016 IN INDONESIA



Chris Raymond, Chief of Party, PQM Indonesia Field Office

The Menkes 33/2016 regulation is one of PQM's greatest achievements in Indonesia to date in terms of the policy's importance, reach and longevity. PQM contributed to the revision through advocacy and technical assistance efforts. Throughout the year, PQM supported the revision of the regulation ('Menkes' in the Bahasa language), which was formally adopted this year. The revision incorporates stronger medicines quality assurance components that the previous regulation lacked. Menkes 33/2016 ensures

proper coordination between the ministry of health and regulatory authority on medicines that are tested through post-marketing surveillance.

The revision was signed into action to include important medicines quality assurance provisions. Specifically:

1. The regulatory authority national postmarketing surveillance sampling strategy must be revised to include recommendations from the ministry of health based on priority public program medicines.
2. Data from the regulatory authority's postmarketing surveillance medicines quality test results must be shared with the Ministry of Health within 10 days for the relevant programs and routinely every three months.

QUALITY ASSURANCE POLICY IN NIGERIA



Chimezie Anyakora, Chief of Party, PQM Nigeria Field Office

PQM provided continuous support in the development and implementation of the Nigerian Quality Assurance Policy. The document is a key national-level policy that establishes quality assurance and quality control regulations for all medical products along various points of the supply chain, thereby securing the supply chain from falsified and substandard medicines. Ultimately, the policy improves the management of critical diseases such as malaria, HIV/AIDS, tuberculosis and neglected tropical diseases.

In the second quarter, the policy was officially adopted by Nigeria's National Council of Health at its annual meeting. The council then recommended sensitization of the policy to six of Nigeria's states. As part of these efforts, PQM was tasked with developing a set of practical guidelines to capture the salient points of the policy as well as developing supporting standard operating procedures. PQM completed the guidelines and standard operating procedures, which were returned to the Ministry of Health for implementation. In the third and fourth quarters, PQM continued its support of the policy's rollout through technical assistance to the Ministry of Health's Food and Drugs Unit, the body responsible for overseeing the policy's implementation and monitoring. PQM is currently developing a robust M&E system in order to track the implementation.

Manufacturing Development in Ethiopia (2015–2025). PQM is a member of the national steering committee and technical working group for the implementation of the national plan and revitalization of the roadmap. PQM provided significant support to the MRA in the development and revision of key regulatory guidelines, policies and procedures.

In Mali, PQM organized a roundtable to engage key local quality assessment partners to identify priority areas of focus in the development of the NQCL's five-year strategic plan based on the roadmap developed previously by PQM.

In FY16, WHO requested comments on several guidance documents, and PQM provided comments on the guidance documents for good manufacturing practices, good regulatory practices and good pharmacopeial practices. Additionally, PQM contributed to the WHO guidance document on Model Regulatory Framework for Medical Devices.

1.2 REGISTRATION, INSPECTION AND LICENSING FUNCTIONS OF MRAs IMPROVED

In Thailand, Guinea and Pakistan, PQM worked to establish and further improve the function of registration systems,

which enhance the ability of countries to process marketing authorizations and thus ensure the medicines available in the country are of high quality.

PQM advocated for and provided technical inputs to the Thai Ministry of Public Health for the development of the country National Malaria Elimination Strategy (2017–2026) and for its Operational Plan (2017–2026) in order to incorporate into the document inspection of medicine supply and distribution as well as drug quality monitoring. PQM evaluated the Guinean regulatory authority's existing registration system, and enhanced its capacity for information management to support medicines marketing authorization and certificates of analysis. In Pakistan, PQM, in collaboration with the Pakistani Drug Regulatory Authority and WHO's Country Office, conducted a two-day workshop to collectively identify areas for improvement on registration processes and practices. The output of the workshop was a draft roadmap for the Division of Pharmaceutical Evaluation and Registration to improve its registration system. In the roadmap, the short-term objective includes developing data standards to partially automate the registration system and, as a long-term objective, to develop an integrated regulatory information management system that will connect all key registration processes.

2 years
↓
4.5 months

By the end of FY16, the Ethiopian Authority, in collaboration with Jimma University, was able to evaluate 467 dossiers, entirely clearing the backlog of new medicine applications (dossiers). These dossiers allow new medicines to register and thus enter the market. Additionally, lead time for fast-track medicine applications decreased from an average of two years to 4.5 months. These so-called fast-track applications are reserved for medicines that address critical unmet health needs including those to treat malaria, tuberculosis (TB) and HIV/AIDS.

Trainings on inspection in Burma and Pakistan developed the skills of inspectors to competently assess various aspects related to this regulatory function. In Burma (also known as Myanmar), PQM facilitated a three-day national training workshop on inspection of pharmaceutical distribution chains, targeted to inspectors representing each state. Following the training, a regional training of trainers was organized in Laos for inspectorates from seven countries in Southeast Asia. In Pakistan, trainings were held on good sampling practice and PMS for federal drug inspectors. Additionally, heating, ventilation and air-conditioning (HVAC) GMP standards were provided for Licensing Division staff.

1.3 STANDARD OF PRACTICES AT NATIONAL QUALITY CONTROL LABORATORIES IMPROVED

PQM builds the capacity of NQCLs to improve the laboratories' standards of operation. Depending on the objectives of the laboratory, raising its standards may help it attain compliance with internationally recognized standards and consequently apply for and attain the corresponding certifications, such as ISO/International Electrotechnical Commission (IEC) 17025:2005 accreditation and/or WHO PQ. ISO accreditation signifies that a laboratory is technically proficient to produce consistently valid test results, which regulatory authorities and medicines manufacturers must rely.

In FY16, NQCLs in Nigeria, Kenya and Ghana successfully maintained ISO accreditation by demonstrating continued technical competence. The maintenance of the Nigerian NQCL's accreditation in Yaba resulted in an agreement with the Global Fund (GF) and Society for Family Health to test medicine samples at the lab, which will help the lab generate income to support sustainability. Additionally, the accreditation has significantly reduced the cost incurred by sending samples abroad, as was the practice prior to the initial accreditation in 2015; this has also resulted in

a significant reduction in the backlog, from over 1,000 samples in 2015 to 200 samples currently. In Kenya, the NQCL initially attained ISO accreditation in 2015; the reaccreditation audit that was conducted in March 2016 unveiled major and minor nonconformities that were due in part to high lab staff turnover. With PQM support, corrective actions were developed, issues were addressed and the lab was successful in maintaining the accreditation. The FDA Laboratory in Ghana maintained its accreditation and expanded its scope to include microbiology and medical devices; PQM supported these efforts through trainings on quality management and key document revision.

At Burma's national QC laboratory, Nay Pyi Taw, PQM provided technical assistance to support the lab's pursuit of ISO accreditation. PQM conducted recalibration and requalification of essential laboratory equipment with hands-on demonstration to the lab analysts. PQM introduced a resource network to identify and compile a pool of qualified service providers located in the region for equipment calibration. This year, Nay Pyi Taw QA staff successfully conducted their first internal audit, completed root cause analysis and developed a corrective and preventive action (CAPA) plan; these are examples of strengthened individual and organizational capacity built on past PQM technical assistance.

Laboratories in Thailand and Vietnam, already ISO accredited, are preparing for upcoming WHO PQ inspections. PQM conducted a five-day assessment of the Pharmaceutical

**1,000 reduced to
200**
THE REDUCTION IN THE BACKLOG
OF SAMPLES WAITING TO BE
TESTED IN THE NIGERIAN NQCL

FIGURE 2: NUMBER OF QC LABORATORIES SUPPORTED TOWARD ISO 17025 ACCREDITATION OR WHO PREQUALIFICATION

Country/Region	Labs
Burkina Faso	1
Burma	1
Cambodia	1
Ethiopia	5
Ghana	1
Guinea	1
Indonesia	14
Kazakhstan	3
Kenya	1
Liberia	1
Mali	1
Mozambique	1
Nigeria	4
Pakistan	2
RDMA	1
Senegal	1
West Bank	1

Technology Service Center Lab of Chulalongkorn University in Thailand to determine the laboratory's progress toward submitting an expression of interest to the WHO PQ program. In Vietnam, PQM conducted a mock audit and verification training in support of the Institute of Drug Quality Control's official WHO PQ inspection.

In Indonesia, following advocacy and advising from PQM and the Indonesia Regulatory Authority, the national accreditation body agreed to revise the accreditation scheme for the national QC lab to expand from product based to method based in line with WHO PQ requirements. Method-based testing will enable the national lab to increase the number of products it can officially test. In addition to the Indonesian lab changing accreditation schemes, PQM also worked throughout the year to prepare the lab toward WHO PQ through the compilation of

laboratory information files, audit preparation, developing procedures for technical operations and providing technical training. Similarly, in Laos, the national QC lab, the Food and Drug Quality Control Center, sought to shift from product-based to method-based accreditation. PQM supported these efforts through proposing corrective actions related to internal policy and procedural conformances uncovered during the second quarter. The Laos lab anticipates submission of an application to an international body in 2017 for method-based accreditation.

In West Bank/Gaza, following PQM's guidance on key technical areas identified, the head of the lab recently confirmed that the Tunisian Accreditation Council has been selected by the Ministry of Health to be the ISO 17025 accrediting body to assess the lab in the near future. As an additional means of catalyzing the accreditation process, PQM assisted the lab with joining the Middle East and North Africa Network of Medicines Control Laboratories; the lab will now be able to conduct interlaboratory testing, which will further enhance its prospects for accreditation.

Following a period of remote technical assistance in Liberia due to Ebola, PQM reinitiated in-country activities in 2016. Key activities included a review of the lab standard operating procedures (SOPs), training on the quality management system (QMS) and analytical testing. Technical assistance to the Cambodian National QC Laboratory focused on developing essential documents (quality manual and SOPs) toward attaining compliance with good laboratory practice to meet official ISO regulatory QC laboratory and technical requirements. The Cambodian National QC Lab intends to attain ISO accreditation by late 2017 or early 2018. PQM supported the Burkina Faso Medicines Quality Control Laboratory to develop an implementation plan to strengthen the laboratory's QMS and supported the revision of key SOPs and QMS documents.

AMPLIFYING THE EFFECT OF TECHNICAL ASSISTANCE: SIMULTANEOUS CAPACITY BUILDING IN NIGERIA, BURMA AND KAZAKHSTAN



“Parallel technical assistance is a really efficient and sustainable way to raise standards across multiple laboratories quickly. The success of this strategy really depends on the visiting lab’s ability to implement the TA independently and in a way that fits the needs of their home lab.”

–Donnell Charles, Manager, Laboratory Quality Management, on his work providing parallel technical assistance to Nigeria and Burma

PQM provided simultaneous technical assistance to multiple laboratories in Nigeria, Burma and Kazakhstan in support of attaining compliance with international standards, recognized by either ISO/IEC 17025:2005 accreditation or WHO PQ. In each of these countries, this parallel approach encourages sustainability and is made possible through strong participation on the part of the MRA. The parallel capacity building also works to harmonize medicines quality testing throughout the country.

As PQM provided technical assistance to one laboratory, typically the strongest performing, these countries engaged staff from other laboratories to participate in capacity-building activities, which in turn amplified PQM’s technical assistance as labs worked toward complying with international accreditation requirements. The unique circumstance of each of these countries underscores that the approach is highly replicable given the prerequisite of strong MRA support and participation.

In Nigeria, PQM focused technical assistance on the lab with the strongest capability, Agulu laboratory, while staff from Kaduna lab visited to benefit from the support. At the time of writing in early FY17, Agulu lab successfully attained ISO accreditation and Kaduna is expected to soon follow. In Burma, similar to the approach taken in Nigeria, the most advanced lab, Nay Pyi Taw, was the first to receive PQM’s technical assistance beginning in 2015. At this time, the other two labs, Mandalay and Yangon, began sending their QA and QC managers to build simultaneous capacity. At the time of writing, Nay Pyi Taw also successfully obtained ISO Accreditation.

In Kazakhstan in FY16, PQM performed initial assessments of three NQCLs in Karaganda, Pavlodar and Kostanay to gauge their compliance with WHO PQ and requirements. During assessments of each lab, staff from the other two labs attended to learn from each other’s experience and to facilitate consistent progress across all three laboratories.

1.4 CAPACITY OF LAB STAFF AND OTHER REGULATORY WORKFORCE INCREASED

PQM invests in the development of quality assurance professionals by facilitating trainings that focus on strengthening a wide range of technical and managerial skills. During FY16, PQM facilitated the training of 1,105 individuals from 19 countries on inspection, GMP, PMS, QC and registration (see Figure 3). This investment in training contributes to highly functional MRAs and results in an increased number of regulatory enforcement actions and improvement in the quality of inspections compared with the previous year.

During FY16, PQM continued its training programs to strengthen the technical capacity of laboratory analytical staff and management as part of its overall strategy to support the MRA’s function. Technical trainings to ensure compliance with international standards of practice are an integral component of the overall targets, for quality control labs at the national and provincial levels.

In FY16, PQM Indonesia reached all 32 provincial and two national QC labs through a combination of national-level trainings (cost shared between the MRA and USAID), as well as intensive technical assistance (TA) and training provided to seven provincial labs. In addition to a \$1 million equipment grant provided by the Global Fund to support NQCL laboratories for TB medicines testing, PQM provided calibration services for 40 high-performance liquid chromatography (HPLC) units and spectrophotometers at various laboratories as part of its package of technical assistance during FY16.

Fourteen national and provincial Indonesian QC laboratories were selected to participate in USP’s Inter-Laboratory Testing (ILT) program during FY16. These 14 laboratories represent roughly 50% of all the QC laboratories currently operated by the government in Indonesia. Under this program,

laboratories tested standardized samples provided by PQM to gather preliminary information on the testing and reporting capabilities of the central and provincial QC laboratories throughout the MRA system. All laboratories successfully completed the ILT program, their reports were collated and their data were reviewed by PQM; subsequently, feedback was sent back to the laboratories. Through this program, labs are exposed to standardized reporting requirements, and the review and feedback provided serves for performance improvement. Labs that have ISO accreditation are required to participate in this type of program to maintain their accreditation.

“ PQM FACILITATED THE TRAINING OF 1,105 INDIVIDUALS FROM 19 COUNTRIES ”

PQM supported four Indonesian MRA staff to participate in a global workshop convened by PQM in Dubai titled “Ensuring the Quality of Anti-TB Medicines—Contributing Toward Ending the TB Epidemic” to bring manufacturers and regulators together to discuss the current approaches in TB treatment and global needs for medicines procurement, quality, etc. The MRA officers who attended are expected to hold a transfer of knowledge dissemination workshop for their colleagues, as well as deliver a larger dissemination workshop to National TB Program staff to ensure harmonization of information during FY17. Indonesian MRA staff and industry members also participated in the training on “Validation and Part 11 Compliance of Computer Systems and Data” to comply with MRA requirements to ensure data integrity, security and availability. Subsequent to the training, PQM sponsored dissemination events at its home institutions to ensure that the knowledge would be shared with colleagues and to build institutional capacity.

As part of an ongoing effort to increase and sustain host country capacity beyond the technical support provided by PQM in Liberia, the QC manager of the NQCL traveled to USP's Rockville laboratory as a visiting scientist and was trained in QC and QA of medicines. He received training on Good Laboratory Practices (GLP), Good Documentation Practices (GDP), calibration of dissolution tests and HPLC. The purpose of the training was to build the lab's capacity to detect substandard medicines in the country in order to sustainably protect the health of the population. Upon returning to Liberia, the QC manager shared his newly acquired knowledge and skills with his laboratory colleagues as an ongoing sustainable training activity.

During FY16, PQM implemented several activities designed to increase the Guinean NQCL's capacity. As an example, PQM installed several pieces of equipment donated by USP, including an HPLC system to conduct assays, which

are compendial methods for determining the identity and quantity of active pharmaceutical ingredients (APIs) in medicines. Results obtained with compendial methods can be used as evidence to support regulatory actions. PQM also provided training for 16 technical lab staff on the proper use of the HPLC system, and a review of GLP and GDP. As another capacity-building measure, PQM supervised a refresher Minilab™ training that was conducted by Guinean NQCL staff.

In Pakistan, laboratory trainings were held on good practices for pharmaceutical quality control and laboratory management for laboratory managers and senior analysts. In parallel, PQM also conducted training on GMP inspection for MRA inspectorates at the federal and provincial levels. Training courses on chlorhexidine (CHX) quality testing and the ILT program have been initiated for federal and provincial QC labs and interested manufacturers. In conjunction with this ILT training, sampling methodologies



DR. YANGA DIJIBA (CENTER) BRIEFING THE BURMESE LABORATORY TEAM ON THE MECHANICAL CALIBRATION TOOL KIT FOR DISSOLUTION TESTING

and techniques were developed for imported chlorhexidine gel products. After receiving the trainings, trainees repeated them for other colleagues at central and provincial inspectorates. During the fourth quarter, PQM conducted the first four-day training of trainers utilizing the country's local resources for the MRA's inspectorate staff. This training focused on HVAC design, qualification and validation to increase capacity and improve compliance for international GMP approval and inspection of HVAC systems. The Pakistani MRA is currently developing a guideline based on the training, the country's first HVAC guideline related to GMP.

To support PMS of medicines in Angola and Burkina Faso, PQM provided Minilab™ training to key staff from the Ministry of Health, MRAs and the National Malaria Control Program, to build the countries' QC capabilities for testing medicines in their markets. Strengthening the capacity of the personnel working at the central level will enable them to then train personnel at various regional levels.

In Burma, PQM conducted trainings on eight analytical tests required for accreditation to analysts from three NQCLs. The knowledge and expertise on all eight scopes of accreditation were enhanced. The PQM team found out that the MRA in Burma Nay Pyi Taw Laboratory had procured a Liquid

Chromatography–Mass Spectrometry system that had never been used due to lack of proper training of analysts. The PQM team provided hands-on training and basic procedures of the machine that will allow analysts to start using the equipment.

In Cambodia, PQM was able to leverage funds from the WHO Country Office to deliver a two-key modules training workshop for 47 analysts at the NQCL. The topic of the first module was ISO/IEC 17025 accreditation and WHO PQ and the second one addressed WHO good practices for pharmaceutical quality control laboratories.

In Mozambique, following several trainings provided by PQM to strengthen the medicine quality system, the NQCL participated in an ISO-accredited proficiency study for the first time. The result of the testing is still pending and, once finalized, will enable comparison of the lab proficiency to other QC laboratories globally. Participation and passing this international proficiency testing will attest to the capability of the lab to perform QC testing and ensure the quality of medicines in the country. To continue maintaining GLP, PQM contracted an ISO 17025-accredited calibration body to calibrate key equipment. Proper calibration and maintenance of the equipment are requisites that, together with staff technical capacity, will help ensure the quality of results produced by the lab.

FIGURE 3: NUMBER OF INDIVIDUALS WHO HAVE SUCCESSFULLY COMPLETED TRAINING

Country	# Male	# Female	Training Type
Angola	18	15	PMS
Benin	6	4	PMS
Burkina Faso	6	11	PMS
Burma	7	53	QC
Cambodia	6	5	QC
Ethiopia	79	24	30 on registration; 22 on inspection; 27 on PMS; 24 on GMP
Guinea	22	4	QC
Indonesia	32	182	179 on QC; 35 on GMP
Liberia	13	2	PMS
Mozambique	7	13	QC
Nigeria	275	183	48 on PMS; 302 on QC; 108 on GMP
Pakistan	46	15	23 on Inspection; 38 on QC
Philippines	2	3	Inspection
RDMA	8	12	QC
Rockville, MD	21	12	GMP
West Bank	2	17	GMP

IR2 | AVAILABILITY OF QUALITY MEDICINES INCREASED

PQM GMP specialists travel to manufacturing sites in order to help companies improve their compliance with international GMP standards and support development of dossiers for submission to the WHO PQ of Medicines Program for certification. Medicines having WHO PQ and/or approval by stringent regulatory authorities are known to meet acceptable standards of quality, safety and efficacy. WHO's list of prequalified medicines is used by procurement agencies and countries to guide their bulk purchasing of essential medicines.

The goal of PQM's work in this area is to increase the supply of locally produced, quality assured medicines, targeting USAID priority health programs. PQM helps increase access to a steady supply of essential medicines of assured quality, safety and efficacy, thus improving local health systems. Technical assistance is provided throughout the application process for WHO PQ, Stringent Regulatory Authority or local National Regulatory Authority approval, from the early stages of the process to the final submission of the application or dossier.

2.1 MANUFACTURING SITES COMPLYING WITH GMP STANDARDS INCREASED

Overall in 2016, PQM worked with nine Core and country programs to provide TA to 51 manufacturers (see Figure 4).

PQM's interventions for increasing the availability of quality assured TB medicines have yielded significant results in FY16. The ability of PQM's technical assistance to be effective and dynamic allows shortages in priority medicines to be thwarted in a timely manner, and in this respect, PQM plays a pivotal role in bridging gaps in manufacturers' capacity in order to meet global health needs.

During the year, the PQM Core TB team provided high-quality technical assistance to manufacturers in support of WHO PQ or other stringent regulatory authority approval of anti-TB medicines. The priority medicines for PQM's support were kanamycin, rifampicin, clofazimine, gatifloxacin, moxifloxacin and rifapentine. The priority medicines for PQM support were identified in close collaboration with the USAID TB team and Global Drug Facility.

KANAMYCIN—INCREASING THE SUPPLY OF THE LIFE-SAVING ANTI-TB MEDICATION



FIGURE 4: PQM TECHNICAL ASSISTANCE TO MANUFACTURERS IN 2016

Countries/Core Programs	# of Manufacturers Received Technical Assistance	Types of Medicine
Core MNCH	6	Magnesium sulfate injection, amoxicillin dispersible tablets, chlorhexidine gel, oxytocin injection
Core NTDs	5	Praziquantel API, praziquantel FPP, albendazole API
Core TB	9	Clofazimine API, clofazimine FPP, linezolid FPP, gatifloxacin API, gatifloxacin FPP, rifampicin API, rifapentine API, rifapentine FPP, kanamycin API
Ethiopia	8	Ethambutole, ciprofloxacin, zinc sulfate, doxycyclin, chlorhexidine
Indonesia	5	Fixed-dose combination (FDC) antiretroviral, 2 FDC, 4 FDC TB, levofloxacin 500 mg
Kazakhstan	1	Levofloxacin, moxifloxacin
Nigeria	11	Zinc/oral rehydration solution, chlorhexidine, amoxicillin, magnesium sulfate, arthemether lumefetrine, pharमतex-artemether lumefetrine, ready-to-use therapeutic foods
Pakistan	4	Chlorhexidine
West Bank	2	Ranitidine

Despite success in the global fight against the tuberculosis epidemic; TB remains a serious public health threat. In 2015 alone, there were an estimated 10.4 million new TB cases worldwide (2016 WHO Factsheet). Most TB cases can be treated with first-line medicines. However, bacteria that cause TB can become resistant to first-line medicines; this causes a condition known as multidrug-resistant TB (MDR-TB). For individual patients, this form of TB means longer, less effective and more expensive treatment. Because patients are infected for prolonged periods, the general public and healthcare workers also face a higher rate of transmission. In 2015, WHO estimated that of the 480,000 people eligible for MDR-TB treatment, only 125,000 (20%) were enrolled in treatment. Therefore, supply and increased access to quality assured second-line medicines, which are used for treatment of MDR-TB is a high priority.

Kanamycin is one of the key second-line medicines used for treatment of MDR-TB. In order to increase the

availability of high-quality kanamycin, during the second quarter of FY16, PQM negotiated the purchasing price with manufacturers based on the costs incurred by the producer in exchange for technical assistance. This intervention had two significant results: The price of quality assured kanamycin fell, becoming available in liquid form to the WHO's procurement mechanism, the Global Drug Facility, for the first time for widespread distribution. The price of 1-g kanamycin solution made available through PQM's intervention is 73% less than the same product from other suppliers (\$0.63 per unit vs. \$2.36 per unit). In addition to the drop in price, the intervention set the lowest price benchmark for 0.5-g and 1-g kanamycin injection solutions on the global public health market, which is expected to drive down the price of kanamycin produced by other manufacturers as well. Ultimately this will allow donors and national TB programs to save millions in public health funding.

Major accomplishments were made for kanamycin finished pharmaceutical product (FPP) and rifampicin API. As a result of PQM's technical assistance, manufacturers were approved by the expert review panel (ERP) and WHO PQ for both products. ERP is composed of a group of independent experts who assess finished pharmaceutical products and make recommendations accordingly to the Global Fund for procurement decisions. With the ERP approval of kanamycin, the problem of potential shortage of this important medicine used for treatment of MDR-TB was addressed. The lower benchmark price for this product also was set.

In 2016, the WHO recommended shortened regimens for treatment of MDR-TB that improve patient outcomes, and reduce the treatment time as well as the cost. Given the benefit of the shortened MDR-TB treatment regimens, it is likely that many MDR-TB-affected countries will implement and expand their use. PQM worked to ensure that the supply of the medicines included in the shorter regimens meets the expected increase in demand. Currently, there is only one supplier of quality assured clofazimine, an MDR-TB shortened regimen medication. PQM identified, engaged and provided technical assistance to one of the manufacturers to develop the API and FPP for clofazimine. It is anticipated that in FY17, clofazimine, an essential medicine that is in dire shortage globally, will be brought to market.

Gatifloxacin is another MDR-TB shortened regimen medication. However, presently, there is no internationally quality assured gatifloxacin on the market. During FY16, PQM worked to identify manufacturers of gatifloxacin API and FPP that have potential for WHO PQ with PQM's support. As a result of information gathering and evaluation, one manufacturer of API and one manufacturer of FPP were identified, and technical assistance has begun.

Similarly, there is currently only one manufacturer prequalified by WHO for moxifloxacin API. Sources of rifapentine API and FPP, recommended by WHO for treatment of latent TB infection are in short supply globally. PQM worked to address these shortages by identifying potential manufacturers for both products, and various forms of technical assistance are underway with these manufacturers.

Neglected tropical diseases (NTDs) disproportionately affect poor populations, and as a result, medicines to treat NTDs are often challenging to attract manufacturers to invest in making quality assured products. To address this challenge, the PQM Core NTD program works to provide technical assistance toward WHO PQ or other stringent regulatory approval to increase the supply of these quality assured life-saving medicines. In FY16, manufacturers were engaged for two priority NTD medicines: praziquantel and albendazole, both of which treat parasitic infections. Some manufacturers received technical assistance on dossier (application to WHO PQ) and GMP inspection of manufacturing activities. Others were assisted in product development studies including technical assistance toward bioequivalence studies; bioequivalence is required in order to make affordable generic medicines. Mock inspections of manufacturing facilities and corrective action implementation feedback were also provided as part of the technical assistance. The PQM Core NTD team collaborated with other global partners invested in working toward increasing the availability of NTD medicines, including the WHO PQ team, WHO NTD and the Bill and Melinda Gates Foundation.

Maternal, newborn and child health (MNCH) are also priorities for the PQM program. The PQM Core MNCH team similarly works to increase the availability of quality assured products for mothers, infants and children through its work with manufacturers and the global health community. In FY16, PQM provided technical assistance to manufacturers of magnesium sulfate, oxytocin and amoxicillin in support of WHO PQ and to support local production. Magnesium sulfate injection is used to treat eclampsia and pre-eclampsia in pregnant women, conditions that involve increasingly high blood pressure during the second half of pregnancy. Oxytocin is a medication to control excessive bleeding after childbirth. Amoxicillin dispersible tablets are used to treat infections in children and are also used in the new WHO shortened regime to treat clinical severe infection in newborns.

In FY16, PQM successfully facilitated a Kenyan pharmaceutical manufacturer to register its chlorhexidine gel (7.1%) product with the Kenya Pharmacy & Poisons Board. This step will allow chlorhexidine, a vital newborn health product that treats umbilical cord infection, to become available in

the country's market. Also, in response to incidents of accidental misuse of chlorhexidine solution due to confusing packaging in 2015, PQM reviewed proposed changes to a manufacturer's cap and stopper for the product in FY16. The proposed changes are aimed at helping to prevent future misuse of the product.

PQM also worked with two manufacturers to facilitate dossier submission for chlorhexidine gel, zinc sulfate tablets and oral rehydration solutions to the East African Community (EAC) for approval and subsequent availability in countries of the EAC region.

Vitamin A deficiency is a public health problem that can cause blindness and increase the risk of infections. High-dose vitamin A supplementation is recommended in infants and children as a solution to the deficiency. In support of the United Nations Children's Fund's global efforts, and to ensure high-quality products are provided to this population, PQM analyzed samples representing 9,640 doses and 13,635 doses of 100,000 and 200,000 international units vitamin A medicines, respectively. Every batch was found to be of good quality.

SUPPORTING MNCH IN NIGERIA: LOCALLY SOURCED QUALITY ASSURED ESSENTIAL MEDICINES NOW WIDELY AVAILABLE



In Nigeria, PQM supported MNCH by providing technical assistance to Nigerian manufacturers that produce oral rehydration salts, zinc sulfate tablets and chlorhexidine digluconate gel, considered priority commodities according to the United Nations Commission on Life-Saving Commodities for Women and Children. These manufacturers, in turn, provided these quality assured essential medicines not only to the market but also to 10 health organizations for interventions across Nigeria as well as in other African countries. The supply of locally produced quality assured MNCH

medicines increased through technical assistance to 12 local manufacturers to improve compliance with international and national GMP standards. As a result, PQM-supported local manufacturer Chi Pharmaceuticals was selected by the United Nations Children's Fund to procure zinc/oral rehydration salts to four countries, with orders expected to supply additional African countries as well. Two public health organizations, the Society for Family Health and Crown Agents, also procured 337,840 zinc/oral rehydration salt packs from Chi Pharmaceuticals for public health interventions in Nigeria. PQM supported Chi to submit a dossier for zinc dispersible tablets, an essential micronutrient, to WHO and currently awaits the outcome from WHO PQ for the product. Another local manufacturer, Drugfield Pharmaceuticals, was chosen by four public health organizations to procure chlorhexidine throughout Nigeria and also selected by three public health organizations to implement public health interventions across Africa.



In addition to the contributions made by PQM's Core programs, PQM country-level interventions in Ethiopia, Indonesia, Nigeria, Pakistan, the Philippines and West/Bank Gaza also made significant contributions toward increasing GMP standards and, ultimately, increasing the supply of quality assured essential medicines.

In Ethiopia, 56 foreign and four local GMP inspections were conducted by the MRA with support from PQM. This is a significant increase from FY15 during which no GMP inspections were conducted due to GMP inspector reassignment to clearing registration backlogs. In FY16, PQM proposed separating this dual responsibility (registration and GMP inspection) while the registration backlog was simultaneously addressed through resourceful collaboration with Jimma University. Through PQM's continued technical support and capacity-building activities, GMP compliance of four local manufacturers has shown improvement. Ethiopia's MRA issued national certification of compliance to four local manufacturers supported by PQM. PQM's technical support, through mock assessment and continuous follow-ups to local manufacturers in Ethiopia, has enabled one manufacturer to submit a tuberculosis medication dossier, Ethambutol 400 mg tablet, to the WHO PQ program. PQM

provided extensive technical support to this manufacturer, which received WHO acceptance for full review. In addition, the manufacturer's bioequivalence and dissolution profile data for the product were also accepted.

In Indonesia, FY16 saw improvement in GMP compliance of local TB and HIV medicines manufacturers as well as progress made by manufacturers toward WHO PQ. The GMP-related activities during FY16 included a number of follow-up facility visits and on-site trainings for manufacturers, including the inception of a new technical assistance strategy to support the training of QC laboratory staff at the manufacturers on GLP and relevant topics as identified. Thus, for FY17, technical assistance will incorporate aspects of GLP training for QC labs in addition to overall GMP support. As quality control data integrity becomes an important assessment component during WHO audits for prequalification, it is important for the manufacturers to have a solid system in place for complying with WHO recommendations for the QC laboratories in addition to the overall GMP aspects of manufacture.

Follow-up GMP site visits were conducted by PQM to PT Phapros (state-owned manufacturer), Zenith Pharmaceutical Laboratories in Semarang, Sanbe Farma/Caprifarmindo

in Bandung, and Kalbe Farma in Cikarang near Jakarta. Highlights include progress made toward dossier submission for two manufacturers that plan to submit product dossiers for Levofloxacin 500 mg tablet in 2017.

“ PQM COUNTRY-LEVEL INTERVENTIONS MADE SIGNIFICANT CONTRIBUTIONS TOWARD INCREASING GMP STANDARDS ”

In Pakistan, PQM conducted assessments of two local manufacturers to support the production and availability of quality assured chlorhexidine digluconate gel 7.1% to treat newborn umbilical cord infection. The assessments were used as a basis for developing a roadmap for the manufacturers to work toward obtaining international accreditation. PQM will continue to support the manufacturers through technical assistance on product formulation, production, and registration. Each of the companies has been working, to varying degrees of progress, toward completing the CHX gel formulation, lab-scale production and conducting stability studies as required by the Pakistani MRA for fast-track registration. Stability study sessions were performed in Karachi and Lahore with technical personnel from the manufacturers going over Pakistan MRA's requirements for stability data analyses of CHX gel. PQM was able to facilitate the evaluation of the submitted dossiers by the Pharmaceutical Evaluation Cell of the MRA and establish a technical evaluation committee by the Drug Registration Board to perform on-site verification of stability data. These guidelines will help to ensure that adequately conducted stability studies provide the evidence for the establishment of the storage conditions and shelf life of products, including CHX gel.

PQM's technical assistance in the Philippines focused primarily on dossier evaluation and CAPA follow-ups. The PQM GMP team visited Hizon Laboratories to follow up on a 2015 assessment conducted by WHO PQ for Levofloxacin, an anti-TB medicine; the trip resulted in a review of CAPA

and the development of a strategic plan on steps toward WHO PQ. The PQM GMP team also conducted a GMP mock audit and dossier review with one manufacturer to review the CAPA plan for the deficiencies observed during the first WHO audit in 2015. PQM also facilitated a key meeting with the Philippine's MRA regulatory officers and the Department of Health/National TB Program to discuss a fast-track registration process and procedures for anti-TB medicines provided through the Global Drug Facility to the National TB Program.

In West Bank/Gaza, one of the greatest challenges for local manufacturing is the lack of capacity to comply with international GMP standards. Once determined to be GMP compliant, the manufacturers are able to market their products overseas. To that end, during FY16, PQM staff and consultants conducted GMP audits of four Palestinian firms: Beit Jala Pharmaceutical Company, Birzeit Pharmaceutical Company, Pharmacare PLC and Jerusalem Pharmaceutical Company. Several of the companies had major deficiencies, though none had any critical deficiencies. The manufacturers began preparing detailed CAPA plans that PQM will review. PQM also conducted a GMP workshop for inspectorate and registration staff from the Palestinian authority focusing on GMP guidelines determined by a standards-setting and working group called the Pharmaceutical Inspection Co-operation Scheme (PIC/S). Potentially, the Palestinian authority's MRA membership of PIC/S will facilitate local manufacturers' access to the international market due to improved GMP compliance.

2.2 CONTRACT RESEARCH ORGANIZATION (CRO) COMPLIANCE WITH GOOD CLINICAL PRACTICES AND GOOD LABORATORY PRACTICES INCREASED

CROs support the pharmaceutical sector by offering research services, such as clinical trials, on a contract basis. Staff from three Indonesian CROs participated in a training, which guided the CROs through the complete equipment qualification, calibration and computer system validation processes from planning to reporting. PQM Indonesia sponsored dissemination events at its home institutions to ensure that the knowledge would be shared with colleagues and to build institutional capacity.



PQM works to combat falsified and substandard medicines by collaborating with local medicines regulatory authorities and national health programs. PQM establishes and enhances PMS systems that encompass an array of activities related to ensuring the quality of medicines circulating in markets and is an important part of overall pharmacovigilance. MQM is a subset of PMS and involves the testing of medicines that are already present in the market. PQM supports MRAs to assess existing quality control systems by selecting sites to monitor based on criteria such as epidemiology, geography, border region and history of trafficking fake medicines. This also includes training field staff in sampling, testing with Minilab™ methods and data reporting, as well as training medicine control laboratory staff in advanced test methods.

3.1 ABILITY TO REPORT THE INCIDENCE OF FALSIFIED, SUBSTANDARD AND UNAPPROVED MEDICAL PRODUCTS INCREASED

PQM assists countries in implementing MQM programs where little capacity exists, and works to enhance existing MQM systems through a wide range of activities, including providing supplies, conducting trainings on use of technologies and inspection processes, strategic planning, strengthening implementation and conducting studies to inform overall medicine quality and PMS approaches. Figure 5 depicts the countries and regional programs that

cumulatively tested 4,501 samples in FY16 through the support of PQM. Regulatory actions against poor-quality medicines in Ghana, Nigeria, Benin and Liberia this year echo the importance of medicine quality monitoring and its impact on overall public health outcomes.

In order to combat falsified and substandard medicines in Ghana, PQM supported the collection of antimalarial and analgesic samples from seven sentinel sites, of which several medicines failed testing. Following these test results, the Ghanaian MRA ordered a recall of all affected batches from the market. Likewise, in Nigeria PQM provided technical support to the MRA's PMS unit to conduct MQM sampling exercises in six geopolitical zones. Technical refresher training on Minilab™ was provided and a sampling protocol was jointly developed to build the capacity of the unit. Data from the surveys showed the presence of poor-quality antimalarial and MNCH medicines. With PQM's technical advice, the Nigerian MRA PMS directorate has put a hold on any further distribution of the affected drugs, conducted a medicine mop-up exercise at various locations and will commence possible prosecution. In Benin, antimalarial samples were collected and tested, and of those that did not comply with quality specifications, several lacked the API. With PQM's technical support, the NQCL submitted an official letter to the regulatory authority requesting regulatory actions on the noncompliant products.

Having medicines quality information is essential in order to increase the ability of local partners to improve on MQM

systems over time. This year PQM, in partnership with local authorities, gathered preliminary information related to the quality of antimalarial medicines in Amazon Malaria Initiative (AMI) countries as well as Burkina Faso. The process and results will help PQM institute good practices for conducting quality monitoring activities with local authorities and ultimately help establish strong PMS programs embedded within national systems.

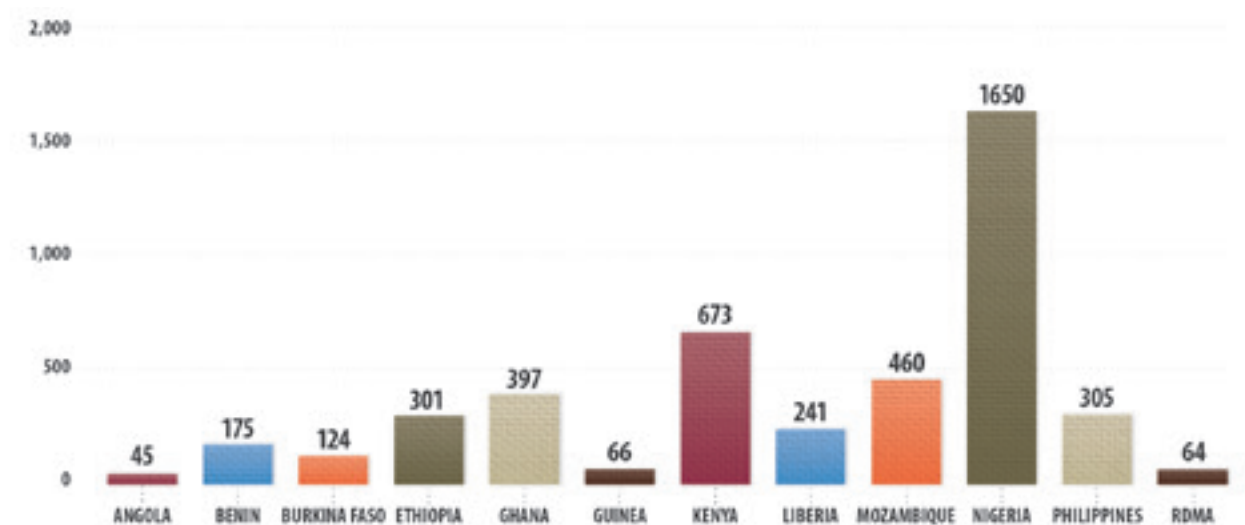
AMI countries located in the Latin America and Caribbean region historically provided routine data on antimalarial medicine quality until 2011, and no results have been reported since then. To address the lack of information, PQM surveyed the QC activities performed on antimalarials in AMI countries over the past two years. Results from this extensive 11-country assessment were reported during the third quarter and show that only countries with strong regulatory systems performed QC in a continuous and sustainable manner; these surveillance activities were performed by the MRAs, while in countries where surveillance was confined to National Malaria Control Programs none was done. Much work is needed across the region to build strong QA systems in all countries. In Burkina Faso, PQM provided technical assistance to the MRA to gather preliminary medicine quality information in Ouagadougou. A total of 124 antimalarial samples were collected, and 11 samples were determined to be doubtful and needed further laboratory testing. Final results are still under review, but the laboratory is working closely with PQM to follow up and develop a course of action.

3.2 COVERAGE OF SCREENING AND TESTING OF FALSIFIED, SUBSTANDARD AND UNAPPROVED MEDICAL PRODUCTS EXPANDED

Part of PQM's work to increase the breadth and capacity of countries to screen and test for substandard medicines includes training local trainers in PMS activities, thus increasing the sustainability and local ownership of QC activities over time. This year PQM worked closely with Guinea's MRA and other key stakeholders to launch the Guinean MQM program during a one-day workshop. In addition to providing an overview of MQM, the workshop served as a forum to develop a sample collection strategy for the purposes of an initial survey and training on monitoring the quality of medicines. Personnel working at the central level increased their capacity in MQM and they will subsequently train personnel working outside of the capital city to improve MQM activities nationwide.

A recent amendment to Kenya's constitution decentralized many functions, including the delivery of health services at the county level. Key stakeholders have been concerned about the ability of counties to procure medicines that meet the regulatory requirements of the national government. To prepare the counties to undertake their new role in procuring quality medicines, PQM collaborated with stakeholders to scale up the MQM program, expanding it

FIGURE 5: NUMBER OF ANTIRETROVIRAL, OI, TB, ANTIMALARIALS AND MCH PMS SAMPLES COLLECTED AND TESTED IN 2016





to include additional counties and ports of entry. As part of PQM's vision to support Kenya's overall strategy of sustaining established capacity, team leaders previously trained by PQM staff supervised the preparation of MQM activities including sampling strategies, refresher training on Minilab™ basic tests and data reporting.

PQM also works to provide guidance toward the expansion of priority medicines tested under national PMS program, advocates to increase PMS activities, and bolsters national MQM capacity and regulatory actions. Successes in these areas this year have been particularly evident in Indonesia, Mali and the Philippines.

PQM continued to advocate for inclusion of priority MOH-provided public medicines in the national PMS priority sampling guidelines in Indonesia. As part of the overall strategy to increase government sector medicines for sampling and testing, and to provide quality control data to disease programs, PQM has been approaching multiple stakeholders to increase support. By utilizing international donor programs such as the Global Fund to inject financing in support of joint activities and provision of equipment, together with technical assistance from PQM, both the MOH and the Indonesian MRA have come together to increase the types of samples included in the national PMS system. The expansion will cover mainly the TB, HIV and other priority vertical program medicines. Going forward, PQM will play a pivotal role by supporting the Indonesian MRA in the rollout of quality control testing, while at the same time coordinating the GF-sponsored activities, including convening workshops,

joint sampling exercises and data sharing for public and private sector medicines with key stakeholders.

In Mali, following the dissemination of the results of last year's round of sampling and testing of antimalarial medicines and the lack of subsequent action by the MRA, PQM worked with Mali's MRA to strengthen regulatory actions on falsified and substandard medicines. The new DPM 2016–2018 action plan calls for the NQCL to decentralize some quality control activities and hire more staff to oversee the implementation of PMS activities at sentinel sites. Likewise, PQM is aiding the redesign of the PMS strategy in the Philippines in collaboration with the Philippine Department of Health, the National TB Program and MRA regional offices and local government units. The new methodology and implementation plan will support the PMS of FDA to move toward sustainability and ownership of quality monitoring activities.

At the global level, PQM developed quality control screening procedures for key MNCH medicines. This included penicillin G benzathine, penicillin G sodium, penicillin G procaine and gentamicin injectable products. PQM also provided technical support for misoprostol quality test procedures. Misoprostol tablets are used for the prevention and treatment of postpartum hemorrhage in women. Due to the instability of the API, it is typically available as dispersion in hydroxypropyl methylcellulose, making it easier to use in manufacturing misoprostol tablets. To date, none of the pharmacopeias had published a monograph of test procedures and specifications for tablets, creating a gap in the ability to

perform quality control testing. To address this gap, the WHO published draft monographs for Misoprostol Dispersion and Misoprostol Tablets for inclusion in *The International Pharmacopoeia*. In February 2016, PQM submitted technical comments including improvements to dissolution and assay recommendations. The development of robust methods will allow for accurate analysis of misoprostol tablets during registration and PMS, resulting in an increased capacity to assess medicine quality globally.

3.3 INNOVATIVE TOOLS AND APPROACHES TO STRENGTHEN MEDICINE QUALITY ASSURANCE INTRODUCED

PMS is a critical regulatory function required to ensure the quality and safety of medical products throughout the supply chain after initial registration by the regulatory authority. It is also one of the most challenging functions. Despite the importance of WHO interventions and recommendations on effective PMS, most low- and middle-income countries (LMICs) are challenged by the lack of clarity and applicability of those recommendations to their resource-limited settings. Consequently, there are significant gaps in LMICs around efficient implementation of PMS. One of the ways that PQM supports local PMS activities is through the introduction and rollout of the Three-Level Approach, a process of three successive, complementary and increasingly complex levels of analysis that may be particularly useful as a first-line inspection in underresourced areas. This innovative approach has proved particularly successful in AMI countries, highlighted by successes this past year.

To support Level 1 assessment of physical and visual inspection in the field, PQM is developing an internet-based application that will be completed and deployed in FY17, initially in Peru and Ecuador in the Americas and in Ghana in Africa. Toward this end, PQM completed a database to be included in the application. The database for Peru contains over 250 products, including all antimalarials registered in the country as well as selected antibiotics and anti-inflammatory medicines. The Ghana database contains close to 100 registered antimalarials. In the past, PQM has supported Peru's MRA and NQCL in the implementation of the Three-Level Approach by helping to develop sampling and testing protocols and training in the use of Minilab™

for Level 2 screening of medicines in the field. To address the need to assess the quality of medicines in the field that are not included in the Minilab™, the National Center for Quality Control (CNCC) established a development and validation program for additional APIs. In support of this initiative, PQM trained CNCC personnel on development and validation of analytical methods. Realizing the global impact that newly developed methods could have, PQM coordinated a collaboration between CNCC and the GPHF to facilitate the inclusion of Peru's newly developed methods in the Minilab™. Since last year, Peru took total ownership of the Three-Level Approach and began implementing it without any PQM support; continuing with this, Peru's NQCL expanded the assistance to regional health offices in performing Level 2 testing by incorporating additional academic institutions to the network of labs providing support. Likewise, following PQM's recommendation, last year Ecuador's MRA included the use of Level 2 screening methods in the PMS guidelines for surveillance of medicines quality. Subsequently, the MRA took ownership of two Minilabs™ originally donated to the National Malaria Control Program in 2005, which had been inactive since 2009. PQM purchased the necessary supplies to replenish those Minilabs™ and supported the participation of two analysts from the reference lab in a training delivered in Peru by CNCC on Minilab™ use and implementation of the Three-Level Approach.

PQM also strives to develop innovative tools and novel approaches to medicines quality evaluation and assurance by interfacing with academia. To address the need for risk-based PMS guidelines for LMICs, PQM's Cross Bureau program convened a consultative workshop with practice and academia experts from the University of Washington, Johns Hopkins University and the WHO Collaborating Center for Advocacy and Training in Pharmacovigilance—Ghana. During the workshop, presentations, case studies and plenary discussions were used to collect views, share experiences and identify best practices that will serve as reference for the development of these guidelines. Based on the discussions and recommendations, PQM also drafted an outline of a framework for implementing a risk-based PMS system. The goal of the guidelines and framework is to ease the burden on quality control and inspection services and help countries utilize a risk-based approach to carry out PMS in an efficient and sustainable way.

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

4.1 AVAILABILITY OF INFORMATION RELATED TO QUALITY OF MEDICINES INCREASED

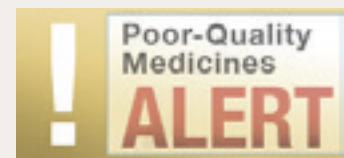
Poor-quality medicines pose a grave threat to patients in developing countries, but their presence remains a largely unknown problem, something that USAID, PQM and national authorities are working diligently to combat. PQM uses a variety of methods to raise awareness among local partners and civil society about the potential dangers of substandard medicines, each tailored to best reach the individual audience. Highlights this year include information sharing at both the global and country levels through studies, seminars, published papers and various PQM-sponsored events such as awareness campaigns, meetings, and inter-country learning experiences.

Administered by PQM HQ is the internationally referenced Medicines Quality Database (MQDB), a real-time, open-source database of more than 14,000 medicines quality test results, including substandard and falsified medicines. MQDB includes data from six countries included in USAID's priority list of countries aiming to end preventable child and maternal deaths (Ethiopia, Ghana, Kenya, Liberia, Mozambique and Nigeria) among others. This year the MQDB had 900 external visitors, and PQM launched the Poor-Quality Medicines ALERT feature within the database. The ALERT provides rapid access to the most recent information on poor-quality medicines identified in PMS activities in PQM countries, including those performed independently of PQM assistance. Currently, PQM is coordinating with the WorldWide Antimalarial Resistance Network to explore ways to integrate the information existing in the two databases.

Another milestone achievement this year was a PQM co-authored article, published in the *Malaria Journal* and presented at a meeting held in Geneva, Switzerland, entitled "Fake Antimalarials: Start With the Facts." The purpose was to disseminate the findings of the artemisinin combination therapy consortium's drug quality program. PQM documented new media reports on incidents of poor-quality medicines and updated a continuous compilation of media reports on medicines quality that is housed on the PQM webpage. In close collaboration with USP, PQM also produced a video available on the PQM website of the importance of ensuring the quality of medicines geared toward a broad audience, including civil society and country partners.



This year, the Poor-Quality Medicines ALERT feature within PQM's Medicines Quality Database was launched on PQM's website. The ALERT now provides rapid access to recent information about poor-quality medicines identified in postmarketing surveillance activities in PQM countries.



For more information, please visit PQM's website, www.usp-pqm.org, or view the MQDB webinar, <https://youtu.be/5ruE3WFlaQY>.



The PQM Core malaria team conducted an important cross-country study this year assessing the diversion of antimalarial medicines from public to private sectors in Malawi, Nigeria and Benin. The study focused on medicines donated by the U.S. government, namely Coartem® and artesunate-amodiaquine. Samples were collected from informal and formal drug stores in both urban and rural areas. Each country study was designed to provide evidence of diversion and data on variations between market prices set by vendors. Gathering additional data on the availability of antimalarials in the market fulfilled a secondary objective to provide additional context on local public health status and help the President's Malaria Initiative (PMI) make informed decisions about future programming. The information will be used to help ensure that donated medicines are reaching their intended markets.

As a follow-up to the implementation of strategies by PQM to strengthen the pipeline of skilled professionals in the pharmaceutical sector, major accomplishments have been made this year to increase and improve medicine quality learning opportunities for healthcare professionals at the global level and in several PQM mission countries.

In FY16, the PQM Cross Bureau team began the development of an e-Learning course on medicines quality assurance. The e-Learning course aims to increase awareness, knowledge and recognition of the importance of medicines quality assurance systems strengthening for the achievement of desired health outcomes and protection of the public against the dangers of falsified and substandard medicines. This course is intended for health program managers and officers, including MOH policy makers; it will also be useful to health professionals working

at national and subnational levels in any program where treatment plays an important role in implementation. However, advocacy groups, civil society and the public in general could also benefit from this basic knowledge on medicines quality assurance. The two-year project is expected to be finalized and made available in FY17.

PQM collaborated with a number of academic institutions to build capacity among educators and help strengthen training for future public health professionals in Cambodia, Ethiopia and Nigeria. This initiative addresses the issue of a lack of an adequately competent regulatory and quality assurance workforce to build strong regulatory systems and improved manufacturing capacity. PQM is supporting two Cambodian universities, the University of Health Science and the International University, to improve academic programs on medicines regulation and quality assurance. These facilities contribute significantly to the health and human resources sector in Cambodia. Approximately 155 pharmacy students per year will benefit from the enhanced curriculum and build a strong foundation in quality assurance of medicines and regulations. PQM also developed and finalized 11 training modules on regulatory inspection for staff at pharmaceutical distribution chains in Regional Development Mission for Asia (RDMA) countries. These modules were designed for trainers and delivered at a regional workshop led by PQM in collaboration with the Laos MOH Food and Drug Department and Bureau of Food and Drug Inspection.

PQM began the initial stages of developing content for a Nigerian e-Learning platform "PQM Academy" in support of the Nigerian MRA's goal of lasting institutional capacity. The course is intended for policy makers, regulatory managers,

INVESTING IN TOMORROW'S PHARMACEUTICAL WORKFORCE AT THE UNIVERSITY OF ADDIS ABABA



A skilled workforce for pharmaceutical quality assurance and regulation is a critical piece of the overall health system. A strong health system ensures access to safe, effective and essential medicine to the public. In most low- and middle-income countries, there exists a pharmaceutical management skills gap.

In order to address the skills gap, PQM collaborated with Addis Ababa University's School of Pharmacy to launch a master's program in regulatory affairs this year. PQM has been involved since the early stages of developing content through to implementation. The first cohort of students was admitted for October 2016. PQM continued to support building the skills of academic leadership by sponsoring two School of Pharmacy management team members to attend

regulatory affairs professional meetings in the United States. In addition, the team visited Howard University, George Washington University and the U.S. Food and Drug Administration. During the visits, the team was able to identify teaching material and reference textbooks for the master's program. The team also identified areas of collaboration with the different institutions and reached an agreement on signing memorandums of understanding with University of Southern California, George Washington University and University of Washington. Based on the agreement, U.S. professors will travel to Ethiopia to teach a number of courses. PQM plans to continue promoting the development of regulatory affairs skills in Ethiopia by providing the necessary financial support and technical review of teaching materials.

government officials, local manufacturers and others interested in learning more about the processes of GMP in pharmaceutical systems. Finally, as a follow-up to PQM's strategies to strengthen the pipeline of skilled professionals in the pharmaceutical sector in Nigeria, PQM also drafted pharmaceutical quality assurance curricula for inclusion in bachelor of pharmacy, postgraduate diploma, master of science and doctorate of pharmacy programs at pharmacy schools in Nigeria. All of these important contributions to educational programs will have sustained and lasting effects on future healthcare professionals and policy leaders in low- and middle-income countries for many years to come.

At the country level, PQM conducted studies and engaged key partners to increase the availability of and access to information about medicines quality assurance issues and raise awareness about substandard medication. Examples from Ghana, Pakistan, Benin, Indonesia, Burma and the Philippines highlight major accomplishments in local advocacy this year.

Postpartum hemorrhage is a major cause of maternal mortality in Ghana, though it can be managed with the use of uterotonics such as oxytocin, ergometrine and misoprostol. The outcome of an FY15 MQM report on the quality of uterotonics indicated that a high percentage of oxytocin and ergometrine available on the Ghanaian market do not meet the required standards of quality, which could have serious implications on maternal mortality in the country. To help combat this serious problem, PQM is providing technical assistance to the Ghanaian MRA to monitor the quality of uterotonic medicines. PQM has played a key role this year by organizing and facilitating a stakeholders' meeting to disseminate the results of a uterotonics study and emphasize the roles and responsibilities of the manufacturers in ensuring the quality of medicines within the country, such as through proper storage and manufacturing practices.

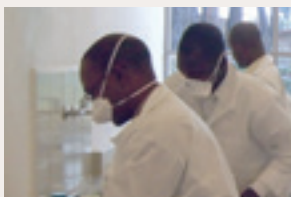
PQM also initiated a series of discussions with overseas manufacturers producing CHX gel, including a multinational company based in the United Kingdom, on possibilities for technology transfer of CHX Digluconate 7.1% to interested local manufacturers in Pakistan.

In Benin, PQM analyzed information on substandard medicines and worked with the national quality control lab to draft and present results at a workshop hosted by Population Services International/Association Béninoise pour le Marketing Social et la communication pour la santé for a communication campaign against falsified artemisinin-based combination therapies. In collaboration with the Philippine MRA, PQM helped prepare a one-day seminar titled "Ensuring the Quality, Safety and Efficacy of TB Drug Products and Other Pharmaceuticals Through Regulation and Promotion of Rational Use" for local government unit staff, pharmacists, supply officers and provincial and city health office staff. The objective of the seminar was to communicate the roles and responsibilities of the MRA and PQM in ensuring the quality, safety and efficacy of TB drug products and other pharmaceuticals, and establish closer collaboration with the local government units. Finally, PQM coordinated a visit for five senior management staff from Burma's MRA to a world-class, state-of-the-art laboratory environment in India. The goal of the trip was to learn about the quality management system, discuss potential cooperation and technical assistance, and strengthen regional cooperation on medicines quality assurance.

In Indonesia, PQM sponsored a seminar during the national Indonesian Pharmacists' Association's annual scientific seminar titled "Developing Pharmacists' Role for Better Quality of Life in the AEC Era." PQM presented on "Dossier Compilation and Product Quality," "International GMP Expectations and Inspections" and "The Importance of Storage in Maintaining the Quality of Medicines." This was a unique opportunity to bring PQM's messages and technical assistance in Indonesia to a national audience of industry and government pharmacists. PQM also supported the Ministry of Health (Directorate of Pharmaceutical Production and Distribution) in Indonesia to conduct a high-level decision maker meeting with local pharmaceutical manufacturers focusing on WHO PQ. In addition to discussing a number of challenges and constraints in implementing WHO PQ projects for priority medicines, strong recommendations were proposed by the government of Indonesia requiring strict compliance with current Good Manufacturing Practice standards for procurement with public funds.

REGULATORY ACTIONS IN ETHIOPIA AND LIBERIA—FIGHTING SUBSTANDARD MEDICAL DEVICES AND MEDICINES

ETHIOPIA



In 2014, the Ethiopian National Quality Control Lab successfully attained an expansion of scope under ISO/IEC 4074:2014 to include testing the quality of medical devices (male condoms). The Ethiopian NQCL is the only laboratory in Sub-Saharan Africa to hold accreditation for testing of medical devices, a noteworthy step in the fight against HIV/AIDS in Ethiopia and throughout East Africa.

In FY16, the lab's quality detection resulted in the recall of nine lots of condoms, comprising 69 million condoms from a single manufacturer based in India. From the total number of purchased condoms, 60 batches were randomly tested and found to be incorrectly sized, lack sufficient lubricating gel and/or have torn when under pressure. The condoms were destroyed and the manufacturer was blacklisted. Were it not for the work of the NQCL, the recalled condoms would have otherwise exposed the public to unintended pregnancy and sexually transmitted diseases.

LIBERIA



PQM began providing technical assistance to Liberia in 2009, at which time the country had no medicines regulatory authority or systems in place to ensure the quality of medicines entering the country. Hence, Liberia was a safe haven for poor-quality medicines until 2010, when PQM assisted Liberia to establish an MRA. The agency started with only three employees in 2010 and has grown to 41 employees

today. The MRA's progress can be seen in the regulatory actions taken this year to combat the circulation of substandard medicines.

In FY16, PQM helped expand MQM activities and supported the MRA's capacity to conduct regulatory actions. In total, 40 new regulatory actions were taken, including the confiscation of poor-quality antimalarial medicines (quinine and amodiaquine monotherapy) from Monrovia and Nimba. In one regulatory activity, a team comprising inspectors from the MRA, a PQM consultant, a county pharmacist, representatives from the Liberian National Police and a local law enforcement official conducted a 10-day cross-county regulatory activity. The team, acting on Minilab™ and compendial test results from previous rounds of medicine quality monitoring, removed several poor-quality medicines from a number of medicine shops and public markets. The team also seized the opportunity to provide updates to stakeholders about poor-quality medicines in circulation. As a means of further bolstering in-country capacity, PQM procured Minilabs™ to assist with MQM activities at sentinel sites, ports of entry and other places to be identified by the National Malaria Control Program and the MRA.

4.2 ENFORCEMENT ACTIONS AGAINST FALSIFIED, SUBSTANDARD AND UNAPPROVED MEDICAL PRODUCTS INCREASED

As a result of PQM's support and MQM routine monitoring, this year the Philippine MRA issued an advisory notice to healthcare professionals and the general public warning them to avoid purchase and use of an illegal Isoniazid/TB product that was found to be unregistered. The FDA authorities will be taking legal actions against the manufacturer for not having a valid Certificate of Product Registration.

4.3 GLOBAL AND REGIONAL COLLABORATION TO ADVOCATE THE QUALITY OF MEDICAL PRODUCTS ENHANCED

PQM raises awareness about the dangers of falsified and substandard medicines and provides information to the public and respective governments by supporting global, regional and local initiatives to promote medicines quality. Activities often include hosting and attending partner meetings, developing regional databases and alert systems, advocating on behalf of partners for additional financial support and encouraging collaboration among stakeholders.

To share information with the global community, PQM coordinated and participated in several international meetings during FY16. Highlights from global and regional collaboration efforts include cooperating on a malaria product surveillance workshop in Southeast Asia and a TB medicine quality workshop in Dubai, and strengthening relationships with the EAC.

A regional workshop was held to raise awareness of the need for substandard/spurious/falsified/falsely labelled/substandard (SSFFC) malaria medical product surveillance and information sharing in Southeast Asia for MRAs in the WHO Western Pacific Region, Association of Southeast Asian Nations (ASEAN) and the Greater Mekong Sub-region. The workshop was convened by the WHO with technical input from PQM. The objectives of the workshop included

strengthening MRA capacity to prevent, detect and respond to SSFFC medical products, develop awareness of the need for robust PMS and reporting in order to protect public health, improve knowledge of laboratory support, field detection technologies and effective sampling methodologies, and identify and train nominated country MRA focal persons in the use of the WHO global surveillance and monitoring rapid alert system. Participants were introduced to the global scale and public health impact of SSFFC medical products and how the WHO rapid reporting scheme will support the work of MRAs. PQM supported this with sessions on regional laboratory development and accreditation, use of field detection equipment, the importance of good distribution practice and supply chain integrity, capacity building of QC laboratories and leadership development.

In an effort to engage with manufacturers of priority TB medicines, PQM held a workshop in Dubai titled "Ensuring the Quality of Anti-Tuberculosis Medicines—Contributing Towards Ending the TB Epidemic." The objective was to raise awareness about pharmaceutical quality and to provide information to manufacturers of anti-TB medicines about opportunities for using PQM technical assistance to strengthen their quality systems. PQM collaborated with the WHO TB program and the Global Drug Facility, as well as various technical subject matter experts, to present trends in TB control and treatment, the WHO PQ process, current GMPs, dossier requirements and data integrity.

The PQM Cross Bureau team presented at this year's American Society of Tropical Medicine & Hygiene Annual Meeting, where MQDB data related to falsified and substandard medical products were presented to approximately 100 participants. The team also presented at the Scientific Exchange "SCIX" 2016 meeting on the assessment of the effectiveness of the CD3+ tool to detect falsified and substandard antimalarials. PQM headquarters and the field office also participated in the 2016 Joint National Tuberculosis Program Review (JPR); PQM provided recommendations to the JPR, particularly on drugs and supplies management for medicine quality monitoring and quality assurance systems. The joint review supports medicines quality assurance efforts among partners.

During FY16, PQM strengthened relationships with key partners, including the EAC and Physikalisch-Technische Bundesanstalt (PTB). PQM has been supporting the EAC initiative on harmonization of regulatory functions and, this year, began the process of formalizing its relationship with the EAC secretariat. PQM technical and programmatic staff attended several workshops and meetings involving EAC and PTB, along with other stakeholders, and contributed to discussions on PMS and regional GMP roadmaps. As a result of the relationships and expanded discussions, PQM made initial plans with EAC and PTB to hold a joint workshop in FY17 to provide training on qualification and validation, as well as dossier assessment.

PQM works closely with multinational partners to advocate for additional financial support for country programs with the goal of increasing the depth and breadth of medicines quality programming within local health systems. This year PQM was influential in garnering significant additional funding for programs in Indonesia, Burma and Cambodia.

Aiming for increased financial sustainability, PQM was able to leverage \$3 million of Global Fund financing to support priority provincial quality control laboratories in Indonesia. An initial \$1 million of reprogrammed TB funds supported the procurement of ion chromatography machines and other needed equipment for testing several TB medicines (amikacin, kanamycin and streptomycin). The remaining \$2 million allowed for capacity building and training in priority NQCLs. Plans for FY17 include supporting 11 provincial NQCLs through procurement of needed equipment, as well as support for extensive “joint sampling” activities between the Food and Drug Monitoring Agency inspectors and the MOH provincial and district health staff. These activities will ensure that medicines are being sampled from government storage facilities, that they are tested using international standards and that the data are reported to the MOH in a timely manner. These activities will promote better follow-up between the MOH, the

Indonesian MRA and manufacturers in the event of poor-quality medicines being found.

As a result of continuous advocacy on medicines quality with key stakeholders and donors in Burma, PQM leveraged \$31,000 from the WHO Country Office that covered two technical training courses held in December 2015. During the fourth quarter, PQM was able to leverage approximately \$40,000 of additional funding from The Global Fund to Fight AIDS, Tuberculosis and Malaria under a regional artemisinin resistance grant to cover the costs of Burma’s NQCL, Nay Pyi Taw, for pharmaceutical chemistry lab equipment and instruments that were purchased by the government.

PQM leveraged \$24,997 from the WHO Country Office in Cambodia to complement the existing President’s Malaria Initiative through the USAID Cambodia Mission. Funds were used to conduct two technical workshops, one for the MRA’s inspectors on regulatory inspection of pharmaceutical distribution chains and the second for NQCL analysts on good laboratory practices. Additionally, Cambodia’s WHO Country Office has agreed to provide \$10,000 to the National Health Products Quality Control Center (NHQC) to conduct trainings on compendial techniques for NHQC analysts in support of ISO/IEC 17025:2005 accreditation. The Global Fund to Fight AIDS, Tuberculosis and Malaria will also provide \$20,300 per year over two years (2016 and 2017) for calibration laboratory equipment and the Cambodian Government will provide \$6,000 to send its key managers and technical staff accredited labs to learn best practices via south-south collaboration. By leveraging almost 50% of the total budget, PQM has successfully mobilized partners to build on USAID’s catalytic investment to support the NQCL in its goal toward ISO/IEC 17025:2005 accreditation.



CHALLENGES, SUSTAINABILITY AND LESSONS LEARNED

CHALLENGES

Challenges are an inevitable part of program implementation, but also serve as an important source of strategy recalibration and experiential-based growth. PQM programs operate in close collaboration with multiple partners, including local governments, national authorities and development organizations, to meet pharmaceutical quality systems strengthening objectives. These close partnerships serve to strengthen program sustainability and local ownership, but can at times contribute to implementation challenges and delays. During this fiscal year, key challenges were experienced across a range of issues, including local regulatory and bureaucratic processes, in-country human resources capacity and funding deficits. While many of the challenges encountered this fiscal year have been beyond the control of the PQM program, country staff, consultants and technical assistants have worked hard to adapt their plans in order to achieve maximum programmatic success and impact.



REGULATORY AND BUREAUCRATIC PROCESSES

Regulatory and bureaucratic processes, while necessary for authorized program implementation, often cause delays in implementation of critical activities. For example, obtaining required approvals and documents such as import permits and tax and customs duty exemptions remains a key challenge in Burma and Indonesia. Approval processes can often take months. The PQM program in Burma has adapted by using available supplies at the NQCL with an agreement to replenish at a later date. The implementation of the PQM Indonesia program was delayed during the first quarter of FY16 due to the complicated process of project registration within the Ministry of Finance.

HUMAN RESOURCES CAPACITY

This year country programs in Cambodia, Laos, Burma, Kenya and the Philippines have reported a lack of skilled human resources among key partner agencies, leading to difficulties and delays in program implementation. For example, the Philippines has seen a high turnover of staff at the MRA and the Local Government of the Philippines sentinel sites. There is also an inadequate number of field office staff and consultants to provide follow-ups on PQM program performance and coordination on the ground. Kenyan partners report high staff turnover and managerial challenges at the NQCL. High turnover of well-trained staff at this location is also cited as a major challenge that detrimentally impacts PQM program implementation, including the maintenance of ISO 17025 accreditation. While human resources capacity and turnover remain challenging in many countries, PQM programs continue to work closely with implementing partners to build capacity by ensuring excellent training for new hires as well as retraining of existing staff.

FUNDING DEFICITS

This year PQM faced a substantial reduction in funding from the PMI-USAID/ RDMA as well as USAID country missions in the Philippines and Cambodia. Country activities were scaled back accordingly and this adversely impacted the ability of country programs to maintain a minimum acceptable level of program support. More than half of the important

program activities in the Philippines and Cambodia, as well as the RDMA (Thailand, Laos and Vietnam) countries, were cut and reprioritized due to the budget reorganization. Medicines quality monitoring, a critical activity in the fight against falsified and substandard medicines, was completely discontinued in Cambodia and RDMA countries due to the lack of funds. Additionally, in Thailand, the lack of funding available for hiring a local consultant led to a communication and coordination gap between PQM and Thai program partners, such as the MOH, Bureau of Vector-Borne Disease Control, Bureau of Drug and Narcotic and the MRA. It has proved critical to have a local native country consultant in place for day-to-day communication, coordination and face-to-face meetings with program partners and the PMI-USAID/ RDMA Mission to ensure the effectiveness and continuity of the program activity implementation on the ground. Likewise, in Liberia, limited funding this fiscal year has meant inadequate preparation of the NQCL for ISO accreditation.

While funding deficits are difficult for program staff to navigate, PQM has been successful in mitigating these deficits by working with partner organizations or local governments to agree to fund PQM activities, thus increasing financial sustainability and collaboration, and facilitating country ownership. For example, PQM was able to leverage \$3 million in Global Fund financing to support PQM's priority provincial quality control laboratories in Indonesia. An initial \$1 million in reprogrammed TB funds supported the procurement of ion chromatography machines and other needed equipment for testing TB medicines (amikacin, kanamycin and streptomycin). The remaining \$2 million allowed PQM to support capacity building and training in priority Indonesian quality control laboratories.

“ **CHALLENGES SERVE AS AN IMPORTANT SOURCE OF STRATEGY RECALIBRATION AND EXPERIENTIAL-BASED GROWTH** ”

LESSONS LEARNED

The experiences of this fiscal year are crucial for the PQM program to continuously improve program delivery, building on the lessons learned, avoiding future pitfalls and seizing opportunities for partnership and improved country ownership. Timely and thorough communication and collaboration have been key themes driving the lessons learned by country programs this past fiscal year.

Constructive engagement with local authorities, including civil societies, has also proved successful in Liberia this year. Collaboration between multiple parties, including the MRA, local police and the civil society led to the recent confiscation of a truckload of poor-quality medicines and health products near the Guinea border in Nimba County.

In Burma and Indonesia, coordination among various implementing partners working to strengthen the capacity of MRAs has been insufficient this past year. For example, only one coordination meeting between the Burmese MRA, WHO, the United Nations Office for Project Services, the National Malaria Control Program and PQM has occurred annually in Burma, far too few to be effective. PQM identified this coordination gap as a major issue and has taken a leadership role to coordinate with key stakeholders to convene more regular face-to-face meetings for updates and thus produce maximum impact. PQM has learned that it is paramount to establish regular meetings (at least quarterly) with the USAID Country Mission activity manager to provide briefings on progress, deliverables and challenges and for timely discussion and guidance. Without this, PQM and Mission staff would be vulnerable to communication and coordination gaps, an experience echoed this year in Cambodia and the Philippines.

The PQM Guinean team worked collaboratively this year with staff from various local health departments, and the MRA and NQCL, to conduct a medicine quality pilot survey. This proved to be a very effective method in launching the MQM activities in Guinea. All participants were highly engaged and welcomed the opportunity to be part of this exercise from the onset. Their participation in the field provided PQM with deeper insights into the status of the private, public and informal pharmaceutical markets, which will help PQM

to engage in more robust MQM activities in Guinea in the future. This positive experience of successful collaboration and timely communication with all partners will be fruitful for the team in the coming year.

Coordination was paramount as the MQM activities in Cambodia, Laos, Vietnam, Thailand and to some extent Burma transitioned from PQM program funding to outside sources, including government and other donors, this past year. As a reduction in PQM funding caused the majority of MQM activities to be postponed, the PQM team learned to initiate and conduct transitions by phasing out MQM activities gradually so that governments could collectively plan better and have a quality assurance mechanism in place. This type of phased transition, which will ultimately aid in sustainability and country ownership, can be learned and adopted by other country programs, particularly when experiencing funding challenges.

SUSTAINABILITY, PARTNER CONTRIBUTIONS AND OWNERSHIP

PQM strives to include local systems strengthening activities throughout its programming in an effort to ensure the sustainability of its impact with the goal that, one day, partners will be capable of assuming responsibility of all processes and operations related to medicines quality and supply. Sustainability, in this context, is defined as the physical resources, processes, regulations and partnerships that enable and facilitate the eventual independent operation and full function of medicine quality and supply activities within local country institutions, partners and programs. PQM works in partnership with local authorities to strengthen various aspects of local health systems, including the health workforce, information systems, health financing, leadership and governance. Country ownership of resources, processes, activities and regulations is paramount to achieving the ongoing sustainability of activities and improvement health systems.

To that end, PQM programs contribute to sustainable development by enabling countries to assume responsibility over trainings and processes, by transferring ownership of medicines quality activities and by diversifying partnerships. Strong commitment this year from government regulators

and local partners in countries such as Nigeria, Peru and Ethiopia resulted in incremental ownership of activities.

“**TIMELY AND THOROUGH COMMUNICATION AND COLLABORATION HAVE BEEN KEY THEMES**”

The leadership of the Nigerian MRA continued to demonstrate a commitment to medicines quality activities and shared responsibility of key processes this year. While Nigeria's NQCL in Agulu prepared for its ISO 17025 accreditation, top managerial staff from Kaduna QC laboratory were sponsored by the MRA to observe training sessions and the accreditation process, thus improving their technical capacity and transferring knowledge to Kaduna laboratory staff as they also prepare for accreditation. These interlaboratory training sessions, facilitated by PQM-trained MRA staff, will continue to increase institutional capacity throughout the country in the coming fiscal year. This training-of-trainers methodology was employed in other PQM-supported countries this year, such as Ethiopia and Liberia. For example, staff from Ethiopia's main NQCL provided on-the-job training to staff from branch labs and those at ports of entry in order to transfer knowledge and skills gained from PQM TA. The Liberian NQCL manager received training at USP's laboratory in Rockville, Maryland, this year to cascade knowledge to other analysts in the national lab, thus sustaining PQM activities.

As part of the AMI in the Latin America and Caribbean region, government MRAs that were previously supported by PQM either assumed complete ownership or continued the successful ownership of medicines quality activities. The most comprehensive local ownership occurred in Peru, where the MRA and the NQCL continued to fully implement medicines quality monitoring, independent of external assistance, including the use of the Three-Level Approach. The success of the Peruvian program has resulted in positive spillover effects for the region as the NQCL provides technical assistance to other countries, thus contributing to regional sustainability and ownership of activities.

The Ethiopian MRA (Ethiopian Food, Medicine and Health Care Administration and Control Authority) is one of the most advanced MRAs that PQM works with and is exhibiting widespread leadership by taking ownership of many tasks previously conducted by PQM, such as equipment maintenance, training activities and PMS activities. In FY16, the MRA assumed the costs of maintenance activities and identified the need to develop internal capacity to assume maintenance responsibilities and thus created a maintenance unit and recruited three biomedical engineers. PQM supported the MRA's efforts by financing training led by the major equipment supplier (Shimadzu, based in Istanbul, Turkey) to enhance the ability of newly hired staff to conduct maintenance activities. Since 2015, essential equipment repair has been transferred entirely to the MRA, which now funds and oversees all human resources. Success in the lab equipment maintenance will help the MRA's NQCL to maintain its accreditation and progress well toward WHO PQ. The four MRA branch labs will also greatly benefit from this in their progress toward ISO 17025. The MRA also began funding specific training activities, such as on-the-job training of staff working in product registration, process validation and analytical method validation. PQM has made a strategic shift in the delivery of trainings by focusing on specialized trainings and allowing the MRA to take the lead on basic trainings. The MRA has also signed an agreement with the Global Fund to provide fee-based testing services, thus helping the MRA to generate funds for its laboratory and sustain its activities for the long term.

Ethiopia's local ownership of PMS activities, highlighted above, has been a major development this past year. Prior to 2016, PQM worked to build capacity at the four MRA branch labs with the goal of starting PMS activities at the branch levels. Previously, only the national lab was conducting PMS testing and worked closely with branch labs to provide technical and financial assistance, training and supplies. This year, for the first time ever, branch labs began rounds of PMS testing conducted entirely by the Ethiopian MRA. The MRA also began budgeting for chemical procurement, sample collection and testing for priority medicines, showing that the MRA made great progress in taking over the funding and ownership of all PMS activities.

.....
USP-U.S.
12601 Twinbrook Parkway
Rockville, MD 20852-1790 USA
1-800-227-8772
www.usp-pqm.org

USP-Switzerland
Basel

USP-India
Hyderabad

USP-China
Shanghai

USP-Brazil
Sao Paulo

USP-Ghana
Accra

USP-Ethiopia*
Addis Ababa

USP-Indonesia*
Jakarta

USP-Philippines*
Manila

USP-Nigeria*
Lagos

*PQM Program
.....

