



PROMOTING THE QUALITY OF MEDICINES

# Promoting the Quality of Medicines (PQM)

**Highlights and Success Stories**  
**January 1, 2015 – March 31, 2015**

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## Promoting the Quality of Medicines (PQM) Program

### PROGRAM BACKGROUND AND FRAMEWORK

Since 1992, the U.S. Pharmacopeial Convention (USP) has worked cooperatively with the United States Agency for International Development (USAID) to help developing countries address critical issues related to poor quality medicines and their appropriate use. During 2000–2009, this partnership operated as the USP Drug Quality and Information program; then, to better meet growing global needs, USAID awarded USP a five-year, \$35 million cooperative agreement to establish a new, expanded program—**Promoting the Quality of Medicines (PQM)**. PQM serves as a primary mechanism to help ensure the quality, safety, and efficacy of medicines essential to USAID priority diseases, particularly malaria, HIV/AIDS, tuberculosis, and maternal and child health. In September 2013, USAID extended the PQM cooperative agreement through September 2019 and increased the budget ceiling by \$75 million, for a total program ceiling of \$110 million.

The PQM program is USAID's response to the growing development challenge posed worldwide by substandard and counterfeit medicines (SCMs). Their availability is increasingly recognized as a serious public health threat, especially in low- and middle-income countries. SCMs can cause treatment failure and adverse reactions, increasing morbidity and mortality, and they may contribute to antimicrobial resistance. They represent not only a waste of scarce resources but also a substantial risk to public health. They further risk undermining decades of health investments, including those made by USAID.

PQM manages a number of activities that reflect a systems-based approach which enables countries to address the problem of SCMs in a comprehensive, systematic, and sustainable manner, as illustrated in the objectives reported below.

#### I. Build capacity and strengthen quality assurance (QA) systems

PQM provides technical assistance to 35 countries, strengthening their national capacity in quality assurance and quality control systems in efforts to combat the availability of substandard and counterfeit medicines.

During this quarter, PQM performed baseline assessments of QA/QC systems in four countries: Burkina Faso, Guinea, Pakistan, and West Bank. Using the findings of these assessments, PQM will propose work plan activities for USAID approval.

Often the first measure PQM introduces in a country, depending on its needs, is to help establish post-marketing surveillance in the form of a system of medicines quality monitoring (MQM). This enables national and international stakeholders to adopt a comprehensive approach that leads to the collection of evidence-based data. The MQM process has proven to be of strategic importance in countries where medicines quality assurance systems are weak by allowing the country's medicines regulatory authority (MRA) to act should SCMs be discovered.

PQM has helped establish and develop medicine quality monitoring activities in 26 countries to date. Through these programs, PQM has helped identify counterfeit and substandard antimalarial, anti-tuberculosis, obstetric, and neonatal medicines in Burma, Cambodia, Ghana, Guatemala, Indonesia, Kenya, Liberia, Laos, Philippines, Senegal, Suriname, Thailand, and Vietnam.

In Senegal, the MQM program is now being implemented by the national lab and is deemed sustainable, as it has been incorporated into the country's post-marketing surveillance activities. PQM no longer implements this program.

Another approach that PQM employs is helping national quality control laboratories (NQCLs) operate with good laboratory practices. This quarter in Cambodia, PQM provided Good Pharmacy Practices (GPP) training for inspectors, pharmacists, and medicines sellers, with a total of 167 participants. Since July 2014, 884 participants have been trained in GPP in the country.

Becoming ISO 17025:2005 accredited or World Health Organization (WHO) prequalified, both globally-recognized standards of proficiency, are also important steps toward strengthening national health systems. So far in FY 15, PQM has assisted eighteen NQCLs in Africa, Asia, and Latin America. The NQCLs of Kenya and Nigeria achieved ISO 17025:2005 accreditations this year, the NQCL of Ethiopia was re-assessed and expanded its scope to Medical Devices (condom testing), and several labs have ISO 17025:2005 accreditations or WHO prequalifications pending. In addition, the USP Center for Pharmaceutical Advancement and Training (CePAT) in Ghana received ISO 9000 Certification and Global Fund recognition this year with assistance from PQM staff.

PQM also assists countries improve and streamline their medicine registration systems to strengthen regulatory authorities' quality assurance. This quarter in Ethiopia, for example, PQM helped draft Guidelines for Registration of Medical Devices, and in Indonesia, PQM supported two workshops, during which the Guideline for Sampling in the public sector was developed and finalized.

Through MQM, improving the technical capacity of NQCL staff, and improving registration practices, PQM provides needed support for countries to better control medicines quality and encourages MRAs to take enforcement actions based on results.

## **II. Help increase supply of QA medicines**

As of the beginning of FY15, PQM is working with 47 manufacturers in 13 countries toward achieving WHO Prequalification status—auditing facilities, offering guidance to prepare dossiers, and providing technical assistance to bring manufacturing systems in line with WHO standards. Notably, 3 anti-tuberculosis (TB) medicines manufacturers have had their medicines become WHO Prequalified with assistance from PQM this year: NCPC Huasheng for Capreomycin active pharmaceutical ingredient (API); Hisun Pharma for Capreomycin finished pharmaceutical product (FPP); and HEC Pharma for Azithromycin FPP.

To inform additional manufacturers of anti-TB medicines how to produce quality-assured medicines by following good manufacturing practices (GMP), PQM conducted a pharmaceutical plenary session on WHO prequalification, at the Fourth Central Asia Trade Forum held this quarter by USAID/Central Asia Republics. The plenary session focused on explaining the WHO Prequalification Program, raised interest in participating, and described how PQM can help in the process.

PQM also provides technical assistance to manufacturers of essential medicines for maternal and child health to improve their GMP compliance. As a member of the technical working groups of the UN Commission on Life-saving Commodities, PQM plays a key role in providing quality assurance support for manufacturers of medicines for maternal and child health.

In addition to working internationally to increase the supply of quality assured medicines, USP staff in Rockville, MD contribute to these efforts by creating monographs for medicines. This year, USP drafted a monograph for Chlorhexidine gel, which is ready for USP expert panel review.

## **III. Combat counterfeit and substandard medicines**

PQM takes every opportunity to raise its profile in advocating for quality medicines and to raise public awareness of the importance of quality-assured medicines to the public health. This quarter, PQM staff gave a seminar on the importance of medicines quality and technical leadership entitled "Why Is Medicine Quality Important?" at the University of Boston's School of Public Health.

Each PQM country program includes activities to raise public awareness about SCMs and the importance of medicine quality assurance. This quarter, PQM prepared a manuscript for publication in the American Journal of Tropical Medicines and Hygiene (AJTMH) that provides a snapshot on the quality of medicines based on data available in the Medicines Quality Database (MQDB). The manuscript was accepted for publication in the AJTMH Malaria supplement on falsified and substandard antimalarial medicines.

In addition to presentations and publications, PQM holds communication campaigns designed to inform the public about the dangers of SCMs. This quarter in Ethiopia, two public awareness-raising workshops were conducted with the aim of combating illegal trade of medicines in the country. In Senegal, previous communication and educative campaigns laid the groundwork to establish an inter-ministerial committee with the aim of combatting counterfeit and substandard medicines in the country.

#### **IV. Provide technical leadership**

PQM advocates globally, nationally, and locally for the importance of quality assurance of medicines to the effectiveness of treatment regimens. In several cases, MRAs have taken corrective action. This quarter in Ghana, for example, the MRA seized substandard and unregistered uterotonics found in various health facilities and destroyed them. In addition, the importers and distributors of these products were identified and invited to a stakeholder forum. Following supervisory visits to MQM sentinel sites in Mali and subsequent confirmatory testing at the country's national lab, information on failed samples was forwarded to the MRA so they could take regulatory actions. In addition, the national lab communicated with WHO-Mali regarding dissemination of the findings through WHO's Rapid Alert System.

Among the challenges to sustaining MQM in countries with limited resources is the expense required to monitor and test medicines quality on a routine basis, particularly in more geographically remote areas and along borders. PQM introduced testing using the Global Pharma Health Fund Minilab<sup>®</sup> in 2005 because of its portability and ease of use, and continues to research other tools that may improve the accuracy and reliability of field-based quality control technology. In conjunction with Boston University, PQM continues to support the development of a new detection technology based on microfluidics. "PharmaChk" is considerably smaller and more transportable than the Minilab<sup>®</sup> and, as testing requires less reference sample, should lower the cost of testing. In FY15, PQM will continue collaborating with Boston University to demonstrate the functionality of PharmaChk.



## Promoting the Quality of Medicines (PQM) Program

### Highlights and Success Stories for Q2: January 1 – March 31, 2015

Since 2009 the Promoting the Quality of Medicines (PQM), implemented by the United States Pharmacopeia (USP), has worked cooperatively with the United States Agency for International Development (USAID) to help developing countries effectively address critical issues related to poor quality medicines. PQM provides the needed technical leadership to build local capacity in medicines quality assurance systems, increase the supply of quality-assured medicines, combat the availability of counterfeit medicines, and advocate for medicines quality worldwide. Through these initiatives, PQM serves as a primary mechanism to help assure the quality, safety, and efficacy of medicines essential to USAID priority health issues, particularly malaria, HIV/AIDS, and tuberculosis (TB).

#### Core Funding

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##### CROSS BUREAU

###### Background

In order to play a technical leadership and advocacy role, and to be in a position to influence national and international medicines quality assurance agendas, PQM plans to attend selected international meetings and participate in the design of proposed activities relating to medicine quality issues. PQM also produces up-to-date information about current issues in medicines quality. In an effort to improve tools to ensure quality control and increase the knowledge base about quality assurance, PQM will develop a field-based quality control tool with increased accuracy, sensitivity, and reliability.

###### Highlights and Success Stories

PQM is working closely with Boston University (BU) to demonstrate the functionality of the PharmaChk device. Using the Systematic Evolution of Ligands by Exponential Enrichment (SELEX) system, BU is developing new probes for several medicines, including Oxytocin and Cotrimoxazole (Trimethoprim/Sulfamethoxazole). BU established a protocol for isolating aptamers for these target drugs. So far, 5 aptamers that bind Oxytocin are undergoing characterization. In parallel to this work, BU is testing Eosin Y as a probe for quantitative testing of Amodiaquine in Artesunate/Amodiaquine tablets.

To disseminate information on the quality of medicines, PQM prepared a manuscript for publication in the American Journal of Tropical Medicine and Hygiene (AJTMH) that provide a snapshot on the quality of medicines based on data available in the Medicines Quality Database (MQDB). The manuscript was accepted for publication in the AJTMH Malaria supplement on falsified and substandard antimalarial medicines.

##### MALARIA

###### Background

PQM has provided support for the President's Malaria Initiative (PMI) objectives using core funds by developing public standards to test existing medicines where standards did not exist before. PQM then established a network of country quality control laboratories to teach chemists about the use of the standards in compliance with Good Laboratory Practices standards. More recently, PQM has been involved in obtaining information at country levels on the extent of diversion of malaria medicines from the public to the private sector. The information obtained will be used by the respective donors to identify risk areas for diversion and take the necessary actions to address the problem.

*Note:* The FY15 Core Malaria work plan has not been approved.

## **MATERNAL AND CHILD HEALTH**

### Background

Since 2009, PQM has been involved in the efforts of the World Health Organization (WHO), UNICEF, and USAID to roll out zinc tablet and oral rehydration salt (ORS) supplementation in the management of children's diarrhea, especially for those children under the age of five. The technical assistance PQM has provided has largely been through quality control testing and good manufacturing practices (GMP) assessments of manufacturers to increase the availability of quality zinc and other maternal and child health (MCH) products, such as chlorhexidine. In 2012, the UN Commission on Life-Saving Commodities for Women's and Children's Health was formed as part of the Every Woman Every Child movement to increase access and use of essential medicines, medical services and health supplies that effectively address causes of death during pregnancy, childbirth and into childhood. Many of the recommendations that evolved from the commission overlap with key USAID priorities being addressed by PQM therefore the assistance PQM has provided is effectively meeting the goals of both initiatives. In order to help increase the global supply of quality assured MCH medicines, PQM will make recommendations to manufacturers to strengthen their quality assurance systems and GMP programs to subsequently achieve WHO prequalification (PQ) status

### Highlights and Success Stories

USP plans to continue its commitment to supporting the development of standards for medicines used globally by partnering with key organizations and other pharmacopeias to specifically address unmet public health needs for quality standards. USP's existing standards-setting capabilities, including its Expert Committees, will support this new standards-setting activity. The initiative targets critical medicines approved outside the U.S. for which no relevant standards exist, and will be conducted in ongoing consultation with the U.S. Food and Drug Administration.

The first monograph developed through this initiative is the chlorhexidine topical gel monograph. Although a monograph exists in the British Pharmacopeia (BP), manufacturer assessments conducted by PQM found many manufacturers were not performing all of the monograph tests, specifically the tests for impurities. This was due either to the lack of equipment or inadequate capacity to use the equipment. To address this issue, yet still maintain a high standard of quality, the new USP monograph allows for the testing of impurities and content (amount of chlorhexidine) in a single HPLC procedure. This is advantageous from both a manufacturing and regulatory perspective since HPLC is common and will reduce analysis cost and regulatory burden.

## **NEGLECTED TROPICAL DISEASES**

### Background

More than 1 billion people—one-sixth of the world's population—suffer from one or more Neglected Tropical Diseases (NTDs). These diseases are called “neglected” because they have been eradicated in most developed areas of the world and persist only in less developed regions.

The aim of the most recent invitation from WHO is to focus on four medicines used in the treatment of NTDs: albendazole, mebendazole, dithylcarbamazine, and praziquantel. These four single ingredient medicines have been shown to be effective in the treatment of lymphatic filariasis, soil-transmitted helminthiasis (STH), and schistosomiasis and have been included in the WHO Model List of Essential Medicines. With this funding from USAID, PQM plans to perform Good Manufacturing Practices (GMP) assessments of manufacturers to ensure that their products are of high quality. In order to help manufacturers achieve WHO PQ status, PQM provides recommendations to strengthen their quality assurance systems and GMP programs.

### Highlights and Success Stories

As PQM has begun working with and communicating with manufacturers of NTD products, particularly Praziquantel, it has become evident that the cost of in vivo bioequivalence (BE) studies in support of

these products may discourage companies from submitting an application to WHO PQ, thus reducing the number of quality-assured sources of this critically important medicine.

There may be an alternative to BE studies, however—a Biopharmaceutics Classification System (BCS)-based biowaiver application. The BCS-based biowaiver application has recently emerged as an alternative regulatory approach, in lieu of a BE study, to demonstrate interchangeability, particularly for generic products. WHO and other regulatory agencies, such as the U.S. Food and Drug Administration, have issued general BCS-based biowaiver application guidance; however, the application of the BCS-based biowaiver guidance requires a case-by-case approach to minimize any risks of making an incorrect bio waiver decision.

The biowaiver eligibility criteria are mainly based on the BCS classification (solubility/ permeability) of the active pharmaceutical ingredient (API). Praziquantel is currently categorized as a Class II compound, meaning it is considered to have low solubility yet high permeability. It is well understood, though, that the classification of Praziquantel was based on the available literature at the time of preparation of the BCS-based biowaiver guideline, which was extremely limited. Any justification that demonstrates the solubility of the API (from low to high solubility) might shift Praziquantel to a Class I (highly soluble/highly permeable) compound. Inherent solubility enhancement of the API, most probably through control of the API polymeric nature during synthesis and/or demonstrating the rapid solubility of the dosage form that supports the condition described under biowaiver, is the primary target for biowaiver alternative proposal.

In light of the above principles, the BCS characterization action plan for Praziquantel drug substance was formulated with defined strategies around four objectives (characterize, isolate, identify, conduct solubility and permeability study) to delineate the current existing bias around the BCS borderline classification and explore the possible alternative route of synthesis to improve the drug substance and drug product performance. The technical approaches for the study were published in the Request for Applications (RFA) to invite potential research institutes. From the most prominent research universities/companies who responded to the RFA, one applicant has been selected to conduct the BCS study and the detailed experimental study is currently in progress.

## **TUBERCULOSIS (TB)**

### Background

PQM provides support to the Global Drug Facility and the Green Light Committee in their efforts to increase the availability of good quality second-line anti-TB medicines (SL-ATBs). PQM assists SL-ATBs manufacturers to ensure an increased supply of quality-assured medicines globally.

### Highlights and Success Stories

As PQM works with manufacturers toward WHO Prequalification, there are many challenges in improving GMP compliance and dossier compilations that need to be overcome. One company has achieved this in the Philippines: Hizon Laboratories Inc., located in Antipolo City, Philippines, has submitted their finished product dossier for Levofloxacin to WHO PQ in March 2015. This dossier was accepted for review, and a WHO PQ GMP inspection will be scheduled in the next quarter. Varichem, a company located in Zimbabwe, submitted (and had their finished product dossier accepted) in December 2014; their inspection is now confirmed for August 2015.

PQM has also worked on addressing global shortages of the Kanamycin product. In order to address this shortage, PQM has worked with incorporating the Original Equipment Manufacturer (OEM) model for Kanamycin. The manufacturer PQM is working with will be submitting their finished product dossier in the next few weeks and providing technical assistance to a second supplier of Kanamycin API and FPP – Hisun Pharmaceutical. They submitted their product dossier and also hosted a WHO PQ inspection last quarter. The outcome of the GMP inspection is still pending and the dossier assessment is still in progress.



## Africa

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### ANGOLA

#### Background

Implementation of large-scale malaria control activities in Angola faces serious challenges because the country's health infrastructure was severely damaged during the civil war. It has been estimated that only about 40% of the population has access to government health facilities. Malaria is a major health problem, accounting for an estimated 35% of the overall mortality in children under five, 25% of maternal mortality, and 60% of hospital admissions for children under five. Malaria transmission is highest in northern Angola, while the southern provinces have highly seasonal or epidemic malaria.

PQM was selected to provide technical, strategic, and operational assistance to strengthen medicines quality assurance in Angola, beginning in 2013. PQM was asked to assist the MOH develop and implement a post-marketing surveillance system for antimalarial commodities in the country.

*Note:* USAID/Angola contacted PQM this quarter, but we are waiting for approval from the MoH before initiating work.

### BENIN

#### Background

In 2014, USAID/Benin determined that more support is required from PQM to assist the NMCP, NQCL, and DPMED speed up procedures for testing of ACTs procured by PMI as well as increase ACT testing in the markets and private health facilities in the Cotonou area.

PQM conducted a consultation visit to Benin to gather updated information on the medicine QA situation, identify gaps, and propose priority activities. Based on the outcome of the visit and the level of funding, PQM proposes to support pre- and post-market quality control of antimalarial medicines by strengthening the capacity of NQCL and DPMED. The NMCP will benefit from the outcomes of these interventions.

*Note:* The work plan was developed and submitted to USAID/Benin for approval.

### BURKINA FASO

#### Background

PQM was selected by USAID/Burkina Faso to strengthen the capacities of the National Drug Authority (DGPML), the National Quality Control Laboratory (LNSP), and other major health programs with the main goal of improving QA/QC systems in Burkina Faso.

#### Highlights and Success Stories

During this quarter, PQM conducted an initial assessment of the country's QA/QC capabilities and met with key stakeholders involved in the regulation, control, management, and distribution of medicines. A workplan is being developed with consultation from various stakeholders.

### ETHIOPIA

#### Background

PQM receives funding from PEPFAR through USAID/Ethiopia to strengthen the capacity of the Ethiopian Food, Medicine and Health Care Administration and Control Authority (FMHACA). The Product Quality and Assessment Directorate (PQAD) laboratory of FMHACA, through the technical and financial support provided by PQM, obtained ISO 17025 accreditation with respect to seven tests in 2011.

PQM also receives funding from PMI to provide technical, strategic, and operational support to strengthen antimalarial medicines quality assurance in Ethiopia. In order to monitor the quality of the country's antimalarial medicines, a medicine quality monitoring (MQM) program has been established, and PQM has supported the program by providing training to technical staff on sampling, testing of medicine samples, evaluation of medicine quality, and other activities. In FY15, PQM also received funding for Maternal and Child Health activities, to carry out post-marketing surveillance, enhance the registration processes of MCH medicines, and support MCH medicines manufacturers to improve GMP compliance and enable them to manufacture new children's formulations.

#### Highlights and Success Stories

Guidelines for Registration of Medical Devices was finalized, published, and distributed to stakeholders. This will have a paramount role in improving the transparency and efficiency of FMHACA, which in turn will be important in the course of improving access to medical devices including those used to treat HIV patients. The Guideline underwent a number of reviews by a team composed of FMHACA and USP-PQM Ethiopia staff.

Three trainings were provided on basic GMP, post-marketing surveillance (PMS) sample collection, and ISO 17025/WHO PQ. A total of 80 staff members have been trained and will contribute to improving the inspection system, QC lab, and PMS. As part of system strengthening, USP-PQM plays a major role in building the capacity of human resources in the regulatory area.

Two public awareness-raising workshops were conducted with the aim of combating illegal trade of medicines in the country.

## **GHANA**

### Background

PQM has focused on providing technical assistance to the Food and Drugs Authority (FDA) to establish a functional medicine quality monitoring program throughout the country and to strengthen the capacity of the FDA's national quality control laboratory (NQCL) toward the goal of ISO 17025 accreditation and WHO prequalification.

### Highlights and Success Stories

FDA Ghana completed the first round of MQM for antimalarial samples, and the reports were issued to USAID/Ghana; the Oxytocin and Ergometrine testing were completed as well. Based on the MQM results, FDA Ghana seized substandard and unregistered uterotonics found in various health facilities and destroyed them. In addition, the importers and distributors of these products were identified and invited to a stakeholder forum.

## **GUINEA CONAKRY**

### Background

PQM was selected to provide technical, strategic, and operational assistance to strengthen medicines quality assurance in Guinea. In January 2014, PQM conducted a rapid assessment of the QA/QC capabilities of the country and met with key stakeholders involved in the regulation, control, management, and distribution of medicines. The outcomes of the QA assessment revealed the immediate need to begin introducing initiatives in support of strengthening the capacity of the Laboratoire National de Contrôle de la Qualité des Médicaments (LNQCM) and the Direction Nationale de la Pharmacie et des Laboratoires (DNPL).

### Highlights and Success Stories

Due to the Ebola outbreak in 2014, travel to Guinea was restricted hence PQM was only able to provide remote technical assistance. The main activity carried out this quarter was the preliminary review of

DNPL law documents. PQM was also able to donate two pieces of lab equipment (GC and UV) to support the DNPL and increase its capacity.

## **KENYA**

### Background

PQM started working in Kenya in 2009 with the support of PMI through USAID/Kenya. PQM created a sustainable protocol for MQM in Kenya, and five sentinel sites for monitoring antimalarial medicines were established. PQM initiated the first round of MQM activities in 2010 by training representatives of the Pharmacy and Poison Board (PPB), the National Quality Control Laboratory (NQCL), and others in sampling strategies, Minilab<sup>®</sup> basic tests, and reporting and managing medicines quality data. Second and third rounds were carried out in 2011 and 2012. Based on MQM findings, PPB has been instrumental in taking regulatory actions by jailing the sellers of counterfeit antimalarials, closing a manufacturer for selling poor quality and unregistered samples, recalling non-conforming samples, and destroying expired antimalarials.

The NQCL obtained WHO PQ status in 2008. In 2011, the NQCL started the process of ISO 17025 accreditation with PQM assistance. In addition to assisting the lab toward ISO 17025 accreditation, and as part of reinforcing the capacity of the NQCL, PQM has been providing technical assistance to lab staff through the Network of Medicines Control Laboratories (NOMCOL). The primary objective of this network is to provide a forum for sharing best practices at the national level on medicines quality; it provides the participating laboratories the opportunity for South-South collaboration on quality control of medicines. Kenya is a charter member of NOMCOL.

### Highlights and Success Stories

The accreditation body, SANAS, conducted an inspection of the NQCL. Based on the findings and completed corrective and preventive actions, the NQCL is expected to become ISO 17025 accredited during the next quarter.

## **LIBERIA**

### Background

PQM helped Liberia to establish the Liberian Medicines and Health Products Regulatory Authority (LMHRA), which was the result of a bill signed into law in 2010. PQM continues to support LMHRA in its efforts to establish priority medicines regulations, manage its regulatory functions, and strengthen the quality control of antimalarial and antiretroviral medicines.

### Highlights and Success Stories

The PQM program in Liberia has been selected as one of the 10 top cases for the USAID Health Systems Strengthening Global Call. PQM's work in Liberia was selected out of 145 cases as an Honorable Mention. For more information, see: [www.hssglobalcall.hsaccess.org](http://www.hssglobalcall.hsaccess.org)

## **MALI**

### Background

PQM has been assisting the MoH of Mali since 2008 in strengthening their medicine quality assurance systems. Activities focus on strengthening the capacity of the Direction de la Pharmacie et du Médicament (DPM) and Laboratoire National de la Santé (LNS) in pharmacovigilance (PV), drug registration, medicine quality control (QC) and monitoring, and providing assistance to the National Malaria Control Program.

### Highlights and Success Stories

In collaboration with LNS, PQM conducted supervisory visits to the sentinel sites of Kayes and Sikasso. During the visits, sentinel site teams received refresher training on sampling and screening antimalarial

medicines using Minilabs. A total of 55 samples were collected and tested during these visits. One sample of fake Coartem, from the informal market, was found.

Sampling and testing of antimalarial medicines was also completed at the sentinel sites of Gao, Koulikoro, and Mopti as well as the district of Bamako, with 100 samples tested at each site. LNS verified the results obtained in the field and communicated the information on failed samples to DPM so they could take action. LNS also communicated with WHO-Mali regarding dissemination of the findings through WHO's Rapid Alert System.

## **MOZAMBIQUE**

### Background

PQM has been working in Mozambique since 2010. Activities have focused on strengthening the quality control (QC) and quality assurance (QA) capabilities of Mozambique's medicines regulatory authority, the Departamento Farmacêutico (DF).

### Highlights and Success Stories

LNCQM completed the first round of MQM in 10 sentinel sites, which included 3 newly-added port areas. The samples are undergoing confirmatory testing at the lab.

## **NIGERIA**

### Background

In 2012, USAID/Nigeria selected PQM to provide technical support to the National Malaria Control Program (NMCP) and the National Agency for Food and Drug Administration and Control (NAFDAC). USAID/Nigeria also selected PQM to support strengthening the capacity of select Nigerian manufacturers that produce zinc sulfate tablets, chlorhexidine digluconate gel, and other maternal and child health (MCH) priority commodities for the United Nations (UN) Commission on Life-Saving Commodities for Women and Children.

### Highlights and Success Stories

Following the assessment by accreditation body ANAB in Q1, NAFDAC's ISO 17025 accreditation was announced in January 2015. The certificate was presented by USAID/Nigeria Mission Director, Mike Harvey, highlighting USAID's support for health systems strengthening in Nigeria.

## **SENEGAL**

### Background

Since 2002, USAID and USP have been providing technical assistance to Senegal to strengthen their medicine QA/QC systems. An MQM program was launched in 2002 at five sentinel sites to monitor antimalarials. In 2009, the program expanded to four additional sentinel sites and began covering antiretrovirals, antituberculars, and contraceptive products.

Senegal's official medicines control laboratory (LNCM) has been working to obtain ISO 17025 accreditation. An important component of PQM technical assistance has been to strengthen the lab's compliance of with international quality management system (QMS) standards.

### Highlights and Success Stories

The MQM program is now implemented by LNCM, and is deemed sustainable as it has been incorporated into the country's PMS. PQM no longer implements this program.

Previous communication and educative campaigns laid the groundwork to establish an inter-ministerial committee with the aim of combatting counterfeit and substandard medicines in Senegal. All Ministries are part of this decree, which was signed by the Minister of Health. PQM is planning a workshop—to take place in Q3—with customs, DPM, and other stakeholders as part of implementing this decree.

### REGIONAL DEVELOPMENT MISSION FOR ASIA (RDM/A), MEKONG MALARIA

#### Key Regional Activities Covering Cambodia, Laos, Thailand, and Vietnam

##### Background

Malaria remains a disease of public health importance in the Greater Mekong Sub-region (GMS), the impact of which is compounded by increasing concerns about the emergence of artemisinin-resistant malaria, which might have arisen from, among other factors, availability and use of poor-quality antimalarials. Although there have been some improvements, there continue to be sporadic incidences of such products in the region requiring intensified and coordinated efforts of intervention.

##### Highlights and Success Stories

###### **Strengthening post-marketing surveillance capacity in key areas**

During Q2 support to FDQCC/FDD/BDFI in Laos was focused on assisting them to obtain additional funding from three sources:

- Global Fund's new funding mechanism which would provide needed funds for both malaria and health system strengthening
- Innovations in English grant system funded by the U.S. State Department to support improved English capacity in the FDQCC lab and FDD
- WHO's Emergency Response to Artemisinin Resistance (ERAR) which needs support to identify the needs for capacity strengthening in post-marketing surveillance of antimalarials complementary to PQM-supported sentinel sites

###### **Strengthening capacity of QC Labs**

Completing QC documents in English continues to be a challenge although some progress has been made. Attempts to increase funding as described above may help.

USP donated a retired gas chromatography machine to FDQCC. The machine has been installed in the lab, but supplies to run it are needed. The lab analysts will need some training to operate this machine to analyze pharmaceutical samples.

###### **Revitalizing in-country and regional collaboration, coordination - BREMERE**

The final submission of an article to the American Journal of Tropical Medicine was made this quarter, and publication is scheduled for April 2015. The article will showcase the efforts of USP globally, and discuss the state of poor quality medicines.

A database for BREMERE alerts is in development, with a first draft completed in Q2. This database will serve as a repository of information (with photos) related to substandard medicines communicated through the BREMERE alert system.

## BURMA

##### Background

The presence of poor quality antimalarials is among the many drivers contributing to antimalarial drug resistance in Burma, and the Mekong region in general. The PQM program in Burma provides a unique set of services to key stakeholders that manufacture, test, and regulate medicines with the goal of reducing the prevalence of poor quality medicines and reducing the spread of resistance in the region.

PQM provides technical assistance to the DFDA to address quality gaps across the antimalarial medicine's value chain in the country to increase the supply of quality assured medicines and uplift the national medicine regulatory system. This includes providing tailored support to the regulatory agency, national laboratory, and engaging with key players. PQM also aims to raise awareness on the quality

issues of medicines and updated information among the key stakeholders and general public to streamline the DFDA's efforts in tackling the poor quality medicines in collaboration with relevant collaborating partners.

#### Highlights and Success Stories

PQM assisted the DFDA to produce a paper on the quality of antimalarials in two border areas of Burma (Tamu and Muse) to be presented at the Burmese Annual Research Congress.

### **CAMBODIA**

#### Background

PQM provides technical assistance to the Royal Government of Cambodia in efforts to strengthen the country's medicines quality assurance program and quality control systems (QA/QC).

The PQM scope of work in Cambodia encompasses three objectives: Improving detection of poor-quality medicines and supporting the MOH to take action against counterfeit and substandard medicines and health products based on the results of testing; strengthening medicines QA/QC through building the capacity of the Department of Drugs and Food (DDF) and National Health Products Quality Control Center (NHQC); and raising awareness about medicines quality issues and improving access to medicines quality information among regulators, health care professionals, and the general public. To improve detection methods and QA systems, PQM helped establish an MQM program to support post-marketing surveillance of the quality of antimalarial and other infectious disease medicines in the marketplace.

#### Highlights and Success Stories

The Ministry of Health and the Ministry of Interior of Cambodia jointly committed to combat counterfeit and substandard medicines and illegal health services in order to protect and promote public healthcare.

This quarter, Good Pharmacy Practices (GPP) training was provided for inspectors, pharmacists, and medicines sellers, with a total of 167 participants. Since July 2014, 884 participants were trained in GPP in the country.

### **INDONESIA**

#### Background

The National TB Control program of Indonesia (NTP) faces many challenges in scaling up its efforts to control the spread of multi-drug resistant tuberculosis (MDR-TB) and extensively-drug resistant tuberculosis (XDR-TB). A multi-pronged approach has been developed by PQM in collaboration with the NTP and the National Agency for Food and Drug Control (NA-FDC) in support of TB control by increasing access to quality-assured anti-tuberculosis medicines from local and imported sources. PQM provides technical assistance to Indonesian manufacturers to support the submission of high-priority anti-TB medicines (1<sup>st</sup> and 2<sup>nd</sup> line) product dossiers for WHO Prequalification. PQM also builds the national and provincial capacity of NA-FDC through the development and implementation of medicines quality monitoring to enhance post-marketing surveillance of anti-TB and antibiotic medicines. In addition, PQM plays an important role by facilitating coordination among the NA-FDC national and provincial laboratories, the NA-FDC regulatory authority, the NTP, and local manufacturers to increase availability of and access to quality-assured, anti-TB and antibiotic medicines in Indonesia.

PQM sits on the Indonesian national Technical Working Group under GFATM and provides input into the overall leadership, management, coordination, and proposal development for the National TB Control Program and the Country Coordinating Mechanism (CCM), and under select Health Systems Strengthening grants. PQM has also been collaborating with the ASEAN Secretariat in Jakarta to develop regional programs for training and building capacity on GMP Inspection under PIC/S and on

BA/BE studies under the auspices of the ASEAN Pharmaceutical Products Working Group in light of ASEAN harmonization in 2015.

The PQM program received new funding from PEPFAR to engage in activities related to the scale up of treatment of HIV and STIs in Indonesia. PQM will begin engaging key partners, including the National AIDS Control Program at the Ministry of Health, international NGOs such as the Clinton Health Access Initiative, JSI, WHO, UNAIDS, and others on a national and local level to strengthen the quality assurance of antiretrovirals, STI medicines, and medicines used in the treatment of Opportunistic Infections associated with HIV infection. In addition, PQM will help develop and implement projects and provide technical input into the development of grant proposals under the New Funding Mechanism of the Global Fund, especially with a focus on HIV and TB joint proposals. PQM will also work with the primary manufacturer and importer of antiretrovirals in Indonesia, Kimia Farma, that is producing the majority of these medicines under a compulsory license granted under a Presidential Decree as part of the TRIPS agreement.

#### Highlights and Success Stories

PQM helped secure \$980,000 in grant funding from Global Fund to support TB medicines testing at BPOM provincial QC labs. This funding will roll out in Q3/Q4.

In collaboration with WHO, PQM Indonesia supported two workshops on the development and finalization of the Guideline for Sampling in the public sector in Indonesia. Coordination meetings among BINFAR, BPOM, and other relevant partners have been conducted over the past several months, and the draft guideline is now complete.

PQM substantially contributed to the National TB Program's 5-year Strategic Action Plan by incorporating specific budgeted activities on Quality Assurance of TB medicines and support for local manufacturers into the MOH's strategy.

Delays in the approval process for the FY15 work plan for Indonesia resulted from extensive changes in senior management at the government partner BPOM, as well as closeout of the previous project registration and the initiation of a new mechanism to conduct activities and provide TA under Indonesia's strict rules of engagement with foreign organizations. During Q2, the PQM team worked closely with BPOM, the Ministry of Finance, and USAID/Indonesia to finalize acceptance of all work plan activities under TB and HIV funding, and to gain approval from both BPOM and USAID to implement the project. PQM will now operate under the general government-to-government Assistance Agreement between The United States and the Republic of Indonesia. To accommodate for additional funding needs, USAID/Indonesia agreed to additional funding support of \$700,000, bringing the total budget for FY15 to \$2,050,000 USD.

## **PHILIPPINES**

### Background

PQM has been actively providing technical and professional assistance to the Philippines Food and Drug Administration (FDA) to enhance its regulatory capacity in evaluation and registration of pharmaceutical products through the introduction and build-up of internationally accepted quality standards, guidance, processes and procedures. Also providing technical assistance to the Department of Health (DOH) – National Center for Pharmaceutical Access and Management (NCPAM), National Center for Disease Prevention and Control (NCPDC) – National Tuberculosis Program (NTP), selected Local Government Units (LGUs) and Regional Offices (ROs) in an effort to strengthen medicine's Quality Assurance and Quality Control system (QA/QC) with emphasis on post-marketing surveillance through Medicines Quality Monitoring (MQM) for anti-tuberculosis and other essential medicines available in the market of the Philippines, and local pharmaceutical manufacturers towards WHO Pre-Qualification (WHO PQ) program.

### Highlights and Success Stories

In an effort to strengthen PQM efforts in the Philippines, USAID/Philippines has approved the hiring of three additional staff (two technical advisors and one office administrator) and the opening of a new PQM field office in Manila. These measures will help ensure efficiency and productivity. Currently, the office administrator has been hired and has begun work, while the process to hire the two technical staffs is ongoing.

## **VIETNAM**

### Background

In Vietnam, PQM has developed partnerships for over a decade with key stakeholders including, the National Institute for Malariology, Parasitology, and Entomology (NIMPE), the National Institute for Drug Quality Control (NIDQC), the Drug Administration of Vietnam (DAV), and the World Health Organization (WHO) -Vietnam. PQM has established nine sentinel sites for medicines quality monitoring (MQM), with three additional sites using leveraged funding from the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM). During FY15, PQM will provide technical assistance under three main objectives: i) Deliver technical assistance and capacity strengthening support for expanding operations and impact of National Quality Control Laboratories; specifically, for HCMC IDQC towards WHO Prequalification; ii) Provide technical assistance and engagement on local methadone production and procurement to support the government to reach their national treatment targets, and iii) Providing technical assistance for integrated delivery of a quality monitoring reporting system in recording and responding to adverse events.

### Highlights and Success Stories

PQM provided technical assistance to the Hanoi Provincial AIDS Center to assess the quality section of their tender and human resources capacity to review bid documents. Follow-up documents have been shared with them as well.

## **Europe and Eurasia**

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## **KAZAKHSTAN**

### Background

According to WHO, Kazakhstan is among the 27 high multidrug-resistant tuberculosis (MDR-TB) burdened countries in the world. TB control, and especially combating MDR and extensively drug-resistant TB (XDR-TB), is a priority in the Health Care Development Programme 2011–2015. The national budget for TB control has been increased to enable rapid scale-up of treatment for MDR-TB patients. Despite these efforts, universal access to treatment has not yet been achieved.

PQM began receiving funding from USAID/Kazakhstan in FY13 with the goal of improving the quality of anti-TB medicines produced by the major medicines manufacturers in the country. PQM's technical assistance will enhance the capacity of these manufacturers to comply with international GMP.

### Highlights and Success Stories

In October 2014, in partnership with the Regional Economic Cooperation/Chemicals, PQM sponsored a pharmaceutical plenary session of the Fourth Central Asia Trade Forum held in Almaty. PQM staff arranged a meeting of Kazakhstani manufacturers of second-line anti-TB medicines (Romat Pharmaceutical Company and Nobel Almaty Pharmaceutical Factory) with representatives of Hanmi Fine Chemicals of Korea, manufacturer of Moxifloxacin API.

As a result of the meeting, Nobel Almaty Pharmaceutical Factory entered into a contract with Hanmi Fine Chemicals for Moxifloxacin API. In January 2015, Nobel purchased the API, manufactured a pilot batch of Moxifloxacin FPP, and started stability studies of the finished product.



Having a reliable source of the Moxifloxacin API will allow Nobel Almaty Pharmaceutical Factory to manufacture high quality FPP, and Nobel will be able to supply a high quality anti-TB medicine to the Kazakhstani market. Nobel is also interested in WHO prequalification of their Moxifloxacin FPP. Thus, the contract between Nobel Almaty Pharmaceutical Factory and Hanmi Fine Chemicals will potentially increase access to WHO-prequalified second-line anti-TB medicines both in Kazakhstan and abroad.

## **UZBEKISTAN**

### Background

According to WHO, Uzbekistan is among the 27 high MDR-TB burden countries in the world. Starting in 2015, the national government will assume greater responsibility for procurement of first-line TB medicines.

PQM began receiving funding from USAID for Uzbekistan in FY14. PQM's technical assistance will enhance the capacity of the local manufacturer to comply with international GMP and strengthen quality assurance systems of the country.

*Note:* PQM has been waiting for a formal request from the Uzbekistan Ministry of Health for technical support from PQM. Meanwhile the activities in Uzbekistan are on hold. Workplan FY15 was not submitted to USAID/CAR.

## **Latin America and the Caribbean**

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### **AMAZON MALARIA INITIATIVE (AMI)**

#### Background

AMI is an initiative whose primary role is to focus the USAID Latin American and the Caribbean (USAID/LAC) Bureau's financial assistance toward improving malaria control and decreasing national morbidity and mortality in LAC countries. Since its inception, AMI has provided assistance to six South American countries (Brazil, Colombia, Ecuador, Guyana, Peru, and Suriname) and subsequently additional countries in Central America and the Caribbean were included. AMI is currently being implemented and coordinated by five international partners: The Pan American Health Organization (PAHO), the U.S. Centers for Disease Control and Prevention (CDC), Systems for Improved Access to Pharmaceuticals and Services (MSH/SIAPS), Links Media, and PQM. PQM's role in AMI is to strengthen country QA/QC systems to ensure the quality of antimalarials throughout the supply chain. During the few years, PQM's emphasis in LAC has been on sustainability, firstly through MRA institutionalization of the Three-level Approach for MQM activities, and secondly, through exploring sustainable mechanisms to facilitate south-south collaborations, in order to utilize the extensive human and technical resources existing in the region.

#### Highlights and Success Stories

During the November 2014 workshop to explore sustainable mechanisms for south-south collaboration for medicines QA, held by PQM in Peru, two committees were assembled to develop two documents: 1. surveillance forms to collect information on country needs, and 2. concept notes to be presented to the MOHs of the countries. Since then, surveillance forms to assess MRA and OMCL capabilities and needs for medicines quality assurance were finalized and distributed to countries. In total, 26 institutions from 15 countries returned their forms. These noted that extensive regional resources exist and discussed how those resources may address needs if collaboration mechanisms are established.

### **GUATEMALA**

#### Background

PQM performed a two-country study requested and financed by USAID's Maternal and Child Health Latin American and the Caribbean (MCH-LAC) Bureau. The objective of the study, carried out in Guatemala and Peru in 2011, was to assess the quality of emergency obstetric and newborn

medicines. The evaluation, performed in the Santa Rosa Health Area in Guatemala, uncovered several quality issues and system deficiencies, including, (1) a 27% failure rate of the tested medicines; (2) inadequate storage conditions at central and peripheral facilities; (3) technical capability gaps at the Unidad de Medicamentos from the Laboratorio Nacional de Salud, Guatemala's Official Medicines Control Laboratory (OMCL); and (4) QC procedural and documentary deficiencies during procurement of medicines by the Ministerio de Salud Pública y Asistencia Social (Guatemalan MoH)

To address some of those issues, USAID/Guatemala obligated funds for PQM from FY11 to FY14. Using remaining FY14 funds, PQM activities in FY15 will be to support the expansion of the OMCL's ISO 17025 accreditation, from a product-based (acetaminophen) to a method-based accreditation. This expansion will require transferring the accreditation from the current grantor, the Guatemalan National Accreditation Body, to ANAB (ex-ACLASS), an international accreditation body.

## **Middle East**

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### **WEST BANK/GAZA**

#### Background

Beginning in FY14, PQM will provide technical support for manufacturers in West Bank/Gaza to meet Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) certification, similar to the support being provided for manufacturers seeking WHO prequalification.

#### Highlights and Success Stories

PQM conducted a baseline assessment of four Palestinian manufacturers, organized meetings with key stakeholders, visited the MOH Palestinian Authority and the NQCL, and conducted a rapid assessment of Palestine's QA/QC capacities.

### **PAKISTAN**

#### Background

Beginning in FY15, PQM will provide technical support to strengthen the Drug Regulatory Authority of Pakistan to ensure the quality assurance and quality control systems of medicines, particularly essential maternal and child health medicines, in the Pakistan market. In addition, PQM will focus on building the capacity of the official Medicines Quality Control Laboratories in the country and assist them to become internationally recognized (such as through WHO PQ). PQM will also provide technical assistance and resources to local manufacturers to achieve internationally accepted standards and requirements to produce quality-assured medicines.

#### Highlights and Success Stories

An assessment of the country's QA/QC systems and an initial assessment of selected manufacturers producing Chlorhexidine gel products both took place, March 27-April 12, 2015. A detailed report on the findings, as well as a workplan, will be distributed in Q3.