



PROMOTING THE QUALITY OF MEDICINES

# Promoting the Quality of Medicines (PQM)

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**Annual Report on Activities  
for October 1, 2013 – September 30, 2014**

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## USAID OBLIGATIONS FOR PQM ACTIVITIES

Implemented October 1, 2013 – September 30, 2014

The complete list of obligations and the funding pipeline will be sent as a separate document.

\$5,755,955	Core funding
\$3,686,751	Sub-Saharan Africa
\$2,669,140	Southeast Asia Region
\$750,000	Europe and Eurasia
\$600,000	Latin America and the Caribbean
\$1,000,000	Pakistan
<b>\$14,461,846</b>	<b>Total obligated</b>

## WHERE PQM WORKS

October 1, 2013 – September 30, 2014

<b>Africa</b>	Angola, Burundi, Ethiopia, Ghana, Guinea, Kenya, Liberia, Mali, Mozambique, Nigeria, Senegal, Zimbabwe
<b>Asia</b>	Burma, Cambodia, China, Indonesia, Laos, Philippines, South Korea, Taiwan, Thailand, Vietnam
<b>Europe/Eurasia</b>	Georgia, Kazakhstan, Uzbekistan
<b>Latin America and Caribbean</b>	Bolivia, Brazil, Colombia, Ecuador, Guatemala, Guyana, Mexico, Peru, Suriname
<b>Middle East</b>	West Bank

This list includes countries where PQM receives USAID Mission funding as well as countries covered under Core funding.

## 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 provided technical assistance to 35 countries in FY14, strengthening their national capacity in quality assurance and quality control systems in efforts to combat the availability of substandard and counterfeit medicines.

One approach PQM has employed is helping national quality control laboratories (NQCLs) operate with good laboratory practices and become ISO/IEC 17025:2005 accredited or World Health Organization (WHO) prequalified, both globally-recognized standards of proficiency. In FY 14, PQM assisted thirteen NQCLs in Africa, Asia, and Latin America. The NQCLs of Ghana and Laos achieved ISO 17025:2005 accreditations this year, the NQCL of Ethiopia was re-accredited, and several labs have ISO/IEC 17025:2005 accreditations or WHO prequalifications pending. In addition, the USP Center for Pharmaceutical Advancement and Training (CePAT) in Ghana received ISO/IEC 17025:2005 accreditation this year with assistance from PQM staff.

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.

PQM also assists countries improve and streamline their medicine registration systems to strengthen regulatory authorities' quality assurance. This year in Ethiopia, for example, PQM drafted guidelines and reviewed backlogs of dossiers, and in Guatemala, PQM installed new web-based registration software and trained users on how to implement it.

Through MQM, improving the technical capacity of NQCL staff through training and internships, and installing registration software, 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**

In cooperation with WHO and the Global Drug Facility (GDF), PQM conducted three workshops (in Indonesia, Morocco, and the Philippines) in FY14 to inform manufacturers of anti-tuberculosis (TB) medicines how to produce quality-assured medicines by following good manufacturing practices (GMP). The workshops explained the WHO Prequalification Program, raised interest in participating, and described how PQM can help in the process.

At the beginning of FY14, PQM was working with 35 manufacturers in 11 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. By the end of FY14, PQM was working with 47 manufacturers in 13 countries. Notably, 3 anti-TB medicines became WHO Prequalified with assistance from PQM this year: Hisun Pharma's Capreomycin active pharmaceutical ingredient (API) and Capreomycin finished pharmaceutical product (FPP) as well as Zhejiang Langhua's Levofloxacin API.

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.

Through its work on GMP, PQM has strengthened its relationships with WHO, GDF, and UNICEF and expanded its role in preparing manufacturers medicines for WHO Prequalification.

In addition to working internationally to increase the supply of quality assured medicines, USP headquarters in Rockville contributes to these efforts by creating monographs for medicines. In FY 14, USP finalized a monograph for DHA-PIP Fixed Dose Combination and drafted one 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. PQM staff participated in several conferences in FY 14, speaking about the importance of medicines quality and the global public health implications of substandard and counterfeit medicines. USP promotes PQM programs through press releases (7 this year) and social media updates. PQM leadership uses every speaking engagement and media interview—local, national, and international—to drive home the message of the importance of medicines quality to successful treatment outcomes.

Each PQM country program includes activities to raise public awareness about SCMs and the importance of medicine quality assurance. This year, PQM published five articles on these topics in five journals: Bulletin of the World Health Organization, American Journal of Tropical Medicine and Hygiene, Malaria Journal, Pharmaceutical Regulatory Affairs, and the Journal of Tropical Medicine and Surgery.

#### **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. In Kenya, for example, the MRA quarantined failed antimalarials found during MQM, and in Liberia, more than 10 regulatory actions were taken against failed products, which included banned monotherapies and unregistered products, as well as counterfeit and substandard products. In Cambodia, the Inter-Ministerial Committee removed the registration numbers of products that failed quality testing and subsequently banned all product registrations from the manufacturer in question. In Burma, the results from MQM activities conducted in two border areas led the MRA to publish a list of illegal medicines found in the market in the national newspaper.

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 FY14, in conjunction with Boston University, PQM supported 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 FY 14, following promising field-testing conducted at the CePAT facility in Ghana, PharmaChk was awarded a \$2 million transition-to-scale grant from Saving Lives and Birth.

## ACRONYMS

AMRH	African Medicines Regulatory Harmonization
ANEQAM	Asian Network of Excellence in Quality Assurance of Medicines
API	Active Pharmaceutical Ingredient
ASEAN	Association of Southeast Asian Nations
ATB	Anti-tuberculosis
BA	Bioavailability
BE	Bioequivalence
BINFAR	Pharmaceutical and Medical Production and Distribution Services
BREMERE	Building Regional Expertise in Medicines Regulation, Information-sharing, Joint Investigation, and Enforcement
CAPA	Corrective and Preventive Action
CAP-Malaria	Control and Prevention of Malaria
CDC	U.S. Centers for Disease Control and Prevention
CHD	Center for Health Development
CHX	Chlorhexidine
CRO	Contract Research Organization
DAV	Drug Administration of Vietnam
DDF	Department of Drugs and Food
DF	Pharmaceutical Department
DOH	Department of Health
DOMC	Division of Malaria Control
DPM	Direction de la Pharmacie et des Medicaments
DQI	Drug Quality and Information Program
FDA	Food and Drug Administration or Authority
FDB	Food and Drug Board
FDC	Fixed Dose Combination
FMHACA	Food, Medicine and Health Care Administration and Control Authority
FPP	Finished Pharmaceutical Product
GCP	Good Clinical Practices
GMP	Good Manufacturing Practices
GMS	Greater Mekong Sub-region
HCMC	Ho Chi Minh City, Vietnam
IMC	Inter-Ministerial Committee
INSP	National Institute of Public Health
IPT	Inter-laboratory Proficiency Testing
LAC	Latin America and the Caribbean
LGU	Local Government Unit
LMHRA	Liberian Medicines and Health Products Regulatory Authority
LNCM	National Laboratory for Medicine Quality Control
MDR-TB	Multi-Drug Resistant Tuberculosis
MOC	Memorandum of Collaboration
MOH	Ministry of Health
MQCL	Medicines Quality Control Laboratory
MQDB	Medicines Quality Database

MQM	Medicine Quality Monitoring
MRA	Medicines Regulatory Authority
MSH/SIAPS	Management Sciences for Health/Systems for Improved Access to Pharmaceuticals & Services
MSH/HCSM	Management Sciences for Health/Health Commodities and Services Management
NA-FDC	National Agency of Food and Drug Control
NHQC	National Health Products Quality Control Center
NIDQC	National Institute for Drug Quality Control
NIMPE	National Institute for Malariology, Parasitology and Entomology
NOMCOL	Network of Medicines Control Laboratories
NQCL	National Quality Control Laboratory
NTP	National Tuberculosis Program
OI	Opportunistic Infection
OMCL	Official Medicines Control Laboratory
ORS	Oral Rehydration Salts
PAC	Provincial AIDS Committee
PAHO	Pan American Health Organization
PEPFAR	President's Emergency Plan for AIDS Relief
PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
PMI	President's Malaria Initiative
PNILP	Programme National Intégré de Lutte contre le Paludisme
PPB	Pharmacy and Poison Board
PQ	Prequalification
PQAD	Product Quality and Assessment Directorate
PQM	Promoting the Quality of Medicines Program
QA	Quality Assurance
QC	Quality Control
QMS	Quality Management System
RDMA	Regional Development Mission for Asia
SL-ATB	Second-Line Anti-Tuberculosis
SOP	Standard Operating Procedure
SSFFC	Substandard/spurious/false-labeled/falsified/ counterfeit
TA	Technical Assistance
TAP	Technical Assistance Program
TB	Tuberculosis
TWG	Technical Working Group
UCAD	University of Cheikh Anta Diop
UN	United Nations
USAID	United States Agency for International Development
USP	United States Pharmacopeia
WB	World Bank
WHO	World Health Organization



## Promoting the Quality of Medicines (PQM) Program Annual Report on FY14 Activities

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.

##### Key Activities

#### **Increase awareness about the importance of medicines quality**

Over the course of the year, PQM staff participated in and presented at several conferences speaking about the importance of medicines quality and the global public health implications of substandard and counterfeit medicines. These conferences included, among others, the ASTMH Global Health Conference, Global Health Mini-University at GWU, JHU Global Access to Medicines Conference, and the Novartis Malaria Initiative Workshop.

To further advocate for the need for medicines quality assurance, PQM published an editorial on the Medicines Quality Database (MQDB) in the Jan 2014 issue of the Bulletin of the World Health Organization and also drafted three case studies (on successful activities in Liberia, Ghana, and Cambodia) for the USAID HSS global call for case studies. USP helped PQM increase awareness about the importance of medicines quality by generating seven press releases and various social media updates.

#### **Produce up-to-date information about current issues in medicines quality**

On PQM's website, a total of 26 new articles, 2 videos, 28 photos, and 28 new or updated resources were added this fiscal year. In addition, 107 new reports were included with the *Media Reports on Medicine Quality*.

#### **Support regional approaches and networks to improve QA/QC of medicines**

This year, PQM representatives attended three meetings (in November 2013, March 2014, and August 2014) of the New Partnership for Africa's Development (NEPAD) African Medicines Regulatory Harmonization (AMRH) Technical Working Group (TWG). NEPAD has designated 10 institutions as Regional Centers of Regulatory Excellence (RCOREs) and drafted guides for the RCOREs to follow.

## **Explore improved tools to ensure quality control or increase the knowledge base about QA**

Dr. Chibwe and representatives from Boston University (BU) and the Center for Integration of Medicine and Innovative Technology conducted field studies of the PharmaChk device at USP's Center for Pharmaceutical Advancement and Training (CePAT) in Ghana in March. Dr. Chibwe and Mr. Roth visited BU in April to carry out post-field testing. In August, PharmaChk received a \$2 million transition-to-scale grant from *Saving Lives at Birth: A Grand Challenge for Development*. This funding will help further PharmaChk's development and bring it closer to commercial production and availability.

*\* Core HIV/AIDS funds also contributed to PharmaChk prototype preparations and field studies.*

## **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.

### Key Activities

#### **Monitor antimalarial quality and the extent of diversion from the public to private sector**

PQM completed studies in Nigeria and Ghana, and the data collected was shared with the relevant stakeholders. However, as a result of the ongoing Ebola outbreaks, several additional studies were not performed.

#### **Improve knowledge about the quality of antimalarials in PMI countries**

During FY 14, USP laboratory staff tested:

- Artemether and Lumefantrine tablets for Kenya
- Sulfadoxine and Pyrimethamine Tablets for Kenya
- Mefloquine Tablets for Myanmar
- Artesunate for Injection and Artesunate Tablets (to support the PharmaChk investigation)

#### **Increase the availability of standards and testing methods for selected antimalarials**

The medicines compendium monograph for dihydroartemisinin-piperazine tablets was completed and is publicly available. Additional monographs for antimalarial medicines are still in development.

### Challenges

The quality and diversion studies were postponed in all West African countries due to Ebola outbreaks.

## **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

#### Key Activities

##### **Increase the supply of quality assured maternal, newborn, and child health medicines**

In FY14, PQM continued to work with manufacturers to increase the supply of quality assured maternal, newborn, and child health medicines. PQM's work expanded to including a magnesium sulphate injection manufacturer. Technical assistance to LaGray Pharmaceuticals was continued in the form of the procurement of validation services for essential utilities (HVAC, water system).

PQM continued work on WHO prequalification of Magnesium sulphate, manufactured by Galychpharm in Ukraine. PQM reviewed the site master file and provided comments to the company. After PQM gave them recommendations for a new API source, Galychpharm began working to get approval for a new API supplier and manufacturer.

##### **Monitor maternal, newborn and child health medicines quality**

The validation data in support of the chlorhexidine topical gel monograph was completed. A new monograph will be drafted that includes a stability-indicating HPLC assay for content and impurities. End-product testing required of manufacturers will be more cost-effective with the new assay. Product testing continued for zinc, amoxicillin, and others.

##### **Support USAID medicine quality initiatives related to UN Commission Activities**

PQM continued to be the leader on issues related to medicine quality for UN Commission activities.

## **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.

#### Key Activities

##### **Increase the supply of quality-assured second-line TB medicines**

Three medicines received WHO PQ: Hisun API and FPP for Capreomycin as well as Zhejiang Langhua API for Levofloxacin. In addition to the PQ approvals, four API MF/FPP dossiers were submitted to WHO.

PQM continues to work with manufacturers in China, Georgia, Ghana, India, Indonesia, Korea, Mexico, Philippines, Taiwan, Vietnam, and Zimbabwe.

##### **Collaborate with GDF and WHO PQ to conduct workshops in a country with a high burden of TB and identify additional promising manufacturers not yet in the PQM pipeline.**

Three workshops were conducted this year in the Philippines, Morocco, and Indonesia. In the Philippines, ten manufacturers attended from Thailand, Vietnam, Cambodia, and the Philippines. Three manufacturers expressed interest in receiving PQM TA. In Morocco, 20+ manufacturers attended the workshop, and three manufacturers expressed interest. In Indonesia, PQM conducted the workshop in conjunction with CPHI Jakarta. 21 participants attended the seminar, and one-on-one meetings were held with manufacturers interested in receiving in-depth information of the WHO PQ program or to discuss their current status.

**Continue to work closely with GDF and WHO and participate in their meetings with manufacturers to discuss prequalification.**

PQM staff traveled to the GDF Stakeholders meeting.

**Conduct operational research to identify substandard/counterfeit second-line medicines on the market**

No issues have been brought to PQM's attention.

**Develop OEM for at least two critical second-line and/or third-line anti-TB medicines**

Work was initiated for 1g Capreomycin (Baush Pharma) and 1 and 0.5g Kanamycin FPPs (Interpharma).

**Support research to improve quality and yield of kanamycin through genetic engineering**

An RFA was drafted and published.

**Obtain comparator products and assist select manufacturers with funding for bioequivalence (BE) studies**

Comparator products and reference standards have been purchased and sent to manufacturers in Korea, Indonesia, Nepal, Vietnam, Zimbabwe, Philippines, and Morocco. A contract was completed and implemented to support Dong-A Pharm's BE study.

**Develop public standards (pharmacopeial and Minilab<sup>®</sup> methods) for screening the quality of second-line anti-TB medicines**

No Minilab or pharmacopeial methods were published.

**Develop Minilab<sup>®</sup> test methods for second-line, or possibly third-line, anti-TB medicines (injectable and tablet/capsule)**

No Minilab or pharmacopeial methods were published.

**Develop USP monographs for prothionamide and terizidone**

No Minilab or pharmacopeial methods were published.

Challenges

If an API manufacturer also manufactures the FPP, the manufacturer is often not willing to sell this API to another manufacturer, for worry of competition, causing vertical integration.

**Africa** \_\_\_\_\_

**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.

Key Activities

An assessment of the MOH was conducted in January 2014. Upon completion of the assessment, a work plan was drafted and forwarded to USAID/Angola. However, due to a change of staff at the mission, PQM has been unable to receive any feedback on proposed activities. Follow-up e-mails sent after the initial visit from Dr. Maria Miralles of USAID/Washington yielded no return feedback.

### Challenges

PQM has not been able to start fully working in-country.

## **BURUNDI**

### Background

Beginning in 2012, PQM was selected to provide technical, strategic, and operational assistance to strengthen medicines quality assurance in Burundi. PQM was asked to propose interventions that will help ensure the adequate quality of antimalarial medicines in the country. In 2013, the President's Emergency Plan for AIDS Relief (PEPFAR) obligated funding for PQM through USAID/Burundi to contribute to the improvement of the quality of HIV-related medical products in the country.

### Key Activities

\*\* Since approval of the work plan was not obtained until August 2014, the implementation of activities is planned to continue until the end of December 2014\*\*

#### **Assess the medicines QA/QC system in Burundi**

PQM met with local stakeholders to conduct a rapid assessment of the QA/QC system in Burundi. The partners included the Directorate of Pharmacy, Medicines and Laboratories (DPML), the National Institute of Public Health (Institut National de la Santé Public, or INSP), the Central Medical Store (Central d'Achat des Medicaments de Burundi, or CAMEBU), the National Council for the Fight against AIDS (Conseil National pour la Lutte contre le Sida, or CNLS), National AIDS Control Program, the World Health Organization-Burundi, and MSH. Following the assessment, PQM developed a work plan that focuses on priority activities for strengthening the capacity of DPML, INSP QC lab, and CAMEBU.

#### **Strengthen the post-marketing surveillance of medicines**

PQM procured laboratory supplies and one Minilab<sup>®</sup> for screening medicines samples. This will be based at INSP which has the mandate to conduct medicines quality control testing. PQM discussed stakeholder responsibilities with local partners regarding monitoring the quality of medicines in Burundi. Training in sampling and screening tests is planned for the end of November 2014. DPML will conduct the sampling in the field. INSP will carry out sample screening (using the Minilab) as well as confirmatory testing.

#### **Strengthen the medicines quality control laboratory of INSP**

PQM procured laboratory supplies and a new HPLC system for the QC lab of INSP. An initial training on Good Laboratory Practices was provided to lab staff. Training in analytical methods will be provided before the end of the calendar year.

In addition to PEPFAR support, the INSP QC lab is benefiting from USP initiatives. The lab has joined the USP Technical Assistance Program and received \$25,000 worth of USP reference standards and reference books. Furthermore, USP is sponsoring the participation of two lab staff in QC training at the Center for Pharmaceutical Advance and Training (CePAT) in November in Ghana.

#### **Strengthen the capacity of the medicine regulatory authority (DPML)**

PQM has identified software for drug registration that could be used by DPML to facilitate the registration process. DPML does not have the ability to carry out such processes in full. PQM will procure the software and facilitate training of DPML staff by December 2014.

## **Strengthen the capacity of CAMEBU**

PQM is in the process of seeking closer coordination with the Association of Central Medical Stores of Africa (ACAME) to provide technical support to CAMEBU in its effort to establish a quality management system. PQM will coordinate with an expert designated by ACAME to support CAMEBU.

## **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.

### Key Activities

#### **Strengthen the performance of Product Registration and Licensing Directorate of FMHACA**

Development of tools:

- Finalized and published Good Manufacturing Practice Guideline for Pharmaceutical Products- 300 published copies were submitted to FMHACA.
- Finalized the Guidance on Training and Qualification Requirement of GMP Inspectors. The guidance was submitted to FMHACA and is awaiting approval.
- Finalized Foreign GMP Inspection Application Form. The guidance was reviewed and submitted to FMHACA for approval.
- Finalized Guidance on writing GMP Inspection Reports. Guidance reviewed and submitted to FMHACA and is awaiting approval.
- Finalized Medicine Manufacturing Establishment Directive and submitted it to FMHACA; awaiting approval.
- Finalized directive for foreign medicine manufacturers GMP inspection and submitted it to FMHACA; awaiting approval.
- Guideline for registration of medicines common technical document (CTD) reviewed and posted on FMHACA's website; this is in the printing process.
- Guideline for registration of medical devices approved and in the printing process.
- Developed draft Guideline for submission of variation in medicines application; the guideline is being reviewed.
- Guidance for Biowaiver draft was prepared and being reviewed.
- Inventory list of tools essential for effective regulatory management was developed and submitted to FMHACA.
- Biological manufacturers GMP inspection check list is being drafted.
- GMP and GCP fee structure drafted and sent to FMHACA.
- GMP inspection manual is being drafted.

Trainings:

- USP/PQM staff provided technical support for in-house training on dossier assessment for 23 FMHACA staff.
- Organized a five-day training workshop on basic GMP for 33 trainees (16 from FMHACA, 16 from veterinary drugs and feed control and administration authority, and 1 from BFPI)

- Provided advanced GMP training for 12 pharmacists from FMHACA and FBPI in Addis Ababa

#### Technical Support:

- Assisted in the assessment of 391 dossiers which have been in backlog for the past two years. The result showed almost 90% of them to be incomplete as per the requirements of the registration process.
- Seven different medicines registration checklists for registration of medicines were updated and sent to FMHACA: 1. Human medicine new application evaluation checklist, 2. New Medicine Pre-screening Checklist, 3. New Medicine by SRA Pre-screening Checklist, 4. Human Medicine Re-Registration Evaluation Checklist, 5. Re-registration Medicine Pre-screening Checklist, 6. New Medicine by SRA Assessment Checklist, 7. Variation Medicine Pre-screening Checklist

### **Strengthen FMHACA's Product Quality Assessment Directorate (PQAD)**

#### **Trainings:**

- A one week training on analytical method validation techniques was given for 18 FMHACA staff
- Supported training of 4 PQAD staff on female condom quality control methods and ISO 4074 at VALENDOR laboratory in Mauritius
- A fifteen-day training was given for 4 FMHACA staff on female condom testing at VALENDOR
- A five day in-country training on male condom testing machine maintenance was given to 8 staff by VALENDOR and ENERSOL

#### **Technical assistance:**

- Supported FMHACA to maintain the seven physico-chemical test methods which have been ISO 17025 certified
- Supported pre-assessment of the PQAD laboratory by WHO assessor
- Maintenance and qualification of VALENDOR branded condom testing machine was carried out. A report on qualification of VALENDOR branded instruments was prepared by VALENDOR and submitted to USP
- The condom lab participated in PT organized by FHI-360 and Enersol
- Supported maintenance and qualification of Enersol condom QC instruments and training 4 FMHACA staff on condom testing machine maintenance
- Supported calibration of 61 PQAD instruments by CCG of Egypt
- Supported maintenance of 2 HPLCs, 1 AAS, and 1 FTIR instruments of PQAD

### **Assist local medicines manufacturers toward GMP compliance and WHO PQ**

- Provided advanced GMP training to 11 staff from local manufacturers in Addis Ababa

### **Strengthen FMHACA branch laboratories**

- Installed laboratory instruments at the Southern Branch of FMHACA and provided training to the lab staff on how to use the instruments
- A two-week hands-on training was given to four branch FMHACA staff on basic analytical techniques and quality management system

### **Strengthen post-marketing surveillance of the quality of ARV and OI medicines circulating in the country**

- Guideline prepared for conducting PMS of ARV and OI medicines circulating in the country
- Laboratory supplies and reference standards required for PMS of selected ARV and OI medicines procured and supplied to FMHACA
- Three workshops were organized to promote public awareness on the problem of the illegal trade of medicines and food in Amhara and Tigray regions

- Collection of samples of antimalarial, ARV and OI medicines completed from all sites
- Testing of PMS samples finalized

### **Strengthen regional/city administration medicine regulators**

- Assessment of Oromia Regional Food, Medicine and Healthcare Regulatory Core Processes undertaken and reports shared with USP/HQ and Oromia region
- Assessments of Southern Nations Nationalities and Peoples Regional Health and Health related Services and Products Quality Control Authority conducted and report shared with the region.
- A five-day training on regulatory inspection and health system supervision was provided to staff from 5 regional/city administration authorities in Accra, Ghana

### **Assist PFSA in establishing internal quality control Laboratory**

- Agreement reached with SCMS/MSH to partition PFSA's laboratory

### **Challenges**

- High turnover of staff in the Product Registration and Licensing Directorate, especially senior staff who had received trainings in-country and abroad. In addition, there is frequent reshuffling of staff between directorates and regional regulatory bodies.
- Slow response from FMHACA delaying implementation of planned activities.

## **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.

### **Key Activities**

#### **Support round 6 of post-marketing surveillance of antimalarial medicines at the 7 sentinel sites in Ghana and encourage the FDA to take enforcement actions based on the results of MQM data**

MQM for FY13 was delayed due to contractual delays, and the last round of testing is currently being tested by the FDA Ghana lab. Additionally, the FDA lab was focusing on preparing for ISO 17025 accreditation, so most efforts were focused on obtaining that goal. After obtaining the accreditation in July, the lab is now focusing on completing the MCH and antimalarial testing. Results for the first round of testing from FY13 were forwarded to PQM, and refresher training for inspectors was later conducted by FDA Ghana in late July 2014. PQM procured necessary reagents and supplies as well as reference standards that would be needed for the confirmatory testing at the lab. Five vials of oxytocin and five vials of ergometrine USP reference standards were shipped to FDA Ghana lab. FDA Ghana is currently working on the testing of the MQM samples, and confirmatory testing is to be completed in October. Training was completed and the sampling and testing is ongoing. As there are no confirmed results, no enforcement actions have been taken; only Minilab preliminary results are available.

#### **Strengthen the capacity of the national Food and Drugs Authority laboratory and assist them toward ISO 17025 accreditation**

Preparations for ISO 17025 were delayed at the beginning of the fiscal year due to the delay in the move of FDA Ghana lab to the new facility. In September 2013, FDA moved to the new site, and PQM assessed the lab's QMS in preparation for the ISO 17025 audit. Throughout Q1, PQM provided consumables that were needed for the accreditation. In November, PQM also helped install key equipment for the scope of accreditation and conducted training on key topics like Good Documentation Practices, Safety in the Lab, Karl Fischer, FTIR, and ISO 17025 training. A confidential report was forwarded to FDA senior management to work on corrective actions to remediate the observations.

PQM also assisted the staff with correcting the findings. In January, a follow-up trip took place to review the improvements after the November trainings. During the February 2014 trip, Ms. Okafor worked with the Quality Assurance Team of the Laboratory Services Department (LSD) to correct observations from PQM's assessment of their Quality Management System (QMS) during the November 2013 visit; key documents were completed and submitted to ACLASS, the accreditation body that will conduct the ISO 17025 audit, and an April 2014 date was set for the audit. The laboratory chemists were also trained for their demonstration techniques and how to properly answer questions during the audit. Key staff were also trained on the following in preparation for the audit: KF, root cause analysis, Loss on Drying, USP-NF General Notices and Understanding Monographs, effectively reviewing laboratory notebooks, and Uniformity of Dosage Unit. Due to procurement issues at FDA, PQM provided key items to prevent delay of the accreditation audit, like ISO traceable pH buffer solutions, dissolution bath covers, HPLC columns, mini printer for the Karl Fischer, and water standard and solutions for the Karl Fischer. PQM conducted technical training with FDA staff in preparation for the audit by ACLASS in April. PQM gave the QA team training on root-cause analysis, reviewed key documents, and helped finalize the documents for submission to ACLASS. Auditor-auditee etiquette training was given to technical and QA staff to prepare them to respond to auditor questions. In July 2014, FDA became officially accredited for eight tests by ACLASS.

### **Provide training for more FDA staff involved in GMP inspections in the use of the risk-based compliance module as well as capacity building for strengthening the GMP Inspectorate Quality System**

GMP training took place at FDA Ghana with key inspectorate in September 2014.

### **Include MQM data in the PQM medicine quality database (MQDB) and analyze trends to provide a basis for informed decision making**

The available results that were completed by FDA Ghana lab were submitted for inclusion in the MQDB. Once the lab completes the stipulated rounds and makes the results available, that data will be submitted to the MQDB. Results from the samples confirmed from the FY13 round 1 have been forwarded to PQM and are being analyzed by PQM consultants for the MQDB. Once the second round of data is complete, it will be included in the database.

### **Collaborate with the Maternal Health Channel of Creative Storm Network to develop public sensitization programs**

Upon further discussion with USAID about the work plan, this particular objective was revised by USAID/Ghana for PQM to focus on testing the MCH samples and the technical aspects of sample collection, testing, and analysis of results. Funds were transferred in July, and samples were collected and are now undergoing confirmatory testing now at the lab. Since emphasis is to remain on MQM, PQM provided all necessary tools, consumables, and standards for MCH testing.

### Challenges

The challenges involve the Public Procurement Act of Ghana which impacts procurement of chemicals, reagents, and consumables in the lab. PQM was able to intervene and provide a number of key consumables that were critical for the ISO 17025 accreditation of the lab. Another challenge faced was technical management attitude and implementation of the quality management system, but PQM was able to work with senior FDA management and the lab to resolve these issues.

## **GUINEA CONAKRY**

### Background

PQM was selected to provide technical, strategic, and operational assistance to strengthen medicines quality assurance in Guinea.

### Key Activities

\*\* Many activities planned for this year have been postponed because of the Ebola outbreak\*\*

PQM conducted the following activities:

1. Trained on Minilab® basic tests, visual and physical inspection, disintegration, thin layer chromatography, good laboratory practices, and good documentation practices
2. Met with relevant partners to discuss implementing the remaining activities for the current fiscal year and planning activities for the next year

The training was provided to 20 participants (18 from the National Quality Control Laboratory and 2 inspectors from Lobe and Kobe regions). As a result of the Minilab® training, the participants were able to test the quality of selected antimalarials using basic test methods and to identify a counterfeit medicine.

During the training, the Minister of Health, Médecin Colonel Rémy LAMAH, other government officials, USAID, and DNPL staff paid an official visit to the lab which was filmed by the local Guinean radio/television media. The video of the ceremony was later broadcast on YouTube. (See <http://youtu.be/F-C3nMMmH54>.)

## **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® 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.

### Key Activities

#### **Continue strengthening medicines quality monitoring (MQM) of antimalarial medicines at the existing sentinel sites and expand it to new sites**

In collaboration with the Malaria control program and PPB, six counties have been added to the existing five sites. PQM procured 6 new Minilabs and delivered them to NQCL, where they were then dispatched to the new counties.

PQM provided training on Minilab basic tests, sampling strategies, and reporting for 22 staff from the 11 sites. PQM visited 3 sites and one port of entry; during these visits, 5 antimalarial samples failed quality testing using Minilabs.

**Continue encouraging regulatory actions by sharing MQM evidence-based data with relevant stakeholders and by raising awareness about poor-quality medicines circulating in the Kenyan market**

Five regulatory actions were taken by PPB on the five non-conforming antimalarials

**Continue strengthening the NQCL laboratory capacity and assist it to improve its QMS and to reach ISO 17025 accreditation**

PQM prepared NQCL for the first ISO 17025 accreditation audit by the SANAS assessor, reviewed SANAS findings with NQCL staff and the director, and discussed ways of addressing the findings with the lab team.

Challenges

The current NQCL management not operating optimally greatly delays the QC testing from the previous MQM round and negatively impacted the planning/implementation of PQM activities.

**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.

Key Activities

\*\* Many activities planned for this year have been postponed because of the Ebola outbreak\*\*

**Continue building the capacity of the LMHRA Quality Control Laboratory**

PQM provided training on preventive maintenance for 3 staff of the LMHRA QC lab, assessed the conditions of the lab equipment after the first lab inspection visit, conduct troubleshooting and repairs on non-operational equipment, and trained equipment users on how to maintain the equipment. The lab staff was able to apply the preventive maintenance techniques that they learned and replaced a part on the purification system. The HPLC is now running without any issues.

The LMHRA QC lab report from the NOMCOL inter-laboratory testing was ranked number one among all 12 members.

**Continue strengthening LMHRA's regulatory capacities**

PQM assisted LMHRA in strengthening registration, inspection, and pharmacovigilance reporting. An inspection tool was developed that was tested successfully in the field by the inspectorate.

Using the results of MQM round 4 and the results of routine inspections of the pharmaceutical premises, the head of LMHRA took more than 10 regulatory actions on failed products. These included banned monotherapies, unregistered products, and antimalarials that were found with no API (counterfeits) or were substandard.

**Strengthen the monitoring of the quality of antimalarial medicines at four sentinel sites and promote regulatory actions**

PQM met with the Malaria Control Program and the head of LMHRA, discussed the next round of MQM activities, and finalized the MQM protocol. PQM also discussed the possibility of organizing a stakeholders meeting to provide updates on recent findings of counterfeit and substandard medicines.

MQM round 5 activities did not take place because of the Ebola outbreak. PQM is planning to carry out these activities during FY15.

Challenges

PMI funds to assist the lab in conducting more compendial trainings are limited. Currently, the lab is conducting mostly assays. LMHRA's government funding was cut by 2/3, and that had a negative impact on having lab consumables and equipment needed for full compendial testing.

## **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.

### **Key Activities**

#### **Strengthen the capacity of LNS to attain ISO 17025:2005 accreditation**

To prepare LNS for ISO 17025 accreditation, PQM is providing technical assistance to strengthen analytical capacity as well as the quality management system of the lab. On the analytical part, PQM procured 2 kits for qualification of spectrophotometers, two sets of standards weights for balance calibration, adequate reagents for Karl Fischer titration, and a new detector of an existing HPLC. The latter will allow the lab to test artemether and lumefantrine simultaneously. PQM provided training to the quality control lab staff in Good Documentation Practice, UV-Vis spectrophotometry, and Karl Fischer titration and assist the lab in prequalifying two spectrophotometers.

The lab staff have acquired skills and understanding on how to:

- Qualify UV-Visible spectrophotometers
- Test medicines using UV-Vis spectrophotometry using pharmacopeias
- Implement good practices to assure the quality of data generated using UV-Vis spectrophotometry
- Document laboratory work properly
- Perform Karl Fischer titration

These instruments are highly used in the lab. The new head of QC lab has been involved in the efforts to strengthen the capacity of the lab. He has supervised follow-up training provided to the lab staff and made sure that the staff implement the training. Following PQM recommendations, he has developed new procedures and new tools that will facilitate the lab internal processes.

In addition to PMI support, LNS is benefiting from the USP Technical Assistance Program (TAP). Through this program, LNS received \$25,000 worth of USP reference standards and reference books. LNS also participated in the inter-laboratory testing (ILT) organized by the Network of Official Medicine Control Laboratories (NOMCoL) sponsored by USP. PQM reviewed the LNS ITL report and provided comments and recommendation for improving the testing, documentation, and reporting of test results. The lab has shown improvement in these areas.

#### **Support MQM program**

PQM provided resources to LNS for conducting one round of sampling and testing antimalarials. A total of 128 samples were collected in the district of Bamako and the sentinel site in Koulikoro. LNS completed the screening of all the samples. PQM reviewed the raw data as well as relating documentation and supervised verification testing of failed and doubtful samples. LNS is currently carrying out confirmatory testing. It also developed a sampling and testing plan for the remaining sentinel sites. Supervisory visits to sentinel sites are scheduled for November through December 2014. To provide a better environment for carrying out screening testing, the Minilabs® will be moved to hospitals at the sentinel sites.

#### **Support coordination of PQM activities**

PQM hired a local consultant to coordinate PQM activities in Mali. The consultant has started working closely with LNS and provided assistance implementing the actions plan relating to strengthening the lab QMS as well as MQM activities. The consultant represented PQM at several partners meetings in the country.

### Challenges

The major persisting challenges facing LNS QC lab are the lack of staff and the inability to retain existing qualified personnel. The lab is facing difficulties in handling their increased workload which has affected the implementation of PQM activities.

## **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).

### Key Activities

#### **Strengthen the capacity of the National Laboratory for Medicines Quality Control (LNCQM)**

PQM provided technical assistance in October 2013 on HPLC troubleshooting to LNCQM staff. In December, PQM traveled to Mozambique to provide additional training for 2 new staff at LNCQM, evaluate the QC testing lab, assess the situation at LNCQM regarding key staff changes, and meet with SWISS cooperation to discuss possibilities for future collaboration. Due to the staff changes, PQM retrained/refreshed on techniques like UV/Vis, HPLC, USP General Chapters, Karl Fischer, and calculation of Dissolution and HPLC results. PQM also procured items for the lab such as lab notebooks, centrifuge tubes, light bulbs for the main laboratory space, filters for the water purification system, parts for the proper installation of the water distiller and other consumables. PQM also prepared staff for a meeting/training that took place in Ghana to discuss inter-laboratory comparison testing. Training was conducted for the technical lab staff for May 2014 to continue to improve the lab's technical capacity.

PQM procured and shipped 4 boxes of lab consumables. Additionally, a batch of reagents and reference standards were provided to the lab to help assist with testing of medicines and to participate in the NOMCOL inter-laboratory testing. PQM also provided training to lab staff on Uniformity of Dosage Unit and Content Uniformity as well as how to properly read and understand the USP and other pharmacopeia.

During Q4, key staff were trained on processing HPLC data; additionally PQM helped the lab resolve and complete the NOMCOL ILT test.

#### **Strengthen the capacity of DF**

During the December 2013 trip, PQM discussed the status of the decree that the DF and Medicamentos e Artigos Medicos (CMAM) are drafting that will allow DF more autonomy to be able to take regulatory actions. PQM offered to assist with drafting the document since PQM has assisted other countries with similar documents. In March/April, PQM facilitated the participation of the DF Director and the Director of LNCQM in USP's International Training Program (ITP) which provided a learning opportunity for the two on USP's technical activities and to meet other regulatory officials from various countries. During the May visit to Maputo, Ms. Okafor met with USAID, the director of DF, and the new CMAM director to discuss PQM's activities in the country and especially the technical assistance provided to DF and LNCQM. The new director was very interested in PQM's activities and asked that a meeting be planned to discuss some of the challenges faced at the regulatory level. During the August 2014 trip, USAID, PQM and DF/LNCQM discussed the lack of regulatory action, and USAID wants PQM to prepare a presentation that could be used at different venues with high officials at meetings with USAID.

PQM discussed the lab taking ownership of some activities; for example, LNCQM management will take ownership of bringing metrology institute on board to calibrate balances.

### **Support MQM program by expansion to the ports of entry**

3 ports were added as sentinel MQM sites, and 3 Minilabs were provided for port screening. LNCQM and DF staff will be responsible for taking the Minilabs to the ports for screening. The Minilabs will be housed at LNCQM as agreed by the director of DF. Minilab training took place at LNCQM in August; about 24 provincial staff were trained.

### Challenges

PQM faced challenges due to the abrupt departure of a staff member who was key in implementing activities at LNCQM. Consequently, activities were left undone and are still not complete due to the transitional period and insufficient training of the new staff by the previous staff. PQM will have to spend time to retrain at least one-third of the staff due to shuffling of activities/responsibilities at LNCQM.

## **NIGERIA-Malaria**

### Background

In 2012, USAID/PMI-Nigeria requested PQM to provide technical support to the National Malaria Control Program (NMCP) and the National Agency for Food and Drug Administration and Control (NAFDAC).

### Key Activities

#### **Strengthen NAFDAC regulatory capacity**

PQM is providing technical support to the NAFDAC central quality control laboratory in its preparation for attaining ISO 17025:2005 accreditation. The focus is on strengthening the lab's analytical capacity as well as its quality management system (QMS). PQM procured laboratory supplies including HPLC columns, tools for monitoring lab environment, and calibration reagents for NAFDAC lab. PQM trained the lab staff in the following techniques including four (\*) topics that are part of the scope of accreditation:

- Dissolution: Theory and Best Practices\*
- UV-Vis Absorption Spectrophotometry\*
- Loss on Drying (LOD)\*
- Disintegration
- Uniformity of Dosage Units\*

The analysts have acquired practical knowledge and understanding on how to:

- Perform dissolution testing according to compendial standards
- Conduct the USP dissolution performance verification testing (PVT)
- Test medicines using UV-Vis spectrophotometry including checks on the system
- Perform loss on drying in accordance with pharmacopeial requirements, and make any necessary corrections for LOD
- Carry out disintegration testing according to pharmacopeial standards
- Conduct uniformity of dosage units test and analyze data based on the harmonized general chapter in the major pharmacopeias
- Document laboratory data in accordance with good documentation practices

PQM provided additional training in good weighing practices, good volumetric practices, HPLC and HPLC troubleshooting to 23 staff from NAFDAC laboratories. PQM evaluated the training of staff by directly observing the staff conducting tests using HPLC, pH, Dissolution, and pharmacopeial standard documents. Following the evaluation, PQM provided lab staff with comments and recommendations for

improvement. Lab staff have made progress in conducting these tests. PQM shared the recommendations and observations with the quality assurance unit.

As for QMS, PQM assisted the lab in implementing the corrective action plan developed previously. The following was achieved:

- The lab environment is being monitored using adequate devices
- Good personal protection equipment were purchased and their use has been instituted
- Good housekeeping in the lab improved
- Participation in Proficiency Testing for HPLC, LOD, KF, pH, UV-Vis spectrophotometry as well as in NOMCoL inter-laboratory testing scheme was completed
- Ten critical standard operating procedures were developed

The lab used to experience frequent power failures. The power generator has been fixed and the lab currently has a steady supply of power.

### **Monitor the quality of antimalarial medicines**

The first round of sampling and testing of antimalarial medicines has been completed. The NAFDAC lab in Yaba drafted a report on MQM activities; NAFDAC-Abuja reviewed the report before sharing the data with PQM. PQM reviewed the testing results and provided comments to NAFDAC. PQM will review the implementation of MQM activities with NAFDAC and the National Malaria Elimination Program and draw lessons for improving the next sampling and testing round.

### **Support the NMCP in finalizing its quality assurance policy for antimalarial medicines and diagnostics**

The completion of the quality assurance policy (QAP) had stalled and little progress was made. After discussions with stakeholders, it was agreed to restart drafting the policy. The National Product Supply Chain Management program took the lead in facilitating the process of gathering documentation useful for drafting the QAP and organizing a workshop to develop a new draft QAP. The draft is expected to be complete by November 2014.

## **NIGERIA-Maternal and Child Health**

### Background

USAID/Nigeria 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.

In support of the UN Commission's goals, USAID/Nigeria is working to increase the availability of relevant MCH medicines in the country. Toward that end, PQM will provide technical assistance on GMP and quality assurance to local medicines manufacturers in collaboration with NAFDAC. PQM will also provide TA to NAFDAC to build its capacity to regulate these products.

### Key Activities

#### **Monitor the quality of maternal child health medicines**

In FY14, PQM analyzed several batches of MCH medicines collected by partner programs. Also included in these batches were samples of batches to be procured.

#### **Strengthen the regulatory capacity of NAFDAC**

PQM continued to support NAFDAC by providing training on various QC techniques including titration, a key technique for analyzing zinc tablets.

#### **Build capacity for Good Manufacturing Practices (GMP) of selected local manufacturers of Zinc sulfate, ORS, Chlorhexidine, and amoxicillin commodities for global and local supply**

PQM provided technical assistance to manufacturers of zinc tablets, ORS, CHX, and amoxicillin DT. This assistance included facility assessments, document review, and dossier preparation and formulation. The key outcome of the assistance was increased technical capacity to comply with WHO GMP and the first African manufacturer of CHX gel.

## **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.

### Key Activities

#### **Strengthen the monitoring of the quality of antimalarial medicines at nine sentinel sites and promote regulatory actions**

PQM, in collaboration with PNLP, organized MQM round 2013 and 2014. A dissemination meeting to share the results with stakeholders will be organized by PNLP and LNCM.

#### **Continue building the capacity of LNCM to reach ISO 17025 accreditation**

PQM provided quotes and a technical description of the HPLC unit that the lab is planning to procure with PMI funds. PQM also facilitated the participation of the lab in the third NOMCOL meeting. This meeting was attended by the Quality Assurance Manager and the Quality Control Manager of the chemistry lab.

PQM reviewed documents pertinent to ISO 17025 accreditation and conducted a QMS audit of the lab. A visit from the accreditation body, TUNAC, is planned for next year.

### Challenges

The cut in PMI funds allocated to PQM greatly limited the technical assistance PQM could provide to strengthen LNCM, DPM, and PNLP.

## **Asia**

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## **REGIONAL DEVELOPMENT MISSION FOR ASIA (RDMA), MEKONG MALARIA**

### 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 in the GMS, which might have arisen from, among other factors, availability and use of poor-quality antimalarials. Although there have been some improvements, there continues to be sporadic incidences of such products in the region requiring intensified and coordinated efforts of intervention.

### Key activities for Burma/Myanmar

#### **Strengthen PMS capacity of Burma Department of Drug and Food Administration (DFDA) and local authorities, primarily at Malaria Containment Zones/Tiers 1 and 2, border checkpoints with Laos, Thailand, and China, through MQM activities to obtain evidence-based data and reduce oral artemisinin-derivative monotherapies.**

Two MQM trainings were conducted in Burma/Myanmar on MQM, with a total of 62 participants. The December 2013 training involved 34 participants from regulatory and other agencies including DFDA,

Vector-borne Diseases Control (VBDC), Department of Medical Research Lower Myanmar (DMR-LM), and WHO. The second training—held in March 2014 in partnership with the Bureau of Drug and Narcotic (BDN) of Thailand—was conducted for 28 newly-recruited pharmacists.

PQM supported sample collection of antimalarial (AMLs) and highly suspected antibiotics (ABTs) with quality problems in targeted areas of the country. In addition, information was collected on the availability of oral artemisinin monotherapies, with findings reported to the relevant agencies, including DFDA and VBDC. This activity was conducted in two border areas (Tamu, on the Burma/India border, and Muse, on the Burma/China border) and 5 sentinel sites (Tanintharyi, Mon, Bago-East, Kayin, and Rakhine). Results from the two border areas are available – 23.5% failed – while results from the 5 sentinel sites are still undergoing confirmatory testing and analysis.

### Challenges

Supervisory M&E visits are still pending due to the political climate, and delays in sample collection and testing have caused some challenges regarding receiving data for all sites in a timely manner. Consequently, there have been delays in administrative and regulatory actions.

### **Continue to strengthen the capacity of the national quality control laboratory of DFDA in Nay Pyi Taw to comply with basic principles of Good Laboratory Practices and help it conceptualize the ISO 17025 accreditation process**

Essential laboratory equipment and hands-on training was provided for DFDA QC lab staff in Nay Pyi Taw successfully carry out post-marketing surveillance and strengthen regulatory capacity. PQM donated one Dissolution tester in November 2013 and one HPLC in February 2014 to DFDA QC laboratory in Nay Pyi Taw.

PQM provided training on Advanced Analysis of Antimalarials using Dissolution (12 participants from DFDA and DMR-LM) in December 2013. This was followed by a training on Advanced Analysis of Antimalarials using HPLC in March 2014, given in collaboration with WHO and Chula Pharmaceutical Technology Service Center (PTSC) (24 participants).

In March and April 2014, PQM conducted 3 site visits to proposed locations for the DFDA Nay Pyi Taw lab relocation. Technical recommendations were submitted to DFDA in April 2014. The new laboratory building was renovated with the Government budget according to the input from PQM and was completed in August 2014.

**Support in-country and inter-country efforts and coordination among GMS countries for cooperation and enforcement through BREMERE, WHO SSFFC medical products working group, INTERPOL's Storm Enforcement Network, and ASEAN Post-marketing Alert System**  
PQM signed the project agreement with Department of Health (DOH), DFDA, and DMR-LM from the Ministry of Health in March 2014.

The new regional PQM consultant participated in Minilab training in Myanmar to increase coordination across the region, including two regional trainings that were conducted in the Philippines. In addition, the Build Regional Expertise in Medicines Regulation, Information Sharing, Joint Investigation and Enforcement (BREMERE) representatives from national testing labs were trained on bioequivalence/bioavailability testing methods

Results of the baseline survey in Burma were submitted to the DFDA for action. According to the results from MQM/PMS activities conducted in two border areas, DFDA announced the list of illegal medicines found in the market in national newspaper for national dissemination. Furthermore, this data was shared with key BREMERE focal points.

### **Purchase and replenish essential Minilab and some QC lab supplies to maintain surveillance activities and confirmatory analyses**

In February 2014, PQM provided 21 essential supplies to DFDA in order to replenish Minilab supplies as well as to be used during trainings. PQM also donated two copies of USP-37 NF-32 to DFDA and another copy to DMR-LM.

**Increase the availability of quality-assured AMLs by improving inspections in supply and distribution chains, enhancing pharmacy practices, and engaging pharmacy school students and faculty in the reduction of CSMs in the country**

The goal was to conduct a training workshop for 8-10 DFDA central inspectors and 15-18 township inspectors (in containment Zones/Tiers 1 and 2) to improve inspection practices in the supply and distribution chains to support the ban on oral monotherapies. While one training workshop was completed in Q2 for DFDA and FDA staff on PMS and MQM, an additional targeted training in this region is needed in the upcoming months to complete this activity.

Discussions on engaging pharmacy school faculty/students on improving syllabi are underway. Key personnel have been engaged at respective schools. This activity will be completed in FY15.

**Participate in and present at meetings and conferences to share the findings and achievements of and challenges to PQM program activities, in national, regional, and international arenas**

Results from the MQM/PMS activities were shared on an ongoing basis with relevant partners including PMI, USAID/Burma, and VBDC.

Key Regional Activities covering Cambodia, Laos, Thailand, and Vietnam

**Continue to strengthen the post-marketing surveillance capacity of Laos Food and Drug Department (FDD) and Bureau of Food and Drug Inspection (BFDI), Vietnam Drug Administration (DAV), and selected local authorities of Thailand**

Work is ongoing to improve the quality of the curriculum for pharmacists in Laos by sharing information from Thai universities and through discussion on translation and reprinting of the *Operational Guide on Improving the Quality of Medicines in Resource-Limited Countries* for Laos and Vietnam. It is hoped that improved training of pharmacists will increase awareness of the need for quality medicines and that they will extend the reach of local authorities to support medicines quality.

**Continue to strengthen the capacity of the national quality control laboratory of Laos Food and Drug Quality Control Center (FDQCC) toward ISO 17025 accreditation, and Support the Chulalongkorn University Pharmaceutical Technology Service Center (PTSC) toward compliance with WHO Prequalification**

Work to improve the scope of accreditation of FDQCC is ongoing. Management review work conducted earlier in 2014 showed minor deficiencies only. Corrective and preventive actions are being implemented; continuing work to improve SOP and QMS documentation is slowed by a lack of human resources. The full assessment of PTSC was cancelled due to the political situation in Thailand and has been rescheduled for FY15 Q1.

**Support in-country and inter-country efforts for cooperation and enforcement through the BREMERE initiative to enhance collective action along with the WHO-led substandard, spurious, falsely-labeled/falsified/counterfeit (SSFFC) medical products working group, INTERPOL-led Storm Enforcement Network, and ASEAN Post-Marketing Alert System (ASEAN PMAS)**

Data collection for the regional comparative report has been delayed in Thailand. The final report for Laos was completed in Q4. Although no substandard or counterfeit medicines were identified, high rates of illegal medicines were found, including injectable artemether. Communication through BREMERE is limited by political and sensitivity concerns. Discussion on potential collaboration and engagement between PQM and ASEAN working groups on pharmaceuticals continued, and a concept note on "Potential Areas of PQM Technical Assistance to Strengthen the Technical and Regulatory Capacity of ASEAN Countries" was developed and submitted to the AOR team.

**Increase the availability of quality-assured antimalarials by improving inspections in supply and distribution chains, supporting selected manufacturing facilities to produce quality Artemisinin-based combination therapy (ACT) medicines, enhancing pharmacy practices, and engaging pharmacy school students and faculty in the reduction of counterfeit and substandard medicines in the GMS**

Inspections and assessments were scheduled for two companies in Thailand and Vietnam but were postponed due to political unrest in Thailand and security concern in South Vietnam. PQM received responses to the manufacturers' questionnaire from two manufacturers (SaoKim Pharmaceutical JSC and OPC Pharmaceutical JSC) in Vietnam, and the PQM GMP Manager paid an initial visit to each company to learn about their capacity and become familiar with their level of GMP compliance. Observations and suggestions were provided to the companies.

**Through existing and proven means and tools, maintain the awareness-raising momentum about the dangers of using counterfeit and substandard medicines in the GMS**

Lao FDD has completed and approved the final report on a study of the effectiveness of IEC material produced to inform consumers about the risks of counterfeit and substandard medicines. The results indicate that further efforts to inform pharmacists about drug resistance are needed, although awareness of counterfeit medicines is high.

Data from samples not yet included in the Medicines Quality Database (MQDB) resulted in a journal submission to the American Journal of Tropical Medicine and Hygiene in Q4. The study compares the regional prevalence of substandard medicines and discusses trends. Publication is targeted for FY15 Q1.

A poster was presented at the FIP conference in Bangkok that focused on the value of the MQDB and trends in reporting. This increased awareness of the database and its utility in tracking global medicines quality.

Challenges

1. The political situation in Thailand has made planning for monitoring, training, and assessments difficult. Activities scheduled for Q3 were postponed indefinitely.
2. Analysis of data on samples collected from 22 provinces in Thailand under Global Fund Round 10 in collaboration with Kenan Asia, Bureau of Vector-Borne Diseases, and Provincial Health Authorities indicated the presence of substandard artesunate monotherapy, chloroquine, primaquine, and quinine in Thailand. Delays in testing in field, and also in central labs, have made drawing accurate conclusions about the level of CSMs difficult, and the prevalence of government-manufactured products among the substandards have created challenges in taking action due to the political situation and sensitivities within the region.
3. Laos has identified high levels of illegal medicines imported, including artemether injectable. Action taken has been limited by political concerns and fraught with delays in testing and reporting.
4. Reduced budget from PMI and ending of GFATM support in FY14 constrained the MQM activities in the region.
5. Ongoing support is needed to improve the capacity in the region to maintain the momentum and efforts addressing the quality of essential medicines, including antimalarials. New funding from Global Fund under New Funding Mechanism is possible; however, the focus on medicines quality seems to be limited.

**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.

### Key Activities

#### **Continue to strengthen the DDF post-marketing surveillance activities at national and local levels by implementing enhanced MQM programs in the country to support enforcement action against poor-quality essential medicines, with the emphasis on antimalarials**

NHQC completed quality testing on five AML samples that were collected in July 2013. DDF-MoH wanted to investigate the cause of these failed samples, but they were told that no more Malarine would be procured or dispensed. The samples with an expiry date of October 2013 were the last batches.

After revising and re-submitting the request, PQM received permission from H.E Chou Yin Sim, MOH's Secretary of State, for sampling and testing of AMLs at public health facilities in addition to private facilities during the comparative study of antimalarials. The country study teams organized an orientation meeting (on objectives of the study and protocol for sampling and testing) and refresher training (on testing by TLC/Minilab) in November 2013. Twelve provincial staff, from 3 MQM sites (Battambang, Pailin, and Mondulakri) and 3 non-MQM sites (Kampot, Kampong Speu, and Siemreap), attended the training. Sample collection from the 6 sites was conducted in November and December 2013. In total, there were 136 samples collected from both the public and private sectors. Basic testing using Minilabs revealed that 1 sample failed: Flamox B.F, INN: Amoxicillin 500 mg, lot No. 141, listed as being manufactured by Bright Future Laboratories Ltd., Cambodia. The IMC Secretariat investigated the cause of failure, and two additional samples were collected and tested to verify the results. A decision has been made to remove the registration number and recall the product from the market.

PQM collaborated with WHO-WPRO to organize a workshop "PQM Technical Assistance toward WHO Prequalification of Antituberculosis Medicines" in March 2014 in Manila, Philippines. The aim of this workshop was to inform senior management and regulatory affairs representatives of medicines manufacturers about the WHO Prequalification Programme, the technical assistance available to them, and the global market outlook for anti-tuberculosis medicines. DDF-MoH and CENAT nominated two representatives from each institution to attend this workshop. Furthermore, two local manufacturers (Pharma Products Manufacturing - PPM and Cambodian Pharmaceutical Enterprise - CPE) also sent representatives to attend this workshop.

Following the workshop, the PQM GMP group conducted assessments in May 2014 of the two identified pharmaceutical manufactures (PPM and CPE) and provided a gap analysis and roadmap for them to work toward the goal of obtaining WHO prequalification.

In order to take timely action on poor quality, substandard, and counterfeit medicines, DDF-MoH prepared Guidelines on Recalling Pharmaceutical Products (including poor quality, substandard and counterfeit medicines). This guideline was reviewed by the DDF-MoH technical working group and pharmaceutical companies for recommendations and comments.

#### **Continue to strengthen the capacity of the National Health Product Quality Control (NHQC) toward compliance with ISO 17025**

PQM is waiting for final construction of the NHQC building in order to provide more technical assistance related to the installation of lab furniture and equipment.

NHQC sent a draft of their Quality Manual to the PQM QMS team for review and comment. The next step is to agree on a time table for receiving and reviewing the Master List of SOPs and the core procedures prior to a site visit so that it can be determined how many procedures will need to be reviewed and estimate the time needed for completion.

NHQC is participating in the NOMCoL Asia-Pacific inter-laboratory testing (ILT) program and is in the process of testing and submitting testing results for review.

**Support in-country, inter-country, and regional coordination, cooperation and enforcement through BREMERE to enhance collective action at national and regional levels.**

MOH-DDF nominated 2 drug inspectors as representatives to communicate and share information with other countries in the region.

**Increase the availability of quality-assured antimalarials through enhanced inspections of distribution chains and pharmacy practices and involve pharmacy school students and faculty members in the reduction of counterfeit and substandard medicines in Cambodia**

In collaboration with DDF/MOH, PQM provided technical assistance in reviewing the Good Pharmacy Practice (GPP) Guideline and training modules, supported the printing of this guideline, and supported the training for pharmacists and drug sellers. Between July-September 2014, GPP training was conducted for 10 provinces (Battambang, Pailin, Kandal, Siemreap, Oddarmeabchey, Thbong Khmom, Kampong Cham, Preah Sihanouk, Pursat and some district of Phnom Penh) and was participated in by 695 pharmacists and drug sellers. By the end of 2014, it is planned to cover 25 provinces.

To engage faculty and final-year pharmacy school students from the University of Health Sciences-UHS and International University-IU in Phnom Penh to improve pharmaceutical practices by establishing and strengthening the QA/QC system in various settings through curriculum/syllabi improvement, an initial discussion with the dean of these 2 pharmacy schools was held. The importance of improving the curriculum by introducing QA/QC into the pharmacy education was discussed, and a proposal to develop a plan of action will be further discussed. However, this activity has been delayed; strong evidence may be needed to convince authorities that a review of the pharmacy curriculum is needed.

**Participate in and present at meetings and conferences to share the findings and achievements of PQM program activities in Cambodia, as well as challenges encountered, in national, regional, and international arenas as necessary**

PQM provided some financial support to the Mekong Bio-Pharma conference held in Cambodia in October 2013 for around 400 participants.

PQM submitted an article entitled “Cambodian Ministry of Health Takes Vigorous Actions in Fight Against Substandard and Counterfeit Medicines” to the Journal of Tropical Medicine and Surgery in February 2014.

PQM’s local consultant, Ms. Lang Siv, attended USAID’s workshop on “Introduction to USAID’s Legal Regulation, Financial Management and Procurement Policies” in March 2014 in Phnom Penh. She also met with USAID’s evaluator team to provide information on PQM participation in the CAP-Malaria project in order to evaluate the project.

Ms. Lang Siv observed the “Refresher Training for Drug Inspectors on Drug Law and Regulation, and Law Enforcement to Ban Antimalarial Monotherapy” conducted in August 2014 in Kampong Cham province. She was also invited to attend the “Dissemination Workshop on Guidelines for Adverse Drug Reaction (ADR) Monitoring and Related Matters, and Recall of Pharmaceutical Products for Import-Export Pharmaceutical Companies, Private and Public Hospitals” in September 2014.

## Challenges

Due to limited funding, MQM activities at 12 sentinel sites were not fully functional. Sample collection and testing were not regularly conducted after the GF R6 budget ended in 2012. Because of this, DDF has focused most on the 3 sentinel sites located in Tier 1 regions (considered the areas at highest risk for drug resistance).

## **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, which is producing some of these medicines under a compulsory license granted under a Presidential Decree as part of the TRIPS agreement. In coordination with the National AIDS Program, PQM will support Kimia Farma on a WHO PQ project with the aim of submitting their nevirapine product dossier for prequalification. PQM will also roll out provincial and district-level sampling and testing for ensuring the quality of ARV, OI, and STI medicines.

**HIGHLIGHT:** A five year, comprehensive and far-reaching MOU was signed in February, 2014 between the heads of USP PQM and the Indonesian NA-FDC. This substantial and unprecedented achievement of long-term partnering with the NA-FDC will ensure that commitments made between the governments of Indonesia and the US (USAID) can effectively be implemented via an established mutual agreement. This was an important milestone in the PQM program for Indonesia and globally.

### **Continue existing technical assistance to TB and HIV medicines manufacturers to obtain WHO prequalification for selected TB medicines**

During FY14, PQM continued providing technical assistance to manufacturers to obtain WHO prequalification with the purpose of supplying the Indonesian national programs with quality-assured 1<sup>st</sup> and 2<sup>nd</sup> line TB products. PQM continued its partnerships with the state-owned manufacturers Kimia Farma, Phapros, and Indofarma for 1<sup>st</sup> line fixed-dose combination medicines to treat TB, and re-engaged with Sandoz Indonesia on its first-line pediatric fixed-dose combination product for TB. PQM also provided technical assistance to manufacturers of second-line TB medicines including Sanbe Farma, Zenith, and Phapros for levofloxacin 500mg. In addition, Phapros is considering submission of a moxifloxacin product, and a new manufacturer, Kalbe Farma joined the PQM technical assistance program for both levofloxacin and zinc sulfate. Kalbe Farma is the largest pharmaceutical manufacturer in Indonesia, so this was a noted accomplishment for the program.

All manufacturers are making considerable progress towards the goal of submitting their product dossier to WHO for prequalification, with the exception of Indofarma. During FY14, the President Director of Indofarma communicated with the PQM team that they must put the project on hold. The reason is that Indofarma is in the process of constructing a new manufacturing facility for their solid dosage products, and would need to resume the PQ project after completion of the new site. The PQM GMP team provided substantial inputs into the blueprint design of the facility, which will comply with current US FDA standards.

A new project initiated during FY14 was to engage the sole Indonesian manufacturer of anti-retrovirals, Kimia Farma, on a WHO PQ project. After discussions with the National AIDS Program manager and Kimia Farma team, the manufacturer agreed to develop a project for either nevirapine or their branded generic ARV Duviral (lamivudine + zidovudine) which are supplying the national AIDS control program in Indonesia. An initial GMP audit was conducted by PQM, and at the end of FY14 Kimia Farma is in the process of implementing their CAPA plan, with good progress and commitment. This project has far-reaching effects, since Kimia Farma is also responsible for the supply and distribution of ARVs for the public sector during the slow transition towards decentralization of procurement to the provincial and district. Kimia Farma still manages the supply and warehousing of the ARVs, while the National AIDS Program and the Health Department slowly shift storage to the provincial and district MOH-run warehouses under the Pharmacy Section in each province/district. Therefore, this represents a big opportunity for engagement by PQM and partners on ensuring medicines quality of ARVs throughout the supply chain.

PQM also supported the government regulatory authority NA-DFC by providing training and workshops on GMP and WHO PQ for manufacturers and for inspectors.

**Continue to assist two Indonesian Contract Research Organizations (CROs) to enhance their compliance with Good Clinical Practices (GCP) and Good Laboratory Practices (GLP) for BA/BE studies on ATB medicines**

PQM conducted final audits and developed CAPA plans with Equilab International and San Clin Eq as the clinical sites for bioequivalence studies conducted as part of the requirements for the WHO PQ product dossier submission. The first line TB medicines in the Indonesian project all have BE study requirements by WHO, yet currently no Indonesian CROs are officially recognized by WHO. PQM is building capacity of the local CROs to conduct BE studies according to WHO standards (EMA, etc.). This will enable local manufacturers to utilize local CROs for BE studies, encouraging the development of human resources, expertise, and economic growth.

During FY14 a new CRO, Pharma Metric Laboratories, joined the technical assistance program offered by PQM. Pharma Metric, a subsidiary of Kalbe Farma, is a well-regarded CRO in Indonesia, and the PQM partnership promises to be a positive collaboration to support the WHO PQ programs.

**Provide technical assistance to the NA-DFC National QC lab towards application for WHO PQ by 2015, and build the capacity of NA-DFC for post-marketing surveillance, medicines quality monitoring, and testing medicines in accordance with local and Global Fund requirements**

PQM provided substantial technical assistance and support to the NA-FDC and the National QC laboratory as part of a comprehensive plan for the lab to achieve WHO Prequalification, and to build the capacity of the NA-DFC in the areas of regulation and inspection on GMP and BE studies. PQM supported the National QC laboratory through assessments, advanced training on compendial methods, Good Laboratory Practices, and developing a plan of action for applying to WHO for Prequalification. The PQM QC team had a number of hands-on practical training on TB and HIV medicines, including advanced training on dissolution and HPLC. Five laboratory staff from the National QC lab spent two weeks at the USP headquarters in Rockville for advanced training co-sponsored by USP PQM and the Global Fund with a focus on HIV and malaria medicines. PQM also fostered regional collaborations and relationships by sponsoring NA-FDC and Provincial A-FDC to attend advanced training workshops conducted by the National Institute for Drug Quality Control of Vietnam with a focus on HIV medicines. In addition, members from the NA-FDC participated in the regional ASEAN-USP Scientific Symposium and its associated training programs on reference standards harmonization and other important aspects for the regulatory authority. PQM also developed action plans for rolling out sampling and testing at the provincial and district levels in conjunction with other agencies as part of a comprehensive strategy for effective technical assistance. By partnering with organizations such as JSI and Global Fund to roll out initiatives at the peripheral levels, PQM's programs will have greater effect in ensuring quality of priority medicines throughout the supply chain.

### **Develop collaborative mechanisms and support for disease programs (NTP, NAP), BINFAR, and NA-DFC to enhance QC capacity in Indonesia**

During FY14, a notable accomplishment was to promote collaboration and coordination between the main players in the pharmaceutical sector in Indonesia, which is a challenging task. The NA-DFC as the regulatory authority, is a separate and distinct institution from the Ministry of Health. Thus, there is traditionally very little organization or coordination between the MOH and the NA-DFC on priority setting for designing the post-marketing surveillance system in Indonesia. In addition, while the MOH is responsible for forecasting, procurement, distribution, storage, etc. it is the NA-DFC which is responsible for monitoring quality of the medicines, inspections, etc. However, the NA-DFC has previously only focused on medicines available in the private sector, and has had very little impact on monitoring medicines for use by the programs from government-held warehouse or health facilities.

In collaboration with WHO, PQM has started to build the relationships between the MOH and NA-DFC through a series of workshops and collaboration meetings, culminating in a national-level edict being drafted by the Director General of Pharmacy (MOH) requiring public sector cooperation with NA-DFC inspectors. A workshop held in July which was convened to disseminate the results from 2 years' of post-marketing surveillance data by NA-DFC for the MOH, and an important output were recommendations on further collaboration and establishing policy-level SOPs for interaction. At the end of FY14 these SOPs were still under development by BINFAR, and PQM will be supporting a number of socialization workshops and interventions to help encourage monitoring and testing medicines from public sector sites. Under the news rules of engagement, PQM will also be supporting roll out of mobile labs for use in screening medicines from both public and private sector facilities using technologies such as the Minilab and others. This effort hopes to provide a solid evidence base on the quality of what is currently available in the programs (public sector) and private markets.

### **Establish USP PQM office as an officially-registered entity in Indonesia**

PQM substantially expanded the PQM Indonesia office throughout the year, including engaging with a local law firm to register the project with the Ministry of Foreign Affairs and apply for Tax Exemption from the Ministry of Finance as required by the Indonesian government to operate legally there. To this end, PQM has made significant progress in the long process towards registration. In addition, by the end of FY14 three full time staff had been hired to support the technical implementation and administration of the program in Indonesia, with 3 more employees anticipated to begin during Q1 of FY15. The substantial scale-up of the office should translate into more effective long-term implementation of the project, as well as provided a higher level of service to the partners in Indonesia.

## Challenges

The main technical challenges in implementing the WHO PQ project with manufacturers in Indonesia include unstable API supply and/or access, due to the need to import all API from various sources in the region. Most of the delays in the timeline for implementation stem from API sources which lack an associated Letter of Access or adequate regulatory status such as CEP or even WHO PQ. Of urgent concern, PQM will be focusing more on solving this issue together with the manufacturers during FY15 to prevent further delays.

There are numerous challenges related to the PQ project with the NA-DFC's national QC laboratory. Limited human resources and limitations in laboratory skills have delayed CAPA implementation and timely progress under the WHO PQ plan. Also, a deficiency in management, especially in the quality assurance aspects of the lab's functioning, has delayed progress.

The process for registering the program legally and officially in Indonesia is labyrinthine and difficult. PQM has managed to proceed with hiring and implementing the project through outsourcing agreement as a temporary solution, however being officially registered will enable USP to provide better support to the country office through administration and finance.

## **PHILIPPINES**

### Background

PQM has been actively providing technical and professional assistance to Philippines Food and Drug Administration (FDA), Department of Health (DOH), National Tuberculosis Program (NTP), selected Local Government Units (LGUs) and Centers for Health Development (CHDs) in an effort to strengthen medicines 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 on the market in Philippines; to enhance the FDA regulatory capacity in evaluation & registration of pharmaceutical products through the introduction and buildup of internationally accepted quality standards, guidance, processes and procedures.

### Key Activities

#### **Maintain MQM with continued Post-Marketing Surveillance at the eight sentinel sites**

MQM activity at sentinel sites continues in monitoring ATB medicines and selected antibiotics. PQM replenished Minilab supplies and inventoried other supplies/reagents. Expired medicines at the site were forwarded to the FDA laboratory for proper disposal.

#### **Strengthen the FDA's capacity and its QC laboratory to enhance the medicine regulatory system**

Ms. Maria Lourdes C. Santiago, Officer in Charge, Center for Drug Regulation and Research, Philippines FDA was sent to Harvard University to attend the Strategic Management of Regulatory and Enforcement Agencies training.

FDA conducted assays on certain medicines requested by NOMCoL Asia Pacific inter-lab testing. Medicines used are Cipro Ethylenediamine Analog USP RS, Cipro HCL USP RS, Artemeter USP RS and Lumefantrine USP RS. The results were reported back to USP HQ.

The agreement between USP Technical Alliance Program and the FDA was renewed for another year.

#### **Collaborate with NTP and other TB partners on relevant disease control programs**

Several meetings and conference calls were held with TB partners and stakeholders in FY 14. Some of these include:

- Pharmacovigilance meeting at FDA with Dr. Kenneth Hartigan-Go, FDA staff, WHO, NTP and SIAPS
- TB group follow-up meeting from the TB group discussion in the convergence meeting at the national level

- Stock-taking meeting at Pan Pacific Hotel hosted by USAID/Office of Health.
- Philippine Coalition Against Tuberculosis (PhilCAT) 21<sup>st</sup> Annual Convention

### **Support local manufacturers towards WHO PQ for 1<sup>st</sup> and 2<sup>nd</sup> line TB medicines.**

PQM's GMP team, together with the PQM in-country consultant, visited Hizon and United Laboratories to help those two manufacturers to respond to CAPAs and prepare dossiers.

#### Challenges

Frequent natural disasters delay the progress of many activities, and the efficiency of coordination and collaboration among USP/PQM with other partners/stakeholders needs to be improved.

## **VIETNAM**

### Background

PQM has been active in providing technical assistance to Vietnam to improve the quality of essential medicines by building the capacity of the National Institute of Malariology, Parasitology and Entomology (NIMPE), Drug Administration of Vietnam (DAV), National Institute of Drug Quality Control (NIDQC), and Ho Chi Minh City (HCMC) Institute of Drug Quality Control (IDQC) to improve the quality of medicines they register, supply, and use in priority health programs. PQM has also been tasked with selecting potential local pharmaceutical manufacturers and capacitating them toward methadone production and strengthening the quality of this product through the supply and distribution chains.

### Key Activities

#### **Providing technical assistance to local methadone production and procurement**

In FY14, with technical assistance from PQM, Vietnam Administration of HIV/AIDS Control (VAAC) launched a national tender, using DFAT funding (HAARP project), to procure 2,300 liters of methadone syrup. Among five local manufacturers that were qualified to compete in the tender, Vidipha and Danapha were the only companies with a product registration license from the DAV. More recently, MoH approved Vidipha to distribute their product directly to three HAARP project provinces (including, Hoa Binh, Tuyen Quang and Bac Kan) without going through the typical six legal distributors, resulting in improved access and affordability of these medicines in country.

#### **Strengthening capacity of the NIDQC and HCMC IDQC quality control labs**

PQM reviewed the Quality Manual and SOPs of HCMC IDQC and collaborated with WHO, Geneva in providing appropriate prequalification support and technical assistance to this laboratory. NIDQC and HCMC IDQC joined the NOMCoL-Asia Pacific network in 2014.

#### **Provide technical assistance for ARV quality assurance through post-marketing surveillance in both the public and private sectors**

Post-marketing surveillance of ARV products in Vietnam will be led by the MoH (DAV - VAAC), and the NIDQC. The NIDQC's GFATM R10 "Strengthening the national drug quality control system" project is successfully underway to assure the quality of ARV, anti-tuberculosis and antimalarial medicines. However, the NIDQC does not have the adequate capacity to conduct advanced analytical testing for the quality of ARV medicines. In collaboration with NIDQC and DAV, PQM is helping these key partners develop a post-marketing surveillance plan which will be a supportive tool for VAAC in QA/QC of ARV medicines subsidized/provided in the national HIV/AIDS program and PEPFAR.

In support of these activities:

- PQM trained an NIDQC analyst at USP HQ for three weeks in May 2014. Some of the expenses for this training were contributed by the HSS grant of Vietnam to NIDQC.
- A ToT technical workshop for quality control system strengthening "Quality Control of ARV medicines using HPLC and Dissolution" was held in Hanoi in August 2014 at NIDQC

- PQM has collaborated with PEPFAR on testing ARVs at NIDQC instead of sending the samples abroad, such as to Singapore or South Africa Labs. This effort will help cut costs and strengthen local capacity.

### **ARV pharmaceutical product quality management practices at treatment sites at the peripheral level**

Due to the decreased funding for Vietnam, PEPFAR has engaged VAAC to begin the transition of pharmaceutical quality management services at the peripheral level to the provinces. PQM was specifically requested by USAID/Vietnam to join the technical assistance team led and coordinated by VAAC. PQM will join the team in a technical assistance capacity and help carry out tasks across 12 provinces with a focus on ensuring the quality of ARVs throughout the supply chain.

In FY14, PQM joined a training workshop held and coordinated by VAAC in Hanoi and HCMC to strengthen the capacity of PACs in ARV pharmaceutical product quality management practices. PQM started discussions with VAAC on planning capacity building activities in the 12 provinces as assigned by PEPFAR/USAID and completed the final selection of the technical and administrative teams to support this activity. PQM has initiated the hiring of appropriate staff to complete this activity.

### Challenges

- Political sensitivity associated with methadone production delayed many aspects of technical assistance provision in Vietnam. Due to this, future activities in regards to methadone will be more related to surveillance of the methadone products versus manufacturing advisory services which were being provided previously.
- Identifying and hiring appropriate talent for Vietnam was a process that took several months
- PQM had planned an assessment trip to HCMC IDQC to determine key areas of support for prequalification and accreditation but it was delayed due to security issues.
- Developing an ARV post-marketing surveillance plan is currently delayed because finding an in country partner and agency (VAAC/DAV/NIDQC) to take leadership in implementation has been challenging. PQM is continuing to have meetings with these agencies to emphasize the importance of this activity and get local buy in.

## **Europe and Eurasia**

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### **KAZAKHSTAN**

#### Background

According to WHO, Kazakhstan is among the 27 high multidrug-resistant tuberculosis (MDR-TB) burden 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 medicine manufacturers in the country. The mechanism traditionally used by the PQM GMP group is the WHO PQ programme. PQM's technical assistance will enhance the capacity of these manufacturers to comply with international GMP standards, thus improving the standard of medicines being distributed locally, as well as opening the distribution channels to the global market. However, over the past year, it has become apparent that manufacturers in the country may not have adequate facilities capable of meeting WHO PQ standards. Therefore, discussions with USAID personnel have been moving away from WHO PQ as a goal and toward education and system-building based on the principles of GMP.

#### Key Activities

PQM conducted a general GMP assessment of the Pavlodar Pharmaceutical Factory (Romat) in October 2013 and have since provided additional recommendations on CAPAs and SOPs that are being implemented by Romat. In Q4, the Romat staff took PQM personnel to visit the construction site of the new facility to view the progress made since October 2013. Romat personnel stated that construction is anticipated to be completed by the end of 2015.

The PQM team and representatives of Romat held a five-day training on the basics of GMP in August 2014. This was attended not only by representatives of Romat but also by pharmaceutical professionals from other second-line anti-tuberculosis medicine manufacturers located in Kazakhstan, as well as representatives of Kazakh regulatory authorities.

PQM held teleconference interviews with a number of candidates for the positions of Quality and Validation consultants for the Romat facility and identified preferred candidates. These consultants developed tentative work plans, and PQM started preparing contracts for the consultants.

PQM made preparations for a WHO PQ Forum to be held in Almaty in October 2014, but this conference has been cancelled due to difficulties confirming key partners' attendance and the limited interest received from regional manufacturers. However, PQM plans to participate in the Central-Asian Trade Forum IV in Almaty in October 2014. PQM and WHO speakers will deliver presentations on GMP requirements and the potential benefits of participation in the WHO PQ programme during the Pharmaceutical session of the Forum. PQM has identified the speakers and started planning for the Trade Forum, including preparation of contracts with the speakers.

PQM has made contact with three Kazakh manufacturers of anti-TB medicines, and all three manufacturers expressed interest in receiving technical assistance from PQM. They were each sent a questionnaire; however, of the three companies who showed interest in the program, only one (Nobel Almaty Pharmaceutical Factory) ultimately responded with a completed questionnaire. PQM GMP personnel will visit Nobel's manufacturing facility around the time of the Central Asia Trade Forum in October 2014.

PQM identified a consultant to translate a set of WHO Prequalification documents into Russian and is preparing the contract.

### Challenges

Given that manufacturers are not at a level of GMP compliance that is expected of a company considering submission to WHO PQ, the activities required in the country are new to the PQM GMP staff. The needs of this region relate more to system-building between the regulatory authority and drug manufacturers. PQM needs to establish contacts within the regulatory authority and needs more information to assess the needs of the region. Additionally, the task of finding qualified consultants to work with Romat proved to be more difficult than had been expected. The time it took to find qualified candidates for a long-term project at the Romat facility was much longer than anticipated by PQM staff.

## **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.

### Key activities

PQM developed a scope of work and anticipated contacts, which were agreed upon by USAID/Uzbekistan and Uzbek partners, to conduct a field gap analysis to identify the status of QA/QC systems for anti-TB medicines and help define priority needs. The visit occurred in August 2014, and PQM was able to meet with representatives of all key government institutions at the Ministry of Health. However, PQM was not allowed to visit and assess the capacities of key institutions, including the MRA, the national QC labs, and the manufacturers who are (or will be) producing TB medicines. For further TA, PQM needs to get a formal request from the Ministry of Health, followed by a comprehensive situation analysis of targeted areas of expertise.

#### Challenges

The poor quality of medicines and their irrational use are certainly contributing to the increase of TB, including MDR and XDR-TB in Uzbekistan. The MOH should understand that a thorough assessment of QA/QC capacities, including selected manufacturers, is highly needed in Uzbekistan. The type of assistance that PQM provides is highly needed, but it can be rendered only if approved by the MOH of Uzbekistan. However, there has been no feedback from the Uzbek MOH after the visit there in August.

## **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's QA/QC systems to ensure the quality of antimalarials throughout the supply chain.

#### Key Activities

##### **Address gaps in QA/QC of antimalarials in malaria endemic states in Brazil**

Routine assessment of antimalarials utilizing the three-level approach was suspended in Brazil in 2008, and since then the quality of antimalarials has not been assessed at dispensing sites from the public or formal and informal private sectors. To address this and other gaps in QA/QC systems throughout the supply chain in endemic areas, PQM sent a technical assistance proposal to the NMCP. The proposal was accepted and relevant activities were subsequently included in AMI's work plan.

##### **Building capacity to perform testing of antimalarials according to Registration Methodologies Suriname**

In recent years, the Suriname MoH committed extensive resources to equip the Official Medicines Control Laboratory (OMCL), and lab personnel attended last year's analytical trainings provided by PQM. To further strengthen the lab's capability to assess the quality of medicines in general and antimalarials in particular, two lab analysts completed internships at USP. The internships were focused on Quality Management Systems and hands-on experience on methodologies required for the analysis of antimalarials.

##### **Regional: Inter-laboratory Proficiency Testing of Artemether-Lumafantrine**

Last year OMCL personnel from Brazil, Colombia, Ecuador, Guyana, Peru, and Suriname participated in training for the pharmacopeial analysis of the Fixed Dose Combination Therapy of Artemether-Lumafantrine, which is the first line of treatment for Plasmodium Falciparum malaria in most AMI countries in South America. This year, the same labs participated in Inter-laboratory Proficiency Testing for this product, with medicines and reference standards donated by USP. Two countries (Ecuador and Peru) completed the testing; the rest are still in process.

## **Identify sustainable mechanisms for south-south collaborations for quality assurance of medicines**

PQM planned a regional workshop as a forum to discuss the development of a sustainable framework for south-south collaborations to strengthen quality assurance of medicines in the countries, utilizing regional professional and technical resources, from public and private organizations, governmental as well as academic. For logistical reasons, the workshop was postponed and will be convened in November 2014. The number of participating countries and institutions has been expanded to include all AMI countries in South and Central America as well as some non-AMI countries. Invitations were sent to MRAs and OMCLs from 18 countries and eight academic institutions from five countries, all in LAC.

## **Development of tool to allow field-access to registered medicines' information**

Originally PQM proposed to develop a virtual library of images of antimalarials in use in AMI countries. Subsequently the scope was expanded for the development of a web database, available also through mobile devices, to allow access to registered medicines' information and images, in support of visual and physical inspection of medicines in the field. The developer has been selected and final scope of work finalized. Development will be financed partially through other PQM funding streams and pilot usage will be implemented in selected countries, including 2-3 from AMI.

## **Bringing awareness about approaches to assess quality of medicines and countries results**

Two papers were published:

1. "Were medicine quality and pharmaceutical management contributing factors in diminishing artemisinin efficacy in Guyana and Suriname?" *Malaria Journal* 2014, 13:7. Pribluda VS et al. This publication puts information attained through PQM activities in LAC in the context of the potential emergency of resistance to artemisinin in the Guyana Shield.
2. "The Three-level Approach: A framework for ensuring medicines quality in limited resource countries" *Pharmaceutical Regulatory Affairs* 2014, 3:1. Pribluda VS et al. The Three-level Approach is utilized by PQM in all regions of the world; however, the initiative of writing this article was generated in AMI because of the institutionalization of the approach by several LAC countries. Main authors include PQM personnel that have been working in the implementation of this approach in AMI countries

## Challenges

The main challenges faced while performing activities in the context of AMI were:

1. The lack of response by certain country stakeholders in Ecuador, Guyana, and Suriname, which precluded performing activities planned in those countries.
2. In Brazil, the lack of response from the regulatory agency to the NMCP significantly delayed the activities planned in that country. Only during the fourth quarter was the work proposal approved by the NMCP and the ensuing PQM activities will have to be initiated next year.

## **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.

To address some of those issues, USAID/Guatemala has obligated funds for PQM since FY11. Using funds obligated in FY13, PQM will continue strengthening QA/QC systems in Guatemala by advancing some of the work addressed in previous years and expanding the scope of work.

#### Key Activities

#### **Installation and launch of an internet based registration software (WEBSiamed) at the Departamento de Regulación y Control de Productos Farmacéuticos y Afines (DRCPFA, Guatemalan MRA)**

This software allows (a) manufacturers and distributors to upload, review, edit, and send electronically all the information for new registration and/or renewals; review the status of the application; communicate with MRA personnel and/or request hearings related to the process; and (b) MRA personnel to give a more expeditious review of the documentation provided, communicate actions related to the review (Approval, Denial or Additional Requests); and also to have direct communication with the OMCL to gain access to QC results. Installation of most of the necessary modules has been completed. Free training sessions to manufacturers and other clients were delivered by a PQM consultant. Online renewal of registrations is fully operational, and by Q3, more than 200 applications had been processed through this mechanism. Installation of final modules and launch for all types of registration was supposed to be finalized during FY14 Q4 but was delayed and will be implemented during FY15 Q1 due to changes in health authorities at various levels of the Ministry of Health.

#### **Building regulatory capacity of DRACPFA personnel**

##### 1. Training on dossier evaluation

This activity strengthened MRA personnel capabilities to properly evaluate the documentation submitted by the manufacturers for new registration and/or renewal of existing ones.

##### 2. Training on equipment and water and air system validation

One of the main roles of MRAs is ensuring that medicines registered and distributed in the country are manufactured in compliance with current Good Manufacturing Practices (GMP), following internationally recognized guidelines for this purpose. After the training, DRCPFA inspectors are better prepared to assess critical processes when auditing manufacturers; this is important because a significant percentage of medicines registered and utilized in Guatemala are manufactured locally

#### **Ensure that the Medicines Unit of the National Health Laboratory (UME-LNS, Guatemalan OMCL) operates in compliance with international standards**

In 2013 the lab requested voluntary suspension from the ISO 17025 accreditation conferred by the Guatemalan Accreditation Organism (OGA). During a visit to the lab and an audit performed in May 2014, PQM verified the readiness of the lab to regain the accreditation; the lab was subsequently audited by OGA and regained its accreditation. A PQM audit also allowed for the development a roadmap for the expansion of the ISO 17025 accreditation, from a product-based accreditation to a method-based accreditation. An audit by the accrediting body for expansion of the accreditation is planned for FY 15 Q2 or Q3.

#### **Support MQM at selected decentralized Health Areas (Áreas de Salud, DAS) utilizing the Three-level Approach**

PQM supported the MRA's pilot implementation of the Three-level Approach (3LA) for MQM in the Huehuetenango Department. All in situ trainings and activities were performed by the MRA and the OMCL, and PQM helped in the development of the protocol and implementation logistics. During this activity, the OMCL trained local personnel in the use of screening tests with the Minilab that PQM donated the previous year.

Subsequently, PQM collaborated with the MRA in the development of a modified regulation for post-marketing surveillance of medicines that includes the 3LA that will be submitted for approval to the Ministry of Health during FY15 Q1. In Guatemala, MQM activities can be performed exclusively by the

MRA. However, besides including the 3LA, the modified version allows the MRA to delegate to local health authorities the implementation of MQM utilizing the 3LA in coordination with the OMCL.

### Challenges

The main challenges faced while performing activities in Guatemala were:

1. The DRCPFA (MRA) generates funds through registration fees, certifications, licenses, etc. However, only a fraction of these funds is returned to the MRA by the MoH. The funds returned are insufficient to support their activities. The personnel are extremely busy functioning under these conditions, which delays the implementation of planned activities. MQM in Huehuetenango could be implemented only because PQM financially supported the transportation and lodging of the MRA personnel that traveled to the site.
2. Similar financial constraints resulted in the temporary and voluntary suspension of the OMCL ISO17025 accreditation in 2013 and are a cause of concern for the maintenance of the re-accreditations and potential expansion next year.
3. The funding from USAID/Guatemala will cease in FY15, due to budget reductions in health elements as well as refocusing activities in specific areas. Since PQM became aware of this during Q3, activities had to be prioritized, to ensure enough funds remain for FY15 to support sustainability of the system changes achieved so far. This resulted in the suspension of some activities included in the work plan.

## **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.

#### Key Activities

Due to ongoing security concerns in the region, travel plans are on hold until further notice.