Promoting the
QUALITY OF MEDICINES Plus

PQM+ Quarterly Report – Program Year 2, Quarter 1

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About PQM+

The Promoting the Quality of Medicines Plus (PQM+) Program is a five-year cooperative agreement (No. AID-7200AA19CA00025) between the U.S. Agency for International Development (USAID) and the U.S. Pharmacopeial Convention (USP) to sustainably strengthen medical product quality assurance systems in low- and middle-income countries (LMICs). PQM+ works to improve medical product quality through cross-sectoral and systems strengthening approaches and the application of international quality assurance standards across the pharmaceutical system. By sharing scientific expertise and providing technical support and leadership, PQM+ helps to create resilient and sustainable local health systems that ensure access to quality-assured essential medicines for HIV/AIDS, tuberculosis, malaria, neglected tropical diseases, and other infectious diseases as well as for reproductive, maternal, newborn, and child health.

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Acronyms

ANAB	American National Standards Society National Accreditation Board
API	active pharmaceutical ingredient
CAPA	corrective and preventive action
COVID-19	novel coronavirus of 2019
CRP	collaborative registration procedure
CTD, eCTD	common technical document / electronic common technical document
DGDA	Directorate General of Drug Administration
DPM	Directorate for Pharmacy and Medicines
DRAP	Drug Regulatory Authority of Pakistan
DT	dispersible tablets (amoxicillin)
EFDA	Ethiopian Food and Drug Authority
FP	family planning
FPP	finished pharmaceutical product
GBT	Global Benchmarking Tool
GMP	Good Manufacturing Practice
HR	human resources
ISO	International Organization for Standardization
ISO/IEC	International Organization for Standardization/ International Electrotechnical Commission
LMIC	low- and middle-income countries
MCH	maternal and child health
MedRS	Medicines Risk-based Surveillance
MNCH	maternal, newborn, and child health
MOH	ministry of health
MoU	memorandum of understanding
MQCL	medicines quality control laboratory
MRA	medicines regulatory authority
MTaPS	Medicines, Technologies, and Pharmaceutical Systems program
NCL	National Control Laboratory
NMRA	national medicines regulatory authority

NTD	neglected tropical disease
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PMI	U.S. President's Malaria Initiative
PMS	post-marketing surveillance
PPE	personal protective equipment
PQM+	Promoting the Quality of Medicines Plus program
PY1, etc.	Program Year 1, etc.
Q1, etc.	Quarter 1, etc.
QA	quality assurance
QC	quality control
QMS	quality management system
QRM	quality risk management
RB	risk-based
RBI	risk-based inspection
SATTA	Stepwise Assessment Tool Towards Accreditation
SF	substandard or falsified
SOP	standard operating procedure
TB	tuberculosis
ToR	terms of reference
TWG	technical working group
USAID	U.S. Agency for International Development
USP	U.S. Pharmacopeia
WHO	World Health Organization
WHO PQ	World Health Organization Prequalification

Overview

The Promoting the Quality of Medicines Plus (PQM+) program sustainably strengthens medical product quality assurance (QA) systems in low- and middle-income countries (LMICs). By sharing scientific expertise and providing technical support and leadership, PQM+ helps create resilient local health systems that ensure access to quality-assured essential medicines for HIV/AIDS, tuberculosis (TB), malaria, neglected tropical diseases (NTDs), and other infectious diseases, as well as for reproductive, maternal, newborn, and child health (RMNCH).

The PQM+ program is pleased to present this quarterly report for Program Year 2, Quarter 1 (October 1 – December 31, 2020). This report summarizes the activities undertaken during this period and presents cumulative progress by objective and source of funding (USAID country Missions and USAID/Washington). PQM+ activities support the priorities of a country's medical product QA system and USAID's commitment to support development objectives in medicines QA systems strengthening. All activities align with at least one of PQM+s five program objectives, which the Results Framework details (see Table 1):

1. Improve **governance** for medical product QA systems.
2. Improve country and regional **regulatory systems** to assure the quality of medical products in the public and private sectors.
3. Optimize and increase **financial resources** for medical product QA.
4. Increase **supply** of quality-assured essential medical products of public health importance.
5. Advance a global medical products QA **learning** and operational agenda.

Table 1. PQM+ Results Framework

GOAL: SUSTAINABLY STRENGTHEN MEDICAL PRODUCT QUALITY ASSURANCE SYSTEMS IN LMICs				
Objective 1: Governance for medical product quality assurance systems improved	**Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved**	**Objective 3: Financial resources for medical product quality assurance optimized and increased**	**Objective 4: Supply of quality assured essential medical products of public health importance increased**	**Objective 5: Global medical product quality assurance learning and operational agenda advanced**
1.1 – Evidence-based medical product quality assurance legislation, policies, and regulations developed/ updated and/or implemented 1.2 – Systems that facilitate transparency and accountability promoted 1.3 – Fragmentation addressed and coordination across entities (public and private) with medical product quality assurance responsibilities promoted 1.4 – Links among the medical product quality assurance systems and other sectors developed and fortified	2.1 – Sustainable systems for market authorization/ registration, inspection, and licensing functions of medical product regulatory agencies improved 2.2 – Sustainable post-marketing surveillance systems and medical product quality control laboratory capacity strengthened 2.3 – Regional harmonization to strengthen medical product quality assurance regulatory capacity and networks supported 2.4 – Adoption of data standards and integrated information systems to support regulatory medical product quality assurance functions supported 2.5 – Competence, efficiency, and expansion of the medical product quality assurance workforce improved	3.1 – Allocation and use of investments for medical product quality assurance systems strengthening optimized 3.2 – Sustainable resources mobilized	4.1 – Pharmaceutical manufacturers for Good Manufacturing Practices (GMP) and medical product regulatory submissions/ dossiers supported 4.2 – Capacity to conduct bioequivalence studies for dossier submissions strengthened 4.3 – Capacity for market intelligence and analytics of public health pharmaceutical markets increased 4.4 – Health coverage schemes that incorporate medical product quality requirements supported 4.5 – Monograph development and use supported	5.1 – Evidence-based approaches and tools developed and/or applied 5.2 – Research and analysis to support medical product quality assurance systems strengthening conducted 5.3 – Advocacy on the importance of medical product quality assurance for public health, including the link between medical product quality and antimicrobial resistance, supported

Highlights

This quarter, the program continued broad-scale implementation of approved work plans for country and core buy-ins, bringing additional staff on board. Program staff at headquarters and in the field adapted to challenges posed by the ongoing COVID-19 pandemic to ensure that PQM+ work and activities continued as smoothly as possible. Highlights from the program's activities follow.

Governance

PQM+'s work related to governance ranged from helping establish public policies to proposing improvements to public policies on medical product QA.

- PQM+ supported the Ethiopian Food and Drug Administration (EFDA) in reviewing and validating the import, export, and wholesale directive. A two-day consultative workshop took place in Addis Ababa with 15 regulatory experts participating. They updated the contents of the directive to adhere to international best practices, aligned the requirement on "remaining shelf life of medicines" with the World Health Organization (WHO) recommendation, and required that all medicines in the supply chain carry unique identification codes, per GS1 standards.
- The program coordinated with the Liberia Medicines and Health Products Regulatory Authority (LMHRA) to complete the mapping of required legislation, identifying 27 regulations that should be developed. Priority regulations will strengthen enforcement actions, medicines registrations, marketing surveillance, and medicines importations. The new regulations will promote good governance of the medical product quality assurance system in Liberia by ensuring transparency, accountability, efficiency, and flexibility.

Regulatory Systems

PQM+ supports countries to improve their regulatory systems, focusing on medical product market authorization, facility inspection, licensing, laboratory testing, and market surveillance.

- PQM+ facilitated the International Organization for Standards (ISO) 17025:2017 reaccreditation assessment of Burma's Department of Food and Drug Administration's Nay Pyi Taw Pharmaceutical Chemistry Laboratory. The accreditation body, American National Standards Society (ANSI) National Accreditation Board, or ANAB, conducted a remote assessment and witnessed all 10 scopes of testing via video conferencing. ANAB granted official reaccreditation to Nay Pyi Taw Pharmaceutical Chemistry Laboratory on December 11, 2020. The 10 scopes are high-performance liquid chromatography (HPLC), dissolution, determination of pH, UV, IR, loss on drying, uniformity of dosage units, Karl Fisher water determination, titration, and melting point. These scopes encompass the critical testing parameters involved in quality testing of the solid dosage form of medicines.
- In Ethiopia, PQM+ built internal self-auditing capacity for EFDA's regional labs, training 33 staff to use the Stepwise Assessment Tool Towards Accreditation (SATTA) and to understand the basics of internal quality auditing. With the enhanced capacity, four of five branch laboratories evaluated their labs using SATTA. After verification/ validation of

the self-assessment findings through supportive supervision, the results will aid in developing branch-specific roadmaps to guide efforts to achieve ISO accreditation. The presence of accredited laboratories at branches will substantially improve EFDAs' capacity to detect falsified and substandard medical products circulating in the Ethiopian market by conducting regular PMS with a broader geographic and product coverage.

- In December, the Drug Regulatory Authority of Pakistan (DRAP) launched the Pakistan Integrated Regulatory Information Management System (PIRIMS), an online platform which will facilitate the integration of registration, inspections, and licensing functions. PIRIMS will increase the ease of doing business for the pharmaceutical industry by ensuring transparency, and accountability in regulatory decisions as well as facilitating pre-market review and post-marketing surveillance activities. It will also greatly reduce the time and cost of bringing new drugs to market.
- PQM+ trained Senegal's multisectoral post-marketing surveillance (PMS) unit on the risk-based PMS (RB-PMS) protocol for essential medicines. Five regions completed sampling of malarial medicines. The teams gathered samples of artemether/lumefantrine tablets and suspension, artesunate injection, sulfadoxine/pyrimethamine tablets and sulfadoxine/pyrimethamine/ amodiaquine dispersible tablets from public and private facilities.

Financial Resources

To enhance financial sustainability, PQM+ promotes risk-based approaches that allow regulatory agencies to focus their resources on the highest-risk challenges.

- With PQM+ support, Nigeria and Mozambique have developed financial sustainability approaches for their labs. In Nigeria, PQM+ is working with the National Institute for Pharmaceutical Research and Development (NIPRD) to review and develop a cost structure that reflects demand for testing, the laboratory's operating costs, and its existing fees and funding. The goal is for the laboratory to determine how to promote sustainability and generate additional revenue to cover the cost of future reaccreditation efforts. Similarly, PQM+ in Mozambique is working with staff from the National Directorate of Pharmacy (DNF) and the quality control (QC) laboratory, known as the Department of Drug Quality Check (DCQ), to build in financial sustainably to attain ISO/IEC 17025: 2017 accreditation.

- This quarter, NIPRD received its first international request for third-party quality control testing of anti-malarial medicines, a result of the lab's new ISO accreditation**.** This marks an important new source of revenue. PQM+ is helping the laboratory determine how to generate additional revenue to cover the cost of future reaccreditation efforts.

Supply

PQM+ is unique among USAID-funded global health programs in that it provides technical assistance to help manufacturers achieve international quality standards by adopting current Good Manufacturing Practices (GMP) in the production of quality-assured medical products.

- RB-PMS entails optimizing resources by channeling limited resources toward areas that present the highest risks to patients. In Bangladesh, PQM+ supported RB-PMS strategies. PQM+ worked with Bangladesh's National Control Laboratory (NCL) to

develop risk-based testing protocols for seven medical products (favipiravir tablets, dexamethasone tablets, hydroxychloroquine tablets, ivermectin tablets, oseltamivir capsules, lopinavir/ritonavir tablets and remdesivir injection) that are on the list of products used to treat COVID-19 in Bangladesh. The country's Directorate General for Drug Administration (DGDA) is also conducting RB-PMS of these products to ensure they are of quality and safe for patient use.

- In Ethiopia, EFDA finalized the report on laboratory test results of 40 PMS samples collected and tested during program year (PY) 1. The samples were alcohol-based hand sanitizers produced by 19 local and two foreign manufacturers. The survey revealed that 9 of 40 (22.7 percent) of the samples failed to comply with requirements. As a follow-up regulatory enforcement action, EFDA issued a recall letter to all manufacturers producing the substandard products. This level of substandard products, especially during the COVID-19 pandemic, signifies the critical need to conduct larger surveys by expanding the scope of products and geographic areas covered.
- PQM+ also supported the Food, Beverage, and Pharmaceutical Industry Development Institute (FBPIDI) and EFDA to finalize an assessment of available capacity and challenges reported by local manufacturers in producing priority medicines. Key findings included: 100 percent encountered problems in acquiring active pharmaceutical ingredients (APIs) in the last six months; 100 percent reported having problems acquiring equipment in the last six months; and 75 percent cited supplier shortages as a challenge. Most local manufacturers are operating at far below their installed capacity. Of eight manufacturers, six produced at below 50 percent capacity in 2019 and 2020. This represents a significant decline in capacity utilization in the last two years. This production occurred across all pre-COVID-19 categories of products. Following the detection of COVID-19 and resulting shortages of some critical products, some manufacturers changed part of their lines to produce alcohol-based hand sanitizers and surgical masks.
- In collaboration with the Medicines, Technologies, and Pharmaceutical Systems program (MTaPS), PQM+ worked with WHO India, JSS Academy of Higher Education and Research, the Indian Pharmaceutical Alliance, the Ministry of Health and Family Welfare, and the Government of India to develop a current GMP online training course to improve the pharmaceutical manufacturing sector in India. This work will build on previous GMP course material that was developed under PQM. The WHO-led course titled "Current Good Manufacturing Practices Online Workshop for Pharmaceutical Units in Active Pharmaceutical Ingredients and Formulations for Access to Quality-Assured Medical Products." Of two modules delivered, one drew 127 participants from the Indian pharmaceutical industry, while 90 people attended the second module.
- PQM+ continued to support Kazakhstan's Nobel Almaty Pharmaceutical Factory to improve its compliance with WHO prequalification (WHO PQ) standards and to complete its dossier for levofloxacin tablets in the common technical document (CTD) format. To mitigate the risk of cross-contamination, Nobel should implement proper quality risk management (QRM). PQM+ provided virtual QRM training for 16 staff members at the Nobel Almaty Pharmaceutical Factory.
- PQM+ reached out to the Association of Pharmaceutical Producers of Nepal (APPON) to discuss capacity-building strategies to improve GMP compliance in the country's local pharmaceutical industry and priority training topics related to GMP compliance.

Learning

PQM+ also aims to advance a global medical products QA learning and operational agenda that includes evidence-based approaches, research, and advocacy.

- In collaboration with Burma's Department of Food and Drug Administration (DFDA), PQM+ organized a technical webinar to share U.S. Pharmacopeia's (USP's) good laboratory practices during the COVID-19 pandemic and explore strategies to prevent and minimize the risk of COVID-19 in labs. More than 100 participants from DFDA, academic institutions, laboratories under various ministries, and private entities attended.
- In November, PQM+ launched a webinar series, with the first session answering important questions: "What are regulatory and quality assurance systems and how do they impact health programs?" More than 130 participants joined from around the globe, many from USAID country Missions and USAID/Washington.

Health Elements

Maternal and Child Health

This quarter, PQM+ completed the English version of the guidance document on risk-based categorization of maternal, newborn, and child health (MNCH) products. This guidance document explains how to define probability and impact risks for priority MNCH products and will facilitate the development of sampling plans using the Medicines Risk-based Surveillance (MedRS) tool in countries. PQM+ also finalized the English and French versions of job aids to assist with amoxicillin dossier preparation and amoxicillin laboratory testing. They function as a quick reference source for regulatory staff who review amoxicillin dossiers for approval and for laboratory staff on testing, highlighting the product's core peculiarities to consider during the review process.

Neglected Tropical Diseases

This quarter, PQM+ engaged two of its Core-FLEX partners—Muhimbili University in Tanzania and Mahidol University in Thailand—to conduct a market analysis of NTD medical products. The analyses will be included in the global NTD medicine donation program. The focus regions are Africa and Asia and the analysis will look at APIs and finished pharmaceutical products (FPPs).

Tuberculosis

In 2020, the presence of nitrosamine impurities was identified in two important anti-TB medicines, rifapentine and rifampicin, raising concerns about the quality of the global supply. To aid the industry in addressing this challenge, PQM+ continued the development of analytical methods for the detection of nitrosamines impurities in these two medicines. Given the sophistication of the methodology required to detect the nitrosamines impurities, quality control laboratories were surveyed to understand their in-house capacity to ensure the suitability of methods under development.

Partners

PQM+ revised its initial approach to partnership engagement and communication based on lessons learned during partner onboarding. This has resulted in the preparation of internal job aids to facilitate the partner engagement process. Additional mechanisms to facilitate bi-directional communication with partners are undergoing review. The goal is to have feedback mechanisms in place to regularly assess programmatic, technical, and operational elements within the consortium.

In Q1, PQM+ was also able to finalize the transfer of USP technical resources to each of its Core-FLEX partners, covering a wide range of technical topics on medicine quality. Future updates to these resources will be available to Core-FLEX partners. This was the second transfer of resources by PQM+ to Core-FLEX partners. In PY1, Core-Flex partners gained access to organizational development resources developed by IntraHealth.

Activities and Progress for Cross-Bureau Activities

PQM+ Cross-Bureau-funded activities primarily focused on raising awareness about the importance of medical product quality, and developing new approaches to strengthen medicines regulatory functions. PQM+ Cross-Bureau activities funded by the Office of Health Systems (OHS)fall under the following program objectives:

- Improve country and regional regulatory systems to assure the quality of medical products in the public and private sectors;
- Optimize and increase financial resources for medical product QA; and
- Advance a global medical products QA learning and operational agenda.

The PY2 workplan for OHS Cross-Bureau activities was approved in November 2020. During the first quarter, PQM+ completed the following activities.

Risk-Based Inspection Methodology Framework

National medicines regulatory authorities (NMRAs) and international regulatory agencies conduct inspections of the range of entities involved in the manufacture, import, distribution, and dispensing of medical products to ensure their compliance with regulatory requirements. Inspections of medical product manufacturers monitor compliance with GMP as part of the authorization process for that manufacturer to produce medical products. NMRAs also conduct inspections to monitor the quality of medical products throughout the supply chain, from the point of manufacture to delivery to the patient, to identify and minimize points where SF medical products infiltrate the system or products degrade during handling, distribution, and storage.

To conserve scarce regulatory resources, PQM+ is developing a risk-based inspection (RBI) methodology. The RBI methodology will allow NMRAs to prioritize the selection and inspection of sites based on risk, directing limited resources to facilities that present the greatest risk to medical product quality. This builds on PQM's experience developing an RB-PMS framework and guidance document to help countries implement more efficient, risk-based PMS sampling and testing. In PY2, PQM+ will develop an RBI guidance document, develop an RBI tool; and field test the guidance and tool.

This quarter, PQM+ identified and commenced initial desk reviews of relevant literature, including the Pharmaceutical Inspection Co-operation Scheme (PIC/S) model for RB inspection for GMP, relevant USP training materials, WHO's *Guidelines on Quality Risk Management*; and the World Bank's *Good Practices for Regulatory Inspection: Guidelines for Reformers*. PQM+ also began reviewing existing tools that guide visual inspection of medicines, potential platforms that can support remote inspection (e.g., conventional video and Avatour) during the COVID-19 pandemic-related travel restrictions, and regulatory information management systems that can handle inspections data. PQM+ drafted an outline of the guidance document, including objectives of risk-based inspection, the process, and technical components.

MedRS Tool

This quarter, PQM+ continued to refine the Excel and online versions of the MedRS tool, based on user feedback. Changes included ensuring consistency in use of terminology, particularly terms used to classify risk factor categories, adding easy-to-understand definitions, and copy editing final content. In addition, after a careful evaluation of limitations of both the online and Excel version of the tool (e.g., number of data entries for sampling facilities), as well as the functional capability (e.g., process for uploading data from the offline to the online version), features (e.g., data backup and security) and user-friendliness, PQM+ created a list of improvements to both versions of the tool that includes a timeline and process for their completion. PQM+ is establishing a core team to implement changes and corrections, where possible, in the Excel (offline) version. An application developer consultant will make the changes and corrections in the online or web-based version.

Model to Estimate the Economic and Health Impact of SF Medicines

PQM+ is developing a model that can help estimate the health and economic costs to patients and health systems incurred by using SF medicines of a given medicine therapeutic class in a country. This activity is an attempt to answer one of OHS' priority research questions: What measurement tools and approaches are most helpful in understanding and estimating the costs that are impacting the health systems strengthening interventions? Model outputs can be used to inform policy decisions about reducing the prevalence of SF medicines.

This quarter, PQM+ laid the groundwork for developing the SF costing model. This included defining the process for developing and testing the model and engaging external partners to participate in developing the model. A panel of experts from USP, the University of Washington, the University of North Carolina, and Harvard University formed, with each institution's roles and scope of work defined. PQM+ also defined criteria for selecting the countries and medicine classes to use in developing and testing the model. PQM+ conducted a mini-survey of PQM+-supported countries to ascertain likely interest and availability of data on key inputs. The survey also solicited information on the medicines that would be of greatest interest to host governments and USAID Missions. Based on the survey results, PQM+ proposed a preliminary selection of countries and medicines that the program will finalize with USAID next quarter.

Common Standards for Pharmaceutical Information Management

PQM+ is collaborating with USAID's MTaPS program to encourage the use of data standards in regulatory submissions and for pharmaceutical information management systems. The goal of this activity is to promote the use of data standards, identify requirements for electronic transmission of regulatory information, and improve ability to integrate data across various

regulatory functions. This quarter, PQM+ had an initial planning meeting with MTaPS to discuss the approach to identifying the standards, roles, and timelines.

Webinar Series

This quarter, PQM+ delivered its first webinar, titled "What are regulatory and quality assurance systems and how do they impact health programs?" This webinar, which occurred in November, had more than 130 participants from around the globe, many from USAID country Missions and the USAID/Washington headquarters. The webinar answered the following questions for participants to expand their understanding and knowledge in medical product quality assurance:

- What are medical product quality assurance systems?
- Who is responsible for them?
- What do regulatory agencies do to assure medical product quality?
- What can be done to sustainably strengthen these systems to help ensure the effectiveness of USAID's health programs?

Priority Activities for Next Quarter

- Risk-based inspection
  - Finalize the structure and content of the guidance document on RB Inspection (RBI).
  - Solicit the interest of select medicine regulatory authorities (MRAs) in participating in an expert panel/working group to develop the RBI guidance document and an RBI tool for LMICs.
  - Define parameters, inputs, outputs, functionality, features, and security for the electronic RBI tool.
  - Identify an information technology (IT) application developer to create the RBI tool.
- MedRS
  - Complete the initial application design with enhanced functionality, features, and capability of the online / web-based MedRS.
  - Finalize all necessary changes and corrections in the online MedRS tool, including migrating existing data from the initial version (MedRS Version 1) into the enhanced version (Version 2).
  - Conduct internal test runs and revise the tool as necessary.
  - Field test the enhanced online MedRS in two PQM+ countries.
  - Launch the final product for full deployment at the country level.
- SF medicines costing model
  - Finalize contractual agreements with SF costing model partners.
  - Convene two meetings of the expert advisory panel to agree on a conceptual framework and further define the parameters, variables, assumptions, and outputs of the SF costing model.

- Finalize selection of the countries and medicine classes for the costing model and engage the PQM+ chiefs of party and USAID Missions in early stages of the work in those countries.

- Common Standards for Pharmaceutical Information Management Systems: Begin compiling common standards related to medicine quality.
- Webinar Series: Develop and deliver the second webinar.

Activities and Progress by Country and Regional Buy-Ins

By the start of Y2, the PQM+ program was working with 17 countries (Bangladesh, Benin, Burkina Faso, Burma, Central Asia Republic/Kazakhstan, Ethiopia, Ghana, Kenya, Liberia, Mali, Mozambique, Nepal, Nigeria, Pakistan, Senegal, Serbia, and Uzbekistan) and the Asia Regional Bureau. PQM+ also received COVID-19 funding from the Bangladesh, Pakistan, and Serbia Missions, and is in discussions to begin work in an additional six countries during PY2. PQM+ also received core funding for Cross Bureau, MCH, NTD, and TB activities. The sections that follow summarize progress on country and regional buy-ins.

Africa Region

Burkina Faso

Malaria is endemic in Burkina Faso and is one of the primary causes of morbidity and mortality. The ministry of health (MOH) reported an estimated 12 million confirmed cases and 3,974 deaths in 2018. The U.S. President's Malaria initiative (PMI) supports the National Malaria Control Program (NMCP) to implement its Malaria National Strategic Plan 2016–2020, which aimed to reduce malaria incidence and deaths in 2020 by 40 percent from 2015 levels.

The country's Directorate General of Pharmacy and Laboratory (ANRP) is the national pharmaceutical regulatory authority. It coordinates all regulatory actions in the pharmaceutical sector, including product PMS. The Directorate of Market Surveillance and Quality Control of Health Products is the technical body in charge of QA/QC. A functional PMS program was established in the ANRP in 2018. ANRP is collaborating with the Directorate for the Control of Drugs and Non-Food Products (DCM/PNA), which falls under the *Laboratoire National de Santé Publique* (LNSP, the National Public Health Laboratory), to sample medical products for post-marketing surveillance.

Building on PQM's efforts, PQM+ continues to work with the main medicines quality stakeholders, ANRP and LNSP, and other stakeholders to: adopt a risk-based, sustainable approach to PMS; strengthen LNSP as it prepares for ISO 17025 accreditation; and assist ANRP in improving collaboration among key stakeholders to strengthen regulatory systems and improve the quality of medicines on the Burkina Faso market.

In PY2, PQM+ is working to:

- Improve **governance** for medical product quality assurance systems.
- Improve country and regional **regulatory systems** to assure the quality of medical products in the public and private sectors.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

This quarter, PQM+ worked to better understand the current state of collaboration between LNSP and ANRP, which will inform development of a memorandum of understanding (MoU) for collaboration between the two agencies. PQM+ conducted a desk review of the documentation that established both institutions and PQM project reports. PQM+ consultants also had conversations with management of both institutions. This desk review indicated that the two institutions collaborate in (a) general activities related to QA of health products, market authorizations, and developing QA strategies; (b) PMS activities; and (c) laboratory capacity building. These areas of collaboration will be elaborated in subsequent meetings to start the development of the MoU.

In addition, ANRP seeks to institute a periodic national QA/QC stakeholders forum. PQM+ helped ANRP develop a preliminary list of all medicines QA/QC stakeholders. It includes several public sector entities (ANRP, LNSP, CAMEG [*Centrale d'achat des médicaments essentiels génériques et des consommables médicaux,* the central medical store and procurement agency]) and several private sector actors, mainly donors. The list will be reviewed, expanded, and validated in a meeting with ANRP and LNSP prior to the planning of the first medicines QA/QC workshop in Burkina Faso.

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

In Q1, PQM+ initiated worked to establish a national PMS technical working group (TWG). PQM+ developed a list of potential members and shared it with ANRP for their input. ANRP reviewed and added to the list, then sent letters to the agencies asking them to nominate members to serve on the TWG. PQM+ shared a generic draft terms of reference (ToR) for the TWG with ANRP that the latter will review and adapt to the Burkina Faso context.

Priorities for next quarter:

Next quarter, PQM+ plans to:

- Assist ANRP to inaugurate the national PMS-TWG and validate the TWG's ToR.
- Orient PMS-TWG members on RB-PMS and train them to use the MedRS tool.
- Assist ANRP and LNSP to draft and validate the MoU for collaboration between the two organizations.
- Conduct training on SATTA and coach LNSP to adapt the tool for internal audits.
- Organize the first medicines QA/QC workshop in Burkina Faso.
- Plan the logistics for the inaugural meeting of the TWG, which will serve as a PQM+ program launch in Burkina Faso.

Ethiopia

The use of poor-quality medical products can endanger treatment, erode public confidence in health programs, and contribute to the development of antimicrobial resistance, which results in

more expensive treatment with unpredictable outcomes. Many LMICs, including Ethiopia, are at particular risk of SF medical products because of lack of effective regulatory oversight and product quality assurance/quality control systems. Furthermore, Ethiopia still imports more than 85 percent of its demand for essential medicines. In the face of global public health emergencies such as Ebola and the COVID-19 pandemic, overdependence on imports for life-saving medicines threatens public health.

In Ethiopia, medicine regulation occurs through authorized bodies at the federal and regional levels. Federally, EFDA registers all medical products; licenses and regulates the production, import, storage, and distribution of transregional medical products; and conducts quality control testing and post-marketing surveillance of products circulating in the local market. All other regulatory activities that EFDA does not mandate fall under the jurisdiction of regional regulatory bodies and city administrations. The lack of clarity in mandates between EFDA and regional regulatory bodies, the absence of a formal reporting relationship between EFDA and regional regulators, and the poor capacity of regional regulators all compromise regulatory oversight of medical products circulating in Ethiopia.

PQM+ is supporting efforts to ensure the availability of quality-assured, safe, and efficacious medicines to address the priority health needs of the people of Ethiopia. PQM+ has been working to build the capacity of EFDA and the regional regulatory bodies for monitoring medical product quality throughout the supply chain and strengthening their collaborative working relationship to create synergy and efficiency in executing their respective regulatory mandates. PQM+ also is building local manufacturers' capacity to meet international standards and ensure that locally produced medical products are of good quality.

During PY2, PQM+ is working to:

- Improve governance for medical product quality assurance systems
- Improve country and regional regulatory systems to assure the quality of medical products in the public and private sectors.
- Increase supply of quality-assured essential medical products of public health importance.
- Optimize and increase financial resources for medical products quality assurance

Progress by PQM+ Objective

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

This quarter, PQM+ helped EFDA finalize the report on laboratory test results of 40 PMS samples collected and tested during the previous program year. The samples were alcohol-based hand sanitizers collected from five locations in Addis Ababa and the and surrounding areas of Ambo, Adama, Debrebirhan, and Woliso. Sample producers were 19 local and 2 foreign manufacturers. The survey revealed that 9 of 40 samples (22.7 percent) failed to comply with requirements. As a follow-up regulatory enforcement action, EFDA has issued a recall letter to all manufacturers producing the substandard products. This level of substandard products, especially during the COVID-19 pandemic, signifies the critical need to conduct larger surveys by expanding the scope of products and geographic areas covered.

To strengthen EFDA's laboratory's ability to monitor the quality of alcohol-based sanitizers, PQM+ procured a digital alcoholometer, delivered this quarter. With this device, EFDA will be better able to determine the alcohol content of products marketed as part of the COVID-19 emergency response.

This quarter, PQM+ trained 33 staff (6 female and 27 male) from branch laboratories and EFDA headquarters on using SATTA and the basics of internal quality auditing. The training helped build capacity to conduct self-assessment/evaluation of the laboratories. After the training, four of five branch laboratories evaluated their labs using SATTA. PQM+ provided remote technical assistance on use of the tool to the branch laboratories. After verification/ validation of the self-assessment findings through supportive supervision, the results will aid in developing branch-specific roadmaps to guide efforts to achieve ISO accreditation. The presence of accredited laboratories at branches will substantially improve EFDAs' capacity to detect falsified and substandard medical products circulating in the Ethiopian market by conducting regular PMS with a broader geographic and product coverage.

Inefficiencies in regulatory processes surrounding the import, export, and wholesale of pharmaceuticals can seriously impact access to essential medicines in a country. Legislation addressing regulatory oversight should facilitate speedy import and wholesale practices. This quarter, PQM+ supported EFDA in reviewing and validating the import, export, and wholesale directive. A two-day consultative workshop in Addis Ababa drew 15 regulatory experts. They reviewed and updated the contents of the directive to adhere to international best practices, aligned the requirement on "remaining shelf life of medicines" with WHO's recommendation, and required that all medicines in the supply chain carry unique identification codes, per GS1 standards. Requirements at ports of entry were revised to ease import processes. The requirements for a pre-import permit for nonregistered products were clearly stated. The competency, roles, and responsibilities of key actors at each level of the supply chain and the administrative measures for failing to meet regulatory requirements were also updated. After incorporation of all inputs from the workshop, the directive was submitted to the management of EFDA for approval.

EFDA seeks to become a WHO-listed authority, which would signal that it has the essential competencies to properly regulate medicines, from product development and manufacture to patient use. Addressing gaps identified by WHO's GBT is a key priority as EFDA seeks a Maturity Level 3 or higher WHO listing. PQM+ is helping EFDA revise and update relevant quality management system (QMS) documentation in compliance with the GBT requirements. During this quarter, PQM+ helped EFDA develop 4 new standard operating procedures (SOPs) and review and update 10 others.

Objective 4: Supply of quality-assured essential medical products of health importance increased

PQM+ worked with government counterparts to explore opportunities for boosting local production of medicines, particularly considering the ongoing COVID-19 pandemic. As part of this effort, PQM+ supported Ethiopia's Food, Beverage, and Pharmaceutical Industry Development Institute (FBPIDI) and EFDA in finalizing an assessment of available capacity and challenges across all categories of medical products that local manufacturers reported in producing priority medicines. The findings of this assessment included:

- 100 percent encountered problems in acquiring APIs in the last six months;
- 100 percent cited the lack of hard currency as the key bottleneck;

- 100 percent reported problems acquiring equipment in the last six months;
- 88 percent cited price increases and transportation blockades as major challenges; and
- 75 percent cited supplier shortages as a challenge.

Moreover, most local manufacturers are operating far below their installed capacity. While one manufacturer reported utilizing 75 to 90 percent capacity from 2016 to 2018, three manufacturers reported capacity utilization of between 25 and 50 percent during the same period, and one manufacturer was operating below 25 percent capacity. Of the eight manufacturers, six (75 percent) were producing below 50 percent capacity in 2019 and 2020. This represents a significant decline in capacity utilization in the last two years.

Overall, the spread of COVID-19 has negatively impacted local manufacturers in multiple ways, including reduction in manufacturing capacity (operations) leading to decrease in revenue; increased overall monthly cost (e.g., unexpected costs including company fumigation and spray, supply of sanitizer, and facemasks to employees); and shortage of foreign currency.

Previously, all manufacturers supplied medicines to the Ethiopian Pharmaceuticals Supply Agency (EPSA). The current assessment revealed that 100 percent of manufacturers have active commitments with EPSA that have not yet been fulfilled. The number of products under active commitment ranged from one to 30, with an average of 14 per manufacturer. Of the 76 priority medicines identified by MOH, 62 (82 percent) can be produced locally. Of the 62 products, 60 (97 percent) are already being produced; the remaining two (three percent) could be manufactured locally if demand exists. Overall, this assessment indicates that local manufacturers, though few, are working below their available production capacity and can contribute substantially to supplying essential medicines to address key public health priorities in Ethiopia. However, this will require a concerted effort among the government and other relevant stakeholders/partners to address challenges the industry faces.

PQM+ worked with EFDA and FBPIDI to produce the evidence about barriers to importing API and finished products. The data were included in the final report that has been shared with relevant stakeholders and partners. The assessment report was discussed in a consultative meeting this quarter involving higher government officials from eight critical stakeholders, including EFDA, EPSA, MOH, FBPIDI, and the Ethiopian Pharmaceutical Manufacturers Association. Participants recommended presenting the findings to a wider audience, including the investment commission, customs, and financial sector (banks). The assessment findings and the results of the stakeholders consultation will provide the evidence for eventual policy decisions.

Priorities for Next Quarter:

Next quarter, PQM+ Ethiopia plans to:

- In coordination with EFDA, build capacity of regional regulatory bodies on inspection and provide support in the conduct of actual inspections;
- Conduct supportive supervision/mentoring to branch laboratories to build capacity of laboratory analysts and validate the self-audit/assessment results;
- Develop laboratory-specific roadmaps for accreditation for three branch laboratories; and
- Assess status of corrective and preventive action (CAPA) implementation by local manufacturers and identify areas for technical support.

Ghana

Malaria is endemic in Ghana and a major cause of illness and death in the country, particularly among children and pregnant women. In addition, maternal mortality is a pressing health concern. Postpartum hemorrhage is the leading cause of maternal death in Ghana. Ghana is 1 of 25 countries that account for more than 66 percent of the world's maternal and child deaths.[1]

WHO recommends oxytocin as a first-line treatment for postpartum hemorrhage. Through PQM's technical assistance, USAID/Ghana focused on building the Ghana Food and Drug Authority (GFDA) capacity to monitor the quality of maternal and child health commodities such as oxytocin. GFDA, now a maturity level 3 medicines regulatory authority, has made great strides in the survey of anti-malarials, with less than 10 percent failure rate in the last survey. But the challenge of substandard, falsified, and unregistered medicines, including those used to treat postpartum hemorrhage, persists in Ghana.

Building on PQM's work, PQM+ is working with the GFDA and other stakeholders to: adopt a risk-based sustainable approach to post-marketing surveillance (PMS); support a local manufacturer to achieve WHO prequalification for artemether/lumefantrine tablets to treat malaria; collaborate with GFDA to assess progress by the three other manufacturers audited under PQM in 2019; identify potential local manufacturers of oxytocin; and collaborate with Ghana Health Supply Chain-Procurement and Supply Management (GHSC-PSM) to start preparing the local pharmaceutical industry and the GFDA for the adoption of GS1 standards.

In PY2, PQM+ is working to:

- Improve country and regional regulatory systems to assure the quality of medical products in the public and private sectors and
- Increase supply of quality-assured essential medical products of public health importance.

Progress by PQM+ Objective

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

In Q1, PQM+ introduced the project to the key stakeholders—FDA Ghana, GHSC-PSM, and Entrance Pharmaceutical Limited. To initiate establishment of a national PMS-TWG, PQM+ drafted a list of potential members and shared it with GFDA for input. GFDA reviewed the list and indicated the need to align this TWG with an established committee for SF medicines to prevent duplication. PQM+ also shared a generic draft ToR for GFDA review and adaptation to the Ghana context and will share it with the other TWG members for their input. PQM+ began to plan the logistics for the inaugural meeting of the PMS-TWG.

PQM+ also worked with GHSC-PSM, Total Family Health Organization, and FDA Ghana to draft a request for expressions of interest for local manufacturers of oxytocin and iron and folic acid tablets. The program will publish it in local newspapers to solicit interest from potential manufacturers who could adopt the necessary technology to produce and supply these medicines on the Ghanaian market.

[1] https://www.usaid.gov/what-we-do/global-health/maternal-and-child-health/priority-countries

Priority Activities for Next Quarter

Next quarter, PQM+ Ghana plans to:

- Assist the Ghana FDA to inaugurate the national PMS-TWG and validate its ToR;
- Orient the PMS-TWG on RB-PMS and providing training on use of the MedRS tool;
- Identify potential local manufacturers for oxytocin, iron and folic acid tablets; and
- Review the registration and procurement processes to identify and provide solutions to registration, procurement, and supply chain gaps that impact the quality of oxytocin.

Kenya

The PQM+ program aims to strengthen the quality of medical products in Kenya by improving governance structures and regulatory systems for medical product quality assurance. PQM+ delivers technical assistance to the Pharmacy and Poisons Board (PPB), the National Quality Control Laboratory (NQCL), the Division of National Malaria Program (DNMP), Department of Family Health, the MOH's Division of Health Products and Technologies (HPT), and the counties to further strengthen in-country stakeholders' capacity to ensure access to quality-assured medical products for the population.

In PY2, PQM+ is working to:

- Improve governance for medical product QA systems and
- Improve country and regional regulatory systems to assure the quality of medical products in the public and private sectors.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

Following inauguration of the PPB's joint pharmacovigilance (PV) and post-market surveillance (PMS) technical working group in quarter 4 of fiscal year 2020, PQM+ introduced the MedRS tool and its use in PMS to the joint PV/PMS TWG of PPB and demonstrated the use of the tool with malaria and reproductive, maternal, neonatal, child, and adolescent Health (RMNCAH) products. MedRS is an RB-PMS tool that PQM launched to help NMRAs develop RB sampling strategies in support of national PMS programs while maximizing available resources. The tool integrates and automates the science and practice of RB-PMS into a single platform.

As part of this support, PQM+ trained 20 of 28 members of the PV/PMS TWG in October on the RB-PMS approach of monitoring the quality of pharmaceuticals and other health products. A second workshop took place in November. During this hands-on workshop, 17 PV/PMS TWG members (11 male, 6 female) received training on using the MedRS tool. Subsequently, PQM+ worked with the PPB and a smaller team of the PV/PMS TWG to enter data on medicines, counties, subcounties, and health facilities into the MedRS tool. The outputs of the MedRS tool will inform development of a protocol for PMS of priority products used in the malaria and the RMNCAH program in Kenya. After data entry is complete, in Q2 PQM+ will support the TWG to develop a universal PMS protocol that can be minimally adapted for use with all other medical products, including PMS of malaria and RMNCAH products.

The PQM+ program also assisted the Division of Health Products and Technologies of the Ministry of Health to develop brief informational packages for the dissemination of the HPT supply strategy and related HPT guidelines and tools. PQM+ took the lead in designing and developing simple infographics and job aids on the quality assurance framework for HPTs. Two drafts were presented at a workshop organized by the Division HPT; one draft was adopted with additional inputs from various stakeholders at the workshop. This infographic will be part of a comprehensive package for dissemination of QA guidance into national pharmaceutical sector governance and health product policies, contributing to strengthening systems and tools for product quality assurance mechanisms of malaria and RMNCAH products at the national, county, and health facility levels.

During the previous quarter, PQM+ assisted the Division of the National Malaria Program (DNMP) to conduct a further technical review of the draft QA framework for malaria commodities by incorporating technical input from stakeholders that focused on products to control the malaria parasite and the mosquito vector.

In November, PQM+ collaborated with the DNMP to conduct a virtual workshop of key stakeholders to validate the draft QA framework for pharmaceuticals and other medical products the malaria program uses. This QA framework outlines the roles and responsibilities of various stakeholders involved in assuring the quality of health commodities used in preventing, diagnosing, and treating malaria. It guides the establishment of a mechanism for coordinating the quality assurance activities of various stakeholders and establishes a coordination mechanism to oversee the quality assurance of health commodities used in control and elimination of malaria in the country.

The scope of malaria commodities covered by the framework include: antimalarial medicines; malaria rapid diagnostic tests; pesticide products; long-lasting insecticidal nets; biologic larval source management products; laboratory consumables and equipment, such as reagents and microscopes; personal protective equipment for indoor residual spraying, such as masks, respirators, hard hats, and gloves; and hand-operated compression sprayers. The 15 workshop participants included representatives from the Division of National Malaria Program, Kenya Medical Supplies Authority, Pharmacy and Poisons Board, National Quality Control Laboratory, Kenya Medical Laboratory Technician and Technologist Board, and PMI implementing partners such as Vectorlink and Afya Ugavi.

PQM+ is assisting the DNMP to collate and incorporate stakeholders' feedback and input from the validation workshop and submit an updated draft QA framework to the DNMP for review and clearance before finalizing, printing, and disseminating it in Q2.

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

In collaboration with the PPB, PQM+ finalized the scope of work for a consultant to conduct a rapid training needs assessment to inform the design of topics for learning (curriculum), the detailed learning content for the platform, and the design of the platform itself. The specific topics have not received the PPB's agreement, but will focus on QA of medical products, PMS, QMS materials (such as organizational policies, quality manual, procedures, work instructions, and job aids) for the PPB, inspections for GMP, good distribution practices (GDP) and good storage practices (GSP), and product registration. In parallel, PQM+ worked with the PPB to finalize the scope of work for another consultant to configure a platform for self-directed learning. For a start, the target audience for the platform will be internal to PPB, focusing on the

approximately 200 employees. PQM+ is evaluating proposals received for both consultancies so that actual work on platform development commences in Q2.

The NQCL is the official regulatory QC laboratory for testing of medical products in Kenya. Only certificates of analysis issued by NQCL are deemed legal for a regulatory action against any poor-quality product. It is therefore critical that the laboratory has the capacity and resources to perform and administer accurate and efficient results.

Last quarter, using the human resources (HR) assessment tool that had been customized for NQCL, PQM+ identified and reviewed relevant background information from several NQCL HR documents and built an NQCL-specific questionnaire for key informant interviews, tailored to collect additional data that could not be obtained from the initial document review. Continuing that work this quarter, PQM+ assisted NQCL to finalize tools and methodology for the HR capacity assessment and prepare a detailed plan for conducting the HR assessment. The HR assessment examines staffing, skills, working conditions, and employee motivation at NQCL. As part of this assessment, PQM+ will facilitate a review of the current management structure, map roles and responsibilities of staff and their skills, review training plans, and review performance management and employee retention policies. To facilitate the HR assessment, PQM+ engaged a consultant in Q1 and onboarded him in mid-December 2020. The assessment will identify key challenges and opportunities that will inform strategies for strengthening NQCL's HR capacity to enable the institution to improve its performance in testing the quality of pharmaceuticals, including those used in the malaria and RMNCAH programs in Kenya.

Priority Activities for Next Quarter

Next quarter, PQM+ Kenya plans to:

- Support the PPB in coordinating and harmonizing technical approaches to PMS implementation in the country. This includes finalizing the RB-PMS protocol and implement a PMS survey.
- Complete the procurement, delivery, and handover of Karl Fischer titrator equipment to the NQCL.
- Support the NMCP to finalize and implement the QA framework for malaria commodities.
- Assist PPB to establish an organizational capacity development platform for self-directed learning (e-learning course).
- Support organizational capacity improvements at NQCL.
- Complete HR capacity Assessment for NQCL.

Liberia

In Liberia, PQM+ is strengthening the country's regulatory system, specifically focusing on supporting the Liberia Medicines and Health Products Regulatory Authority (LMHRA) and its quality control laboratory. This quarter, PQM+ facilitated the development of a list of priority regulations that support implementation of the LMHRA Act of 2010. PQM+ also supported the mapping of required legislation and sponsored a trip for senior staff of LMHRA to travel to the Ghana FDA on a study visit. Following the study visit, the LMHRA organized a special committee for drafting the regulations. PQM+ has also facilitated establishment of a PMS-TWG, inaugurated December 18, 2020, with a chair and vice chair elected.

In PY2, PQM+ will help to:

- Improve governance for medical product QA systems, and
- Improve regulatory systems to assure the quality of medical products in the public and private sectors.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

The lack of regulations to support the LMHRA Act of 2010 has been a major challenge to improving governance of medical product quality assurance in Liberia. During Q1, PQM+ laid the foundation for good governance and regulatory practices by building consensus through discussion with LMHRA on the purpose and design of proposed regulations and a strategic plan.

PQM+ coordinated with the LMHRA to complete the mapping of required legislation by reviewing the LMHRA Act of 2010 and other documents, like the institutional development plan based on the WHO Global Benchmarking Tool for self-assessment and the strategic plan of 2011. The LMHRA and PQM+ have identified 27 regulations that need to be developed. Priority regulations will strengthen enforcement actions, medicines registrations, marketing surveillance, and medicines importations. Once these regulations are in place, they will promote good governance of the medical product quality assurance system in Liberia by ensuring transparency, accountability, efficiency, and flexibility.

PQM+ arranged and supported a five-day (November 29 – December 3, 2020) study visit to the Ghana FDA for LMHRA's managing director and two other senior staff. The PQM+ Liberia consultant accompanied the LMHRA delegation to Ghana. The visit has strengthened collaboration between the LMHRA and the Ghana FDA. It also allowed the LMHRA to learn from Ghana's successes (including regulations development) through in-person workshops, where FDA staff gave 14 presentations and site visits to laboratories in Accra and the Tema port. As a result of the visit, LMHRA set up a committee for drafting priority regulations. It will depend heavily on lessons learned from Ghana and PQM+ will continue to provide technical guidance.

Figure 1: The LHMRA delegation and Ghana FDA lab managers participate in a study tour roundtable talk.

The most recent LMHRA three-year strategic plan expired in 2015 and has not been revised or updated. LMHRA leadership now intends to develop a new strategic plan. PQM+ coordinated with the LMHRA to complete the terms of reference for a consultant to support development of a five-year strategic plan. The procurement process is ongoing.

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

In October, the LMHRA lab relocated to a temporary facility in King's Farm, Careysburg, about 39 kilometers from central Monrovia. To support the laboratory relocation, PQM+ advised on

equipment decommissioning and installation, packing, transportation, documentation, and inventory of equipment and chemicals.

PQM+ also developed a standard registry for equipment, chemicals, and apparatus. The LMHRA is using the registry as a resource as it inspects the laboratory's inventory. Additionally, PQM+ has completed its review of the LMHRA's new laboratory design and submitted its comments to the LMHRA for consideration.

On December 18, 2020, the LMHRA, with the support of PQM+, successfully launched the PMS-TWG for Liberia. The launch was attended by 26 stakeholders (including online participants) from the LMHRA, Liberia National Police, Liberia Pharmacy Board, WHO, Liberia Drug Enforcement Agency, Ministry of Heath Supply Chain Unit, National Malarial Control Program, National AIDS Control Program, Central Medicines Stores, National Tuberculosis Control Program, and the Ministry of Health Neglected Tropical Disease Control Program. This TWG will oversee PMS activities in Liberia to ensure an integrated and harmonized system.

PQM+ assisted the LMHRA to develop a ToR for the TWG and helped organize the inaugural meeting. Members of the TWG elected a chair (from the Central Medicines Stores) and vice chair (from the National Malarial Control Program). LMHRA heads the secretariat in accordance with the PMS-TWG ToR. FrontPage Africa of Liberia printed a story on December 23.[2]

Priority Activities for Next Quarter:

Next quarter, PQM+ Liberia plans to:

- Coordinate the LMHRA Committee on Regulations Development to begin drafting priority regulations;
- Continue to support PMS activities by coordinating with the new PMS-TWG to draft PMS protocols and plan one round of PMS;
- Continue support to get the LMHRA laboratory operational, to include procurement of reagents and minilabs to support PMS activities; and
- Hire a consultant to help develop the LMHRA's five-year strategic plan.

Mali

Over the past decade, the government of Mali has engaged in widespread institutional reform. The proposed establishment of a national pharmaceutical regulatory agency was declined in 2019 for major revision. DPM has yet to submit a revised proposal. The DPM is working to mobilize national support for this initiative. It hopes to share case studies of successful precedents in francophone Africa to convince the Institutional Development Unit of the need to establish a national pharmaceutical regulatory agency.

In PY1, PQM+ facilitated the establishment of a multisectoral PMS-TWG, co-chaired by both DPM and *Laboratoire National de Santé* (LNS, the National Health Laboratory), with participation from the health inspectorate, all disease programs, the procurement agency, the pharmaceutical wholesaler's association, and other allied professional bodies. PQM+ worked with this TWG to develop national guidelines and a protocol on RB-PMS using the MedRS tool

[2] https://frontpageafricaonline.com/health/lmhra-usp-pqm-set-up-post-marketing-surveillance-technical-working-group-for-liberia/

for antimalaria and MCH medicines. This approach and process will strengthen the risk-based medicine PMS system in Mali.

In PY2 PQM+ will:

- Improve country and regulatory systems to assure the quality of medical products.

Progress by PQM+ Objective

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

In Q1, the multisectoral PMS-TWG received training on the RB-PMS protocol for antimalaria and MCH medicines. Sampling of medicines (artemether/lumefantrine tablets, artesunate injection, quinine injection, artemether injection, oxytocin injection, diazepam injection, amoxicillin dispersible and medroxyprogesterone injection) in four regions—Segou, Sikasso, Koulikoro, and Kayes—was planned. LNS and DPP completed the necessary administrative processes to start the sampling. Four teams were deployed to each region between December 9 and 24 to sample from public and private facilities. The sampling teams included staff from LNS, DPM, the malaria control program, and the MCH division of the ministry of health.

Priority Activities for Next Quarter

Next quarter, PQM+ Mali plans to:

- Supervise the testing of antimalarials and MCH medicines;
- Assist PMS-TWG to review the RB-PMS data and compile the report; and
- Support LNS management in instituting a performance management system.

Mozambique

Mozambique's National Directorate of Pharmacy (DNF) was established in 2017 as a transitional organization, working toward becoming an autonomous NMRA. It was created from the Pharmacy Department of the Ministry of Health after the promulgation of the revised pharmaceutical law. Further technical support is required to help the QC laboratory, known as the Department of Drug Quality Check (DCQ), attain ISO/IEC 17025: 2017 accreditation, and for DNF to attain maturity level 3 in the WHO GBT program and ISO/IEC 9001:2015 accreditation.

In PY2, PQM+ will help to:

- Improve governance for medical product QA systems;
- Strengthen regulatory systems for quality medical products; and
- Optimize and increase financial resources for medical product QA systems.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ proposed a program implementation framework that lays out the roles and responsibilities of DNF and PQM+. PQM+ also proposed a stepwise approach to achieving sustainability of DCQ. The draft has been shared with DNF for its feedback.

The establishment of the DNF as an autonomous NMRA required development of key regulations to establish required processes, practices, and systems for its regulatory functions. Building on PQM's technical support, in collaboration with the MTaPS program, PQM+ will continue providing this technical assistance to the DNF. PQM+ updated the laboratory regulation of DCQ to reflect the laboratory's status as a department under the new DNF and added clauses that will aid good laboratory practices.

Objective 2: Regulatory systems to assure the quality of medical products in the public and private sectors strengthened

PQM+ updated the ISO/IEC 17025: 2017 accreditation roadmap for DCQ with detailed steps and timelines. PQM+ initiated procurement of reagents, reference standards and books, proficiency test samples, and internet services for the laboratory. PQM+ also developed a draft equipment status report on the condition of major and support equipment to perform QC testing.

As a step toward building an effective workforce, PQM+ assessed the capacity of personnel in two DNF departments. PQM+ assessed capacity of staff of the Department of Evaluation of Medicines, Vaccines, and Biological Health Products to evaluate dossiers and of the Department of Pharmaceutical Licensing and Inspection to conduct good manufacturing practice inspections. In collaboration with partner IntraHealth, PQM+ developed a training needs assessment tool to identify gaps on these topics and inform the development of robust training plans.

Objective 3: Financial resources for medical product quality assurance optimized and increased

Mozambique's DNF does not currently generate enough funds to attain financial self-reliance. DCQ does not receive adequate funds from the government health budget or other funding streams to maintain its day-to-day operations and fulfill its service function. PQM+ presented and discussed basic financial management principles for laboratory sustainability with leadership and key staff and developed a draft sustainability framework.

Priority Activities for Next Quarter

Next quarter, PQM+ Mozambique plans to:

- Continue to work on PY1 activities that were delayed or postponed dur to COVID-19.
- Continue working on updating the laboratory regulation; and
- Implement activities outlined in the ISO 17025 roadmap for DCQ.

Nigeria

According to the 2018 Nigeria Demographic and Health Survey, one in eight children die before turning 5 years old. Maternal mortality caused by prolonged obstructed labor, unsafe abortion, septicemia, hemorrhage, and eclampsia remains a serious problem in Nigeria.[3,4] Malaria remains the country's leading public health problem, disproportionately affecting children younger than 5 years and pregnant women. Nigeria also has a high incidence of communicable and noncommunicable diseases.

PQM+ is working to ensure the quality of medicines and other medical products with an emphasis on USAID and Government of Nigeria (GON) priority malaria and MCH medicines and family planning commodities. PQM+ works with stakeholders in the public and private sectors to increase local pharmaceutical manufacturing capacity and to sustainably strengthen regulatory systems at the national and state levels. PQM+ also is strengthening quality management systems and building laboratory capacity in quality control testing in compliance with international standards.

In PY2, PQM+ will:

- Improve country and regional regulatory systems to assure the quality of medical products in the public and private sectors;
- Optimize and increase financial resources for medical product QA; and.
- Increase the supply of quality-assured essential medical products of public health importance.

Progress by PQM+ Objective

Objective 2: Regulatory systems to assure the quality of medical products in the public and private sectors strengthened

PQM+ is working with the Pharmacists Council of Nigeria (PCN) to strengthen medical product quality assurance and regulatory systems at the state level to improve access and availability of malaria, MCH, and family planning products in three states. The focus is on medical product retail outlets, which are community pharmacies and patent medicines shops. PCN and PQM+ conducted an assessment to understand the challenges in addressing quality assurance as it pertains to these outlets. The state-level assessments took place in Bauchi, Sokoto, and Ebonyi states using structured questionnaires via Google Forms. Using a purposive sampling approach, interviews took place with key state-level stakeholders, including representatives of the following institutions and organizations:

- State Ministry of Health
- State Primary Health Care Development Agency
- State Drug Revolving Funds/Medicine Agencies
- Wholesalers

[3] National Population Commission (NPC) [Nigeria] and ICF. 2019. Nigeria Demographic and Health Survey 2018. Abuja, Nigeria, and Rockville, Maryland, USA: NPC and ICF.
[4] USAID 2015-2020. Nigeria Country Development Cooperation Strategy (https://www.usaid.gov/nigeria/cdcs)

- Retail outlets (pharmacists and patent and proprietary medicines vendors (PPMV)]
- Pharmaceutical Society of Nigeria (PSN)
- Association of Community Pharmacists (ACPN)
- National Association of Patent and Proprietary Medicines Dealers (NAPPMED)
- Nongovernmental organizations implementing programs at the state level
- Pharmaceuticals Inspection Committees and PPMV Licensing Committees
- Pharmacists Council of Nigeria at the state level

The state-level assessments identified state-specific gaps that relate to medical product sale, QA, and regulatory systems. PQM+ validated the findings in collaboration with key stakeholders such as PCN (headquarters and state staff), state-level inspectors, PSN, ACPN, and NAPPMED at a dissemination and action plan meeting. Other participants were representatives of USAID/Nigeria, the Federal Ministry of Health Food and Drugs Services Department, National Products Supply Chain Management Programs, WHO, nongovernmental organizations such as the Clinton Health Access Initiative and the Institute of Human Virology Nigeria. During this meeting, each state, with support from PCN and PQM+, developed a state-specific action plan. When implemented, these action plans will improve the capacity of the state-level inspectors, quality assurance systems at CPs and PPMVs, and, hopefully, the quality of medical products and services offered at these outlets.

Figure 2: Stakeholders gather for the Nasarawa State dissemination and action plan meeting.

Objective 3: Financial resources for medical product quality assurance optimized and increased

Building on the ISO/IEC 10025:2017 reaccreditation of the National Institute of Pharmaceutical Research and Development (NIPRD) in PY1, PQM+ is helping the laboratory determine how to generate additional revenue to cover the cost of future reaccreditation efforts. PQM+ is helping NIPRD review and develop a cost structure that reflects demand for testing, the laboratory's operating costs, and its existing fees and funding. This started with a hands-on capacity building workshop called "Financial Management Principles for Sustainability of NIPRD's Central Laboratory, Budgeting and Pricing." At the workshop, 52 NIPRD staff learned about and started using a PQM+-developed tool for laboratory budgeting, costing and pricing. This intervention is timely, on the heels of the laboratory's recent ISO accreditation (see box).

Immediate Reward from ISO Accreditation

NIPRD received its first international request for third-party quality control testing of some anti-malarial medicines in Nigeria as an outcome of the ISO accreditation of the laboratory.

Objective 4: Supply of quality assured essential medical products of health importance increased

This quarter, PQM+ continued to provide technical assistance to local manufacturers of essential MCH, malaria, and nutrition products as these manufacturers seek WHO prequalification of their products. Examples of this support include:

- PQM+ reviewed data prepared by a manufacturer of magnesium sulfate 50 percent w/v injection prior to its submission in response to queries as part of WHO prequalification. That manufacturer also submitted samples of the product in its commercial pack to WHO PQ for evaluation.
- PQM+ helped the manufacturer close out CAPAs following a third-party audit of its aged plant to prepare to supply 250,000 doses of amoxicillin dispersible tablets for export.
- More than 160 patients participated in a palatability study for a zinc sulfate product, which should help conclude this study so the dossier can be submitted to WHO PQ.

As part of the GMP roadmap project, PQM+ conducted a two-day virtual workshop on implementing an effective CAPA system. More than 70 participants from a diverse cross-section of companies attended.

Priority Activities for Next Quarter

Next quarter, PQM+ Nigeria plans to:

- Conduct a gap assessment of PCN toward ISO 9001:2015 to inform development of a roadmap for its accreditation.
- Conduct stakeholder meetings to explore the possibility of community pharmacies and patent medicine shops procuring from drug revolving funds or medicine agencies in the three focus states.
- Provide support to NIPRD for migration to a local accreditation body, which will reduce the cost of future accreditations.
- Support manufacturers toward WHO PQ:
    - Review responses to WHO PQ requests for additional product data/information for magnesium sulfate injection dossier under review.
    - Review the bioequivalence study report of sulfadoxine + pyrimethamine (SP) tablet produced and the updated SP tablet dossier.
    - Provide support for compilation of an SP dossier based on updated product data.
    - Review a zinc sulfate dispersible tablet palatability study report.
- Continue implementation of recommendations from the GMP road map

Senegal

The Government of Senegal has developed a five-year (2019–2023) integrated strategic plan for the Directorate for Pharmacy and Medicines (DPM) and the National Medicines Control Laboratory (LNCM). The government's vision is to build "an efficient system of regulation and control, which ensures the development and application of quality standards and which guarantees access to medicines and other quality health products that are effective and safe for the entire population."

The plan cites areas of weakness for the DPM and the LNCM that include scarce financial resources, insufficient human resources, poor information systems, and lack of coordination and communication among relevant stakeholders engaged in the medical product QA system. To address these areas, the strategic plan outlines seven general objectives. PQM+ is contributing to the first and third: "Establish an appropriate institutional framework for the optimal implementation of pharmaceutical regulatory and control functions" and "Evaluate and control the quality of drugs." PQM+ is also addressing two subobjectives under those general objectives: meet the conditions for WHO certification and ISO 17025 accreditation of LNCM, and ensure PMS of medical products.

During PY1, PQM+ facilitated the establishment of a national PMS unit that includes DPM, LNS, the health inspectorate, all disease programs, the procurement agency, the pharmaceutical wholesalers' association, and other allied professional bodies. PQM+ worked with this unit to develop national guidelines and a protocol on RB-PMS for the MedRS tool for antimalaria medicines. During PY2, PQM+ continues to build on this progress.

In PY2, PQM+ will help to:

- Improve country and regional regulatory systems to assure the quality of medical products in the public and private sectors.

Progress by PQM+ Objective

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

In Q1, PQM+ trained the multisectoral PMS unit on the RB-PMS protocol for antimalaria and MCH medicines. Sampling in several regions—Dakar, Kolda, Djourbel, Kaolack, Kedougou, and Tambacounda—was planned and the DPM completed the necessary administrative processes to start the sampling. Three sampling teams were deployed to cover two regions each between December 14–24 to sample artemether/lumefantrine tablets and suspension, artesunate injection, sulfadoxine/pyrimethamine tablets and sulfadoxine/ pyrimethamine/ amodiaquine dispersible tablets from public and private facilities. The sampling teams included LNCM, DPM, and malaria control program staff.

In addition, this quarter PQM+ procured External Quality Assurance Assessment Scheme (EQAAS) Phase 10 proficiency testing samples for LNCM. Participation in this proficiency testing scheme will help LNCM demonstrate its competence in the techniques used in the PMS protocol. This will confirm the reliability of LNCM test results and strengthen its application for ISO/IEC 17025 accreditation.

LNCM received the EQAAS samples in December. It must complete the tests (colorimetric sulfates identification test and a complexometric titration of zinc sulphate tablets) within two months.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Supervise the PMS testing of anti-malarial medicines;
- Assist the PMS unit with reviewing the RB-PMS data and compiling a report; and

- Review the EQAAS Phase 10 proficiency testing data and report before submission to WHO.

Asia Region

Asia Bureau

PQM+'s technical assistance funded by USAID's Asia Bureau aims to promote regional regulatory convergence and reliance. PQM+ will work through regional health networks that include the Association of Southeast Asian Nations (ASEAN) Pharmaceutical Product Working Group (PPWG) and the South-East Asia Regulatory Network (SEARN) to strengthen regulatory and quality assurance systems. This work will build on support provided through the PQM program, as well as leverage the current PQM+ work in Southeast and Central Asia. The PY2 workplan was approved in November 2020, except for work on the GMP online training course, which was approved earlier.

Progress by PQM+ Objective

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

In collaboration with MTaPS, PQM+ developed a concept note that was shared with the ASEAN PPWG secretariat to discuss potential areas of support through the regional platform to member countries. PQM+ participated in a meeting convened by the ASEAN PPWG to discuss the concept note. PQM+ is currently awaiting the decision of the ASEAN PPWG before detailed planning can commence.

PQM+ is working in collaboration with MTaPS, WHO India, the JSS Academy of Higher Education and Research (JSS AHER), the Indian Pharmaceutical Alliance (IPA), the Ministry of Health and Family Welfare, and the Government of India to develop a current GMP online training course. This work will build on previous GMP course material developed under PQM. The activity is in response to an assessment of pharmaceutical manufacturers in India conducted by the WHO South-East Asia Regional Office (SEARO) and WHO India with an interministerial involvement of the Government of India. Assessment findings led to recommendations to improve the pharmaceutical manufacturing sector in India. The WHO-led course was titled "Current Good Manufacturing Practices (cGMP) Online Workshop for Pharmaceutical Units in Active Pharmaceutical Ingredients (API) and Formulations for Access to Quality-Assured Medical Products." Of two modules delivered, one drew 127 participants from the Indian pharmaceutical industry, while 90 people attended the second module. The first part of the course focused on knowledge enhancement. The second, planned to start in 2021, is a three-month mentorship phase with PQM+ involvement. In that section, the leader of each course will mentor participants to help effect change in practice.

This quarter, PQM+ developed and delivered two modules for the course that started in November and ended in December. The modules were "WHO Certification Scheme: Certificate of Pharmaceutical Product (CPP)" and "Laboratory Information Management System (LIMS)." PQM+ also peer-reviewed two modules developed by MTaPS on stability testing and "Good Manufacturing Practices—A Comparative Review of International Norms." WHO plans to roll this course out to other countries.

Also, during this quarter, PQM+ worked to engage its partner Mahidol University in Thailand to conduct a regulatory landscape analysis of the medical product quality assurance system for SEARN and ASEAN member countries. The aim of this analysis is to understand the situations of SEARN and ASEAN member country MRAs and to identify common challenges that can benefit from regional solutions. PQM+ worked with Mahidol University to develop the USAID contract package that must be completed before the University can undertake this work.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Continue to support the WHO-led collaborative GMP online training course delivery and rollout;
- Finalize Mahidol University's contract and start the landscape analysis of medical products quality assurance systems for SEARN and ASEAN member countries; and
- Continue discussions with ASEAN PPWG to agree on key technical areas of support.

Bangladesh

This quarter, PQM+ focused on implementing activities under program objectives 1, 2, and 4 in the approved work plan for PY2 and completing activities from the last quarter of PY1. PQM+ Bangladesh is helping the Directorate General of Drug Administration (DGDA) institutionalize good governance practices related to transparency, accountability, and communication with stakeholders; the National Control Laboratory (NCL) to strengthen its medicines quality monitoring system focusing on vaccines; and manufacturers to increase production of quality-assured first-line anti-TB medicines.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ completed an internal review and helped edit the DGDA's draft annual report for 2019–2020. This report highlights the DGDA's key achievements and performance and helps DGDA comply with the 2009 Right to Information Act, which requires that every authority publish a report on its decisions and activities each year.

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved.

The pharmaceutical market in Bangladesh is large and it is critical for the government to optimize use of its regulatory resources to protect the public health. This includes optimizing PMS and/or monitoring the safety of medical products after their release in the market. PQM+ promotes risk-based approaches to PMS that consider and assess multiple types of risk factors and prioritize activities to maximize the utility of the surveillance. PQM+ is helping DGDA scale up PMS of priority medical products in two new geographic divisions, Sylhet and Mymensingh.

In October, the director general of the DGDA organized a virtual consultative meeting to discuss how to strengthen the vaccine testing laboratory and relevant regulatory functions to achieve WHO maturity level 3. This would enable DGDA to oversee vaccine regulation and lot release in accordance with WHO prequalification criteria. WHO, PQM+, MTaPS, and other stakeholders

attended the meeting. The director general reallocated human resources and formed teams within the DGDA to address the following: GBT assessment; legal provision review and adoption; guidelines implementation; SOP review and development; CAPA completion; financial optimization; establishment of QMS; and dossier review. These new teams are tasked with completing all necessary activities to achieve WHO maturity level 3, with a special focus on vaccines. They will help DGDA become an effective and functional regulatory agency that can perform according to international standards.

In November, PQM+ procured two Minilab™ screening tools for the surveillance department of the DGDA. The Minilab™ is a portable device that allows for rapid quality verification of priority medicines, such as anti-infective medicines, and the detection of SF pharmaceuticals in the field. With these additional Minilabs™, the DGDA will be able to provide field-based screening of medicines as part of risk-based PMS in all eight divisions of Bangladesh.

One of the DGDA's key goals is to be a pre-accession member of the Pharmaceutical Inspection Co-operation Scheme (PIC/S). To help achieve this goal, PQM+ is working with the DGDA's focal person to review the PIC/S pre-accession applicant audit checklist and ensure that all of the audit requirements are met.

This quarter, PQM+ also met with the management team of the NCL vaccine unit and the DGDA's focal person to discuss the DGDA's goal of achieving WHO PQ for the NCL vaccine unit in 2021. Participants identified the areas of support required to build capacity for vaccine testing and lot release functions. They selected three vaccines as priorities (meningococcal, hepatitis-B, and cholera vaccines) toward applying for PQ. It was agreed that all laboratory analysts require extensive training on QMS and QA/QC.

As part of building the laboratory's capacity, PQM+ provided guidance and training in the following:

- How to prepare and use the standard testing procedure (STP) following the standard format along with the system of distribution, control, and archiving.
- How to use compendia for vaccine testing.
- Prepared a list of annual procurement requirements: vaccine standards, chemical/reagent and media, and organisms for the microbiological laboratory.
- Identified existing equipment in the vaccine laboratory with its unique identification number along with its brand name, model number, and serial number.
- Assisted in preparing job descriptions for new staff in the vaccine laboratory.
- Assisted the NCL physiochemical lab staff with validating the thin-layer chromatography (TLC) method using the established protocol and provided guidance on reporting.

Objective 4: Supply of quality assured essential medical products of public health importance increased

Building on PQM's work with manufacturers, PQM+ continued to support ACI Pharmaceuticals in addressing the CAPAs identified during PQM's inspection of the company in 2019. This quarter, PQM+ provided technical guidance and recommendations to ACI Pharmaceuticals to manufacture quality-assured, first line, fixed-dose combination anti-TB medicines. By December, 70 percent of the CAPA had been addressed. ACI Pharmaceuticals is in the product development stage of a three-drug fixed-dose combination working toward registration and WHO prequalification.

Priority Activities for Next Quarter

PQM+ plans to:

- Review existing legal provisions regarding laboratory service subcontracting with third-party private laboratories and conduct a landscape assessment of third-party private laboratories;
- Support the DGDA to complete review of and submit the PIC/S pre-accession applicant audit checklist;
- Conduct a dissemination meeting on the National Quality Assurance Guideline (NQAG);
- Provide training on RB-PMS guidelines and sampling and screening tools;
- Help develop SOPs for new equipment in the vaccine laboratory;
- Help develop a training program on testing scopes and compendial methods for the vaccine laboratory and subsequently provide the training; and
- Assist in analytical method validation for HPLC in the physicochemical laboratory

Burma

The PQM+ Program in Burma is working to build the capacity of Burma's Department of Food and Drug Administration (DFDA) toward a resilient medical product quality monitoring system. PQM+ aims to assure the quality of medicines in the country, with focus on antimalarials, and thereby contribute to the National Malaria Control Program's effort to eliminate malaria by 2030.

In PY2, PQM+ will help to:

- Improve country and regional regulatory systems to assure the quality of medical products in the public and private sectors.

Progress by PQM+ Objective

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

In Q1, PQM+ facilitated the ISO 17025:2017 reaccreditation assessment of DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory between November 24 and 26, 2020. The accreditation body, the American National Standards Society (ANSI) National Accreditation Board (ANAB), conducted a remote assessment and witnessed all 10 scopes of testing via video conferencing. All parties worked 12-hour days during the assessment to overcome the time difference. The assessment concluded without any nonconformities, and ANAB granted official accreditation to Nay Pyi Taw Pharmaceutical Chemistry Laboratory on December 11, 2020.

Figure 3: DFDA laboratory analysts demonstrate manual titration during the remote assessment.

Despite COVID-19 pandemic disruptions, the DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory will continue to provide, with confidence, accurate and reliable quality testing

of medical products to support front line workers, thanks to the ISO 17025:2017 reaccreditation supported by PQM+ and USAID/PMI.

PQM+ Burma organized a technical webinar titled "Good Laboratory Practices during the COVID-19 Pandemic" in collaboration with DFDA, and conducted webinars on December 9 and 11, 2020. In the webinars, specialists from the USP Reference Standards Laboratory shared best practices implemented at USP laboratories to prevent and minimize the risk of COVID-19 in the workplace. A total of 112 participants from DFDA and other organizations, including academic institutions, laboratories under various ministries, and private entities, attended the webinars. Since the beginning of the pandemic, participants reported having limited opportunity to get in touch with experts and expand their knowledge.

PQM+ is also in discussion with DFDA senior management on relocating the Nay Pyi Taw Pharmaceutical Chemistry Laboratory. DFDA management approved the relocation budget in December 2020, and reconfiguration work is expected to begin in January 2021. PQM+ and DFDA will begin preparations for WHO prequalification of the laboratory after relocation.

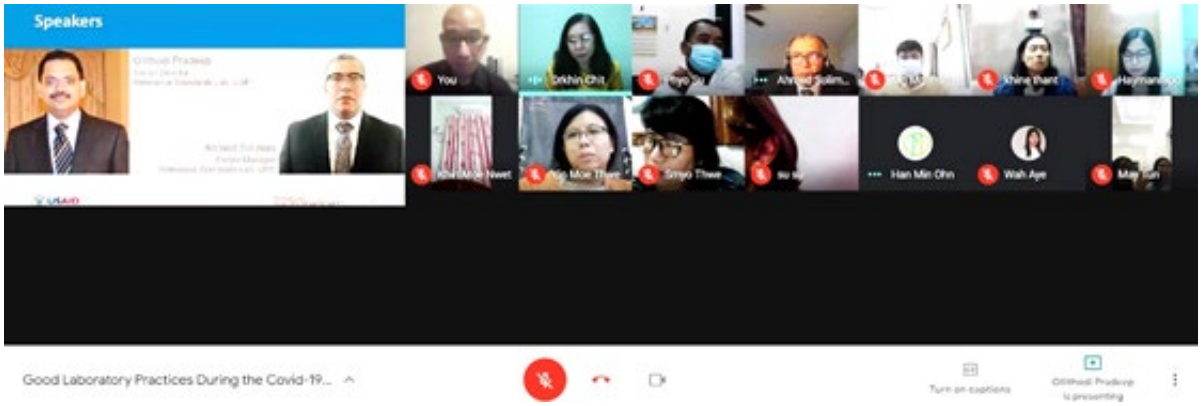

Figure 4: A total of 112 participants, ranging from laboratory technicians to deputy director generals, from 14 organizations attended the PQM+ webinar, shown in a screenshot here.

PQM+ and DFDA distributed a PMS pre-assessment questionnaire to four field offices (Yangon, Mandalay, Bago, and Kayin) to identify gaps in the current system. Responses from Mandalay and Bago field offices were delayed due to a nationwide surge in COVID-19 cases and repurposing of DFDA staff to COVID-19 response work.

Priority Activities for Next Quarter

Next quarter, PQM+ Burma plans to:

- Organize a consultative meeting between DFDA and USAID/Burma for a potential COVID-19 response activity to provide technical assistance to DFDA on the quality assurance of personal protective equipment (PPE);
- Oversee relocation of the DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory and reconfiguration of the Mandalay Pharmaceutical Chemistry Laboratory;
- Organize two webinars on issues related to medicines quality testing in collaboration with DFDA;
- Develop a regular training plan for DFDA laboratory staff to use in-house; and
- Assess the current PMS system at DFDA field offices and develop an action plan to implement a risk-based approach to PMS.

Nepal

PQM+ provides technical assistance to Nepal's Department of Drug Administration (DDA) to strengthen medical product QA and QC systems at the federal and peripheral levels (i.e., subnational and provincial levels in all seven provinces). In addition, PQM+ is strengthening the capacity of laboratories to conduct quality testing at the National Medicines Laboratory (NML) and its corresponding entities at the provincial level. PQM+ is strengthening private medicines testing laboratories and local medicine manufacturers, including both public and private allopathic and ayurvedic manufacturers. Finally, PQM+ is working across all stakeholders (including the National Health Research Council, the Logistics Management Section of MoPH, the Association of Pharmaceutical Producers of Nepal, and others) to build awareness of the health and economic threats posed by SF medical products and the need for strong regulatory systems.

In PY2, PQM+ will help to:

- Improve country and regional regulatory systems to assure the quality of medical products in the public and private sectors and
- Increase supply of quality-assured essential medical products of public health importance.

Progress by PQM+ Objective

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

This quarter, PQM+ coordinated with DDA, NML, the Nepal Medical Council, the Nepal Pharmacy Council, the Nepal Pharmacy Association, the Association of Pharmaceutical Producers of Nepal, the MTaPS program, and other stakeholders to advocate for revitalization of the Drug Advisory Council and Drug Advisory Committee. The advisory council and committee are helping the Government of Nepal review regulations, policies, and strategies to ensure the availability of quality, safe, effective, and affordable medicines in the country.

PQM+ worked with DDA and NML leadership to finalize plans for activities related to workforce development. The first step is to identify needs and challenges through an exhaustive assessment, which will inform a workforce development plan for the DDA and NML. This quarter, PQM+ and leadership from the two institutions agreed on the assessment guidelines, tools, key informants list, and interview schedule. PQM+ will conduct the interviews and focus group discussions next quarter.

PQM+ also continued its assistance to DDA and NML to strengthen the PMS system. The program submitted a revised preliminary assessment report to DDA and NML for review. The program also shared the risk-based PMS approach, guidelines, and tools with DDA and NML counterparts. PQM+ proposed the establishment of a technical working group to review the existing PMS policies and procedures for their alignment with a risk-based approach. The program team and DDA and NML counterparts reviewed the existing PMS plan and available capital and operational resources for implementing the PMS plan.

PQM+, in coordination with the NML, completed a desk review of NML policies, procedures, and tools related to governance, HR, service delivery, information management, finance, performance management, etc. All required documents and additional data were collected and

analyzed to identify gaps in existing policies, procedures, and tools. The program team drafted a report and shared it with the NML team for review and input. PQM+ will assist NML to finalize and disseminate the report next quarter. The program also helped NML prepare to implement the SATTA and craft an institutional development plan for NML ISO 17025 accreditation.

In collaboration with MTaPS and the DDA, PQM+ provided input on the draft outline for several components of the new drug law, including PMS, QA/QC, GMP inspection, and others, as well as on the quality management systems for DDA.

Objective 4: Supply of quality assured essential medical products of public health importance increased

PQM+ reviewed the Nepali GMP code for inspection of medical product manufacturers, importers, and distributors to determine the gaps and inconsistencies with international standards (e.g., International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use Q9 on Risk Management) and WHO guidelines. The program also reviewed the information collected through a preliminary questionnaire. The team drafted and shared a report of findings with DDA and stakeholders for their feedback.

PQM+ reached out to the Association of Pharmaceutical Producers of Nepal (APPON) to discuss capacity building strategies to improve GMP compliance in the local pharmaceutical industry of Nepal. The program ascertained industry interest and discussed priority training topics related to GMP compliance.

PQM+ initiated discussions with stakeholders (e.g., DDA, NML, APPON, Nepal Medical Council, Nepal Pharmacy Council, Chemists and Druggists Association, Logistic Management Section) on the Nepal pharmaceutical strategy and proposed a landscape analysis of the market for essential medicines in Nepal. The program shared the concept with USAID/Nepal, implementing partners (e.g., GHSC-PSM, MTaPS), the Ministry of Health and Population (MoHP), and professional bodies and associations. PQM+ began acquiring preliminary information on essential medicines, their market availability, MoHP priorities, and industry interest. The program also worked to finalize administrative arrangements with a PQM+ partner (IQVIA) so the latter can conduct a study on the essential medicine market in Nepal.

PQM+ Nepal reached out to leadership of the Logistics Management Section of MoPH, GHSC-PSM, and other partners (provincial health departments, public sector hospital administrations, and public health programs) to collect information on procurement policies and procedures; the number of medicines being procured and tracked through the logistics management information system; and challenges in procurement of quality-assured medicines on the local market. The program will analyze the documents and relevant information to inform recommendations on procurement and supply management of quality-assured health products.

Priority Activities for Next Quarter

Next quarter, PQM+ Nepal plans to:

- Hold consultative meetings with stakeholders (e.g., DDA, NML, NPC, Nepal Medical Association, APPON, CIP) to obtain buy-in for the development of a Medical Product Quality Assurance steering committee;
- Complete the rapid assessment of human resources for regulatory systems and medicines quality assurance at federal and provincial levels;

- Finalize the assessment report on the status of risk-based PMS in Nepal: findings, gaps, and recommendations;
- Conduct a SATTA at the NML;
- Endorse and operationalize a TWG on inspection;
- Finalize the GMP code assessment report and action plan;
- Initiate the design and adoption of GMP training material;
- Finalize the scope of work for a landscape analysis and engage partners in designing the study;
- Finalize priority medicines for WHO prequalification;
- Finalize a request for expressions of Interest; and
- Complete the review of procurement guidelines, procedures, and other relevant information.

Pakistan

Pakistan's regulatory system has limited capacity for medicines quality surveillance, contributing to the proliferation of SF medical products. Lack of regulatory enforcement and availability of centers to conduct reliable bioequivalence studies reduces confidence in the efficacy of generic medical products manufactured in the country. Inconsistent government policies for the pharmaceutical sector have undermined the private sector's potential role in improving health outcomes. The PQM+ Pakistan program is addressing these challenges through four areas: improving governance of medical product QA systems; strengthening medical product regulations; enhancing private sector engagement; and reducing the availability of SF medical products. PQM+ works closely with the Drug Regulatory Authority of Pakistan (DRAP).

In terms of specific country objectives, the PQM+ work plan focuses on advancing medicines quality assurance elements to enhance Global Health Security Agenda initiatives; curbing antimicrobial resistance; promoting maternal, neonatal, and child health; addressing communicable diseases; and engaging the private sector in achieving better health outcomes and contributing to economic development.

In addition, PQM+ coordinated with the Mission to support the official launch of the Pakistan Integrated Regulatory Information Management System (PIRIMS). This regulatory framework was developed in partnership with DRAP. PIRIMS will support integration of registration, inspections, and licensing functions in the first phase with other functions, such as lot release, lab integration, and PMS, to be added in the second phase. Laboratory testing and PMS results can also be processed in PIRIMS. The system will increase the ease of doing business for the pharmaceutical industry by ensuring transparency, traceability, and accountability in regulatory decisions.

The launch ceremony for PIRIMS took place December 2 in Islamabad. USAID/Pakistan Deputy Mission Director Michael Nehrbass virtually attended the event, saying: "We are pleased to partner with the Government of Pakistan to ensure this system complies with international standards, strengthening health services across the country." Other attendees included the special assistant for the prime minister on health, Dr. Faisal Sultan of the Ministry of National Health Services Regulation and Coordination (MoNHSRC); Mr. Asim Rauf, CEO of DRAP; officials from health departments; and representatives from the pharmaceutical industry, media, and academia.

In PY2, PQM+ will help to:

- Improve governance for medical product QA systems;
- Improve country and regional regulatory systems to assure the quality of medical products in the public and private sectors; and
- Increase supply of quality-assured essential medical products of public health importance.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ completed a detailed gap assessment for the development of medical devices regulations for DRAP. The assessment considered international regulations for medical devices including regulatory structure, device classification, device approval, and PMS. The gap assessment also considered the indicators from the GBT. Based on the gap assessment results, PQM+ laid out short- and long-term recommendations for DRAP. These include strengthening human resources related to medical equipment and devices, developing an integrated information management system, setting up a conformity assessment body to evaluate medical devices, planning for high-priority equipment protocols, and developing a protocol for refurbished and remanufactured equipment.

In Q1, the PQM+ team conducted gap assessment of the appellate laboratory, NIH in Islamabad, against the ISO 17025: 2017 standard. The assessment identified all gaps and the need to develop protocols for method validation and method verification, uncertainty measurements, analyst qualifications, and authorizations of test result validity. The gap assessment was followed by development of a CAPA plan and more than 50 new SOPs. In addition, PQM+ drafted the quality manual and application for proficiency testing, which is now ready for submission to the accreditation body.

Objective 2: Country and regional regulatory systems to assure the quality of medical products in public and private sectors improved

PQM+ continued to help the National Control Laboratory for Biologicals make progress against its CAPA plan. DRAP requested that PQM+ include lot release data in PIRIMS. PQM+ visited the lab to understand the existing lot release mechanism and propose a design prototype.

Figure 5: PQM+ completed a gap assessment of the Public Health Laboratory of the Institute of Public Health in Lahore.

PQM+ completed a gap assessment of the Public Health Laboratory (PHL) of the Institute of Public Health (IPH), Lahore. The laboratory was assessed relative to the ISO 15189 standard, which is the international standard that medical diagnostic laboratories across the globe follow for developing quality management systems. The gap assessment report has been shared with laboratory management to inform development of a CAPA plan.

PQM+ Pakistan and the WHO Prequalification Team established a partnership for peer audits to strengthen the quality control laboratory system in Pakistan. Due to a recent intense second wave of COVID-19, the WHO/PQM+ peer audit preparatory visit for DTL-Multan was postponed. As the COVID-19 situation improves, the visit will be rescheduled.

PQM+ reviewed the laboratory information file of DTL-Bahawalpur for WHO PQ and shared observations with the laboratory staff. The staff has addressed the observations and the file is now ready for submission to WHO.

Antimicrobial consumption (AMC), which quantifies the consumption of antimicrobial agents, plays a key role in antimicrobial resistance surveillance. AMC data support comparative analysis at the country level and evaluation of the impact of regulatory interventions. Access to AMC data had been limited in Pakistan. To address this, PQM+ collaborated with DRAP to develop the AMC dashboard. Pharmaceutical industry users can submit data relating to production/batch, sales, distributors, resellers, and patients through the PIRIMS interface. The modules developed for the AMC dashboard respond to both DRAP and pharmaceutical end users' requirements.

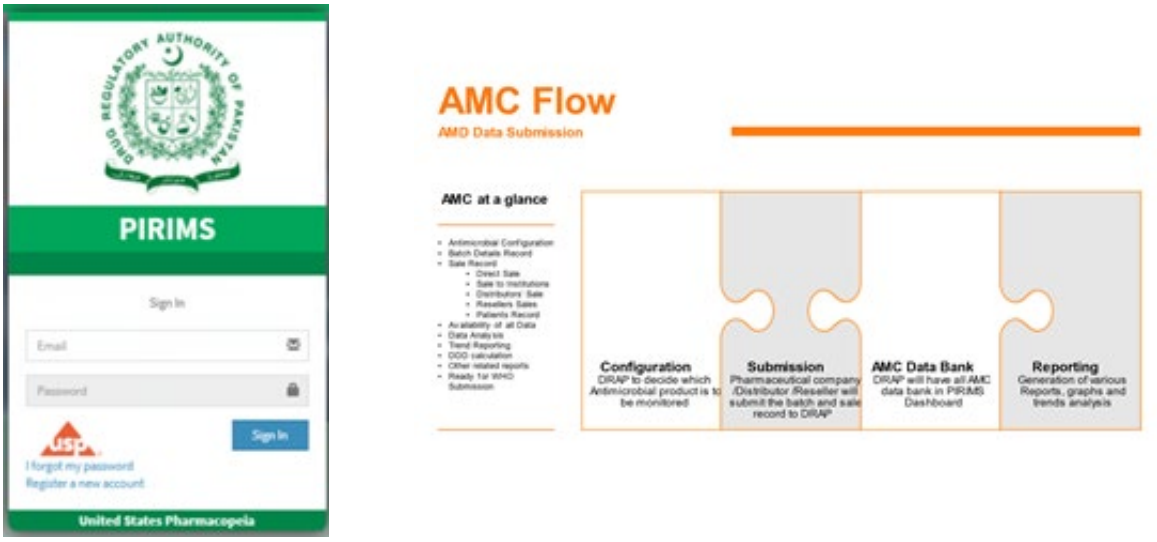

Figure 6: PIRIMS sign-in page (left) and AMC Dashboard

Objective 4: Increase supply of quality-assured essential medical products of public health importance.

In previous quarters, PQM+ developed a draft concept note on a National Biopharma Strategy and Private Sector Engagement Plan. In Q1, the program shared the concept note with Mr. Atif Bukhari, chairman of the Board of Investment (BOI), at a meeting at the prime minister's office in Islamabad. PQM+ discussed how to bring new investment and industrial reforms to increase export potential, diversify into knowledge-based sectors, and reach a new level of global economic connectivity. The parties agreed to develop a 10-year National Pharmaceutical Development Strategy. In a follow-up meeting with the director general of BOI, key stakeholders from the public and private sectors were identified. PQM+ discussed support for establishing a small joint working group that will develop baseline background material for future consultations.

PQM+ also had a virtual meeting with Ms. Maria Kazi, joint secretary for the Africa region at the Ministry of Commerce, and her team. PQM+ briefed the ministry about USAID's PQM+ program activities in Pakistan. The joint secretary appreciated the efforts by USAID and the PQM+ program and showed interest in collaborating with PQM+ to develop the biopharma strategy.

PQM+ is providing technical assistance to DRAP to adopt and implement Identification of Medicinal Products (IDMP) standards. PQM+ procured five IDMP ISO standards to use as normative references. PQM+ shared the draft roadmap to implementing IDMP standards with DRAP and is awaiting feedback. The PQM+ IDMP consultant has reviewed the data nomenclature used in PIRIMS and has recommended changes to align with IDMP standards.

Priority Activities for Next Quarter:

Next quarter, PQM+ Pakistan plans to:

- Conduct a virtual follow-up meeting with BOI over the Biopharma Strategy;
- Provide virtual training for DRAP on IDMP standards and develop national IDMP standards;
- Hold a consultative meeting with DRAP and stakeholders on contract manufacturing;

- Revise the proposed competency framework for DRAP regulatory functions based on WHO's recent draft guidelines;
- Submit the DTL Bahawalpur laboratory information file to the WHO PQ team;
- Conduct a joint peer audit of DTL Multan, Lahore, for WHO PQ audit preparation;
- Follow-up on CAPA progress of IPH Lahore for ISO 15189 accreditation; and
- Support Appellate Laboratory ISO 17025:2017 activities:
  - Conduct proficiency testing once samples are received;
  - Complete uncertainty calculations of all scope parameters;
  - Follow up on all applicable method verifications; and
  - Conduct an internal audit and a first management review meeting.

Europe and Eurasia Region

Central Asia/Kazakhstan

The PQM+ program is working to strengthen Kazakhstan's medicines regulatory system. In particular, the program provides technical assistance to the National Center for Expertise of Medicines and Medical Devices (NCEM) to: strengthen the medicines registration system; support medicines quality control laboratories (MQCLs) to test the quality of medicines reliably and accurately according to the international standards; strengthen the GMP inspectorate and prepare the country to apply for accession to PIC/S. The program also focuses on increasing the supply of locally manufactured quality-assured TB medicines in the local market by providing technical support to the pharmaceutical manufacturer Nobel Pharmsanoat and the Association of Pharmaceutical Manufacturers.

In PY2, PQM+ will help to:

- Improve country regulatory systems to assure the quality of medical products and
- Increase the supply of quality-assured medical products.

Progress by PQM+ Objective

Objective 2: Country regulatory systems to assure the quality of medical products in the public and private sectors improved.

This quarter, PQM+ continued technical assistance in responding to the gaps identified in the medicines review and registration system during the WHO GBT assessment. PQM+ reviewed NCEM's SOP on assessing registration dossiers in accordance with national regulations and prepared recommendations on updating the SOP.

The WHO collaborative procedure for accelerated registration of prequalified finished pharmaceutical products is a fast-track process for registration of quality-assured medicines. Although a member of the WHO collaborative registration procedure (CRP), Kazakhstan does not use this mechanism for medicines registration. In Q1, PQM+ continued technical assistance to operationalize the use of WHO CRP to ensure availability of WHO prequalified medicines in the country. A final version of the SOP for review and registration of WHO-prequalified

medicines was developed. In addition, NCEM is finalizing a guideline for manufacturers/ applicants for faster registration of WHO-prequalified medical products under the CRP procedure with PQM+ assistance. Once these documents are finalized and approved, the country will have a straightforward process for registering WHO-prequalified medicines through CRP, which will help expand availability of these medicines on the local market.

The WHO GBT assessment of Kazakhstan identified gaps in market surveillance and control. Last quarter, PQM+ developed a customized risk-based PMS guideline using the data received from an assessment questionnaire completed by NCEM. This quarter, PQM+ supported NCEM in establishing a risk-based PMS. PQM+ provided additional clarifications on the guideline and guidance on specific topics, such as mechanisms and procedures to mitigate risks associated with medicines that do not undergo full compendial testing under the current QA system, as well as the criteria for products subject to PMS. PQM+ also provided comments on NCEM's draft rules for market sampling. Some of these will be reflected in the national regulations, which are being updated.

In Q1, PQM+ continued providing technical assistance to the Almaty and Karaganda MQCLs to help them achieve and maintain WHO PQ. WHO's peer audit of Almaty MQCL was scheduled for November 2020 but was postponed due to COVID-19 travel restrictions. In the meantime, PQM+ continued assistance to Almaty MQCL in preparation for WHO PQ. PQM+ participated in a virtual internal audit of the Almaty laboratory to verify compliance with ISO 17025:2017 standards and WHO's Good Laboratory Practice (GLP) guidelines. PQM+ virtually observed the laboratory's demonstration of analytical and microbiological methods and discussed their QMS. After completing the internal audit, PQM+ had several follow-up conference calls with the Almaty laboratory to discuss preparing the audit report and CAPA plan. PQM+ will follow up with the Almaty laboratory on preparing and implementing the CAPA plan.

The Karaganda MQCL received WHO prequalification in March 2020, but WHO identified the validation of computerized systems as needing improvement. This quarter, PQM+ conducted two virtual training sessions, three hours each, on computerized system validation for the Karaganda MQCL. More than 40 people attended, including representatives of Nur-Sultan and Almaty MQCLs, as well as the quality assurance and IT departments of the NCEM headquarters. This broad participation builds capacity at the central level.

Given COVID-19 restrictions and reduced workload, the NCEM is deciding whether the Nur-Sultan MQCL is needed. Pending this decision, work at Nur-Sultan is currently suspended.

PQM+ is supporting also supporting Kazakhstan to prepare for ascension to PIC/S. PIC/S membership will open access to the reliant GMP inspection mechanism with other PIC/S member countries and other resources for further capacity development, eventually contributing to increased access to quality-assured medicines in country.

This quarter, PQM+ continued to assist the GMP inspectorate with preparations for PIC/S membership. PQM+ met with the working group of representatives from the Committee for Medical and Pharmaceutical Control (formerly the Committee for Quality Control and Safety of Goods and Services) and NCEM. The working group addresses organizational structure, QMS, training procedure, and legislation for the Inspectorate. PQM+ provided two virtual trainings this quarter for the inspectorate. They are described below.

- The GMP Inspection Methodology training took place over three days and included three training sessions of three hours each, as well as hands-on practical tasks. The courses covered important aspects of GMP inspection, such as the inspectorate's key

responsibilities, soft skills for inspectors, the inspection process, key inspection steps, inspection conclusion, follow-up activities, and quality assurance. The training was attended by 81 representatives of the Committee for Medical and Pharmaceutical Control and NCEM.

- In December, PQM+ provided a virtual training on distant good practice in pharmaceutical industry (GxP) assessments. The training included two training sessions that covered options for the inspectorate during a pandemic, regulatory approaches, and triggers for distant assessment, preparation for distant assessment, virtual inspections, and follow-up activities. This training was of particular importance as the number of on-site inspections was reduced, shifting to virtual inspections due to COVID-19. More than 30 people attended.

In addition, PQM+ presented an annual report on progress to the senior management of the Committee for Medical and Pharmaceutical Control of MOH and NCEM. The report gave special emphasis to the priorities in 2021 (including changes to legislation and industry compliance with GMP). The action plan was agreed to during the meeting.

Objective 4: Supply of quality-assured essential medical products of public health importance increased

PQM+ continued to support the Nobel Almaty Pharmaceutical Factory to improve its compliance with WHO PQ standards and to complete its dossier for levofloxacin tablets in the CTD format. Cross-contamination among levofloxacin, cephalosporins, and other products is a challenge. To mitigate the risk, Nobel should implement proper QRM. During this reporting period, PQM+ provided virtual QRM training for factory staff (16 participants). The training covered the basic principles of QRM: understanding risks, failure, cause, and effect. There was a discussion of root cause analysis and steps in QRM. The last part of the training described risk analysis tools that can be applied by a pharmaceutical manufacturer.

Based on the training, Nobel will revise its risk management SOP and develop additional SOPs related to QRM; these documents will be reviewed by PQM+. Nobel will use these SOPs for risk assessment of levofloxacin production. Nobel will also work on preparation of levofloxacin dossier for submission for WHO PQ.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Address findings related to good regulatory practices from the GBT assessment in collaboration with the NCEM;
- Provide technical assistance to the NCEM on the WHO CRP for accelerated registration of medicines to develop capacity and finalize procedures to ensure its use for registration of WHO PQ medicines, including TB medicines;
- Identify and provide concrete support to NCEM on PMS;
- Continue to provide targeted capacity building on QMS, such as training and SOP development, for MQCL to achieve WHO PQ;
- Continue to provide training and support on PIC/S to the working group to respond to issues that arise during preparation for PIC/S application;

- Initiate dialogue with the NCEM director on collaborating with the scientific education center on capacity-building efforts; and
- Support risk assessment and dossier development for Nobel Almaty Pharmaceutical Factory for WHO PQ for levofloxacin.

Uzbekistan

Uzbekistan is graduating from Global Fund-supported procurement of TB medicines to domestically funded procurement and plans to gradually increase the allocation of funding for procurement of second-line TB medicines. The government's strategy is to ensure that domestically produced, quality-assured medicines are available for procurement. In recent years, the government of Uzbekistan introduced several initiatives to strengthen the local production of quality-assured medicines in the country. In support of this strategy and generally to ensure quality of medicines on the local market, PQM+ is providing technical assistance to the Agency on Development of the Pharmaceutical Industry ("the agency") around medicines regulatory systems strengthening. This includes improving the medicines review and registration system, supporting MQCLs to test the quality of medicines reliably and accurately, and preparing the GMP inspectorate for PIC/S accession. The program also focuses on increasing the supply of locally manufactured, quality-assured TB medicines by providing technical assistance to pharmaceutical manufacturers. This quarter, USAID and the agency signed a memorandum of understanding that underlines both agencies' commitment to championing PQM+ activities in Uzbekistan.

In PY2, PQM+ will help to:

- Improve country regulatory systems to assure the quality of medical products and
- Increase the supply of quality-assured medical products

Progress by PQM+ Objective

Objective 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

GBT represents the primary means by which the WHO objectively evaluates country regulatory systems. PQM+ facilitated a virtual meeting with the agency's working group on registration, during which PQM+ presented the concept of WHO GBT and overview of GBT functions and indicators. In Q1, the working group completed a questionnaire on GBT's registration and marketing authorization indicators. After reviewing the responses, PQM+ identified priority areas in need of technical assistance. The action plan will be developed in discussion with the working group.

In the previous quarter, PQM+ provided technical assistance to the agency to develop procedures and guidelines for the WHO collaborative procedure for accelerated registration of prequalified finished pharmaceutical products. This quarter, PQM+ facilitated coordination among all interested stakeholders—the agency, National TB Program (NTP), Global Drug Facility (GDF), and the Global Fund—to ensure use of WHO CRP for fast-track registration of the latest order of first-line TB medicines. This will speed up importation and access to these products. In addition, PQM+ organized an orientation on CRP for representatives of the NTP and GDF by staff of the agency. Now, they are ready to prepare documents for submission to

the agency for CRP. PQM+ will continue to facilitate communication among stakeholders to support registration of prequalified TB medicines using CRP.

PQM+ is providing technical assistance to the agency to prepare for PIC/S GMP ascension. PIC/S membership will open access to the reliant GMP inspection mechanism with other PIC/S member countries and to other resources for further capacity development, eventually contributing to increased access to quality-assured medicines in Uzbekistan.

PQM+ is working with the agency's working group to develop the capacity and improve the structure of the GMP inspectorate. In Q1, PQM+

- Facilitated development of legislation on the GMP inspectorate structure;
- Identified changes needed for the GMP guide;
- Supported preparation of the draft quality manual as described by the PIC/S standard;
- Finalized three SOPs on developing SOPs, training inspectors, and a code of ethics;
- Prepared the matrix of inspectors and their competencies to help identify gaps and needs for future training;
- Developed a basic list of topics and areas for inspectors to obtain further training; and
- Developed a conflict-of-interest form for inspectors to sign prior to inspection.

This quarter, PQM+ also completed the first three-day online training for the entire GMP inspectorate (48 participants) on the inspection methodology. The training covered key responsibilities of a pharmaceutical inspectorate, the organization of an inspection, and the soft skills required for inspection.

PQM+ also developed an annual report on PIC/S activities and areas of support needed from the agency leadership to meet PIC/S standards. The report was presented and discussed with senior management of the agency.

PQM+ is also supporting two of the five MQCLs – Tashkent and Andijan - to strengthen their QMS and eventually meet the criteria for WHO PQ. Following an assessment of the two MQCLs in January 2020, PQM+ conducted several targeted capacity building efforts such as training and development of SOPs and guidelines to improve their QMS. PQM+ prepared an implementation plan to address the gaps identified during the assessment. PQM+ will discuss ways to address gaps with the Tashkent and Andijan MQCLs working groups.

The agency also requested assistance reviewing the architectural designs for the MQCLs that will be built as part of "Pharma Park," a large complex that will house the agency, MQCLs, university, and manufacturers. PQM+ reviewed the design and layout of the laboratories that are under construction to ensure that they meet the best practice in international standards.

Objective 4: Supply of quality-assured essential medical products of public health importance increased.

PQM+ is assisting Nobel Pharmsanoat to prepare the product dossier for levofloxacin, a second-line TB drug, for WHO PQ. Per PQM+ recommendations, Nobel is working to mitigate the risk of cross-contamination between penicillin and levofloxacin at its production site. In Q1, Nobel developed the analytical method to check the environment for cross-contamination. The samples were submitted to Tashkent MQCL for testing. Nobel will develop a report based on the sample results from Tashkent MQCL for PQM+'s review.

PQM+ developed a list of documents on product development needed for dossier preparation and GMP compliance and provided these to Nobel, which is preparing them for PQM+'s review. Nobel has assigned two staff to coordinate with PQM+ on GMP compliance and cross-contamination risk mitigation.

PQM+ facilitated discussions and forged consensus between the Association of Manufacturers and the agency to organize a webinar on the electronic CTD. WHO PQ requires submission of dossiers in the CTD format. The agency also plans to make CTD format mandatory for dossier submission in the future. A total of 38 participants from the agency and two the Association of Manufacturers members were introduced to the eCTD concept. PQM+ plans to develop the capacity of the regulators to provide such trainings in the future.

Priority Activities for Next Quarter:

Next quarter, PQM+ plans to:

- Identify areas of WHO GBT for PQM+ technical assistance;
- Facilitate discussions between the agency and stakeholders to enable use of WHO CRP for accelerated registration of TB medicines;
- Continue to develop the GMP inspectorate's capacity, structure, and functions;
- Develop an implementation plan for the Tashkent and Andijan MQCLs;
- Initiate plans for technical assistance to establish risk-based PMS in Uzbekistan; and
- Review the cross-contamination analysis report and provide feedback.

COVID-19 Response Activities

Bangladesh

Since June 2020, PQM+ has been supporting:

- regulators to mitigate shortages of COVID-19-related medical products;
- manufacturers for the local production of quality-assured PPE and medical devices; and
- the National Control Laboratory to boost its capacity to test priority COVID-19 medical products to protect patients from SF medical products.

This quarter, PQM+ supported the preparation of a protective personal equipment (PPE) manufacturing facility inspection checklist for DGDA inspectors. PQM+ assisted DGDA with making required revisions to its existing standards for N95/KN95 respirators. PQM+ also translated the checklist into Bengali. PQM+ helped the DGDA draft an authorization checklist/guidance for ventilators based on current best practices.

PQM+ supported NCL to develop risk-based testing protocols for seven medical products (favipiravir tablets, dexamethasone tablets, hydroxychloroquine tablets, ivermectin tablets, oseltamivir capsules, lopinavir/ritonavir tablets, and remdesivir injection) that are widely used for the treatment of COVID-19 in Bangladesh. PQM+ also is assisting DGDA in conducting RB-PMS of these products to ensure their quality and safety for patient use.

DGDA convened 18 stakeholders to review and provide feedback on these draft deliverables, sharing hard and soft copies of 10 deliverables (e.g., visual inspection checklist for gowns, coveralls, fabric masks, surgical masks, N95/KN95 respirators; general guidance on risk-based approach to registration of COVID-19 related medical products). PQM+ headquarters staff also conducted a technical review and edit of the documents.

Following this review, PQM+ presented two important deliverables via a webinar in late December. The deliverables were the technical and regulatory aspects of PPE in the COVID-19 response in Bangladesh and the general guidance on a risk-based approach to registration of COVID-19-related medical products in Bangladesh. Almost 50 participants from DGDA, USAID, manufacturers, and private PPE laboratories attended.

To help regulators, manufacturers, and other stakeholders work to ensure quality and standards of COVID-19 medical products, PQM+ will disseminate new tools and guidelines in Q2. The first will be on testing protocols of COVID-19 medicines planned for DGDA and NCL management and analysts. The second is for COVID-19 product manufacturers' regulatory focal persons on general guidance for risk-based registration and the procedure of EUA/NOC. The third will be a webinar to review the checklist/guideline for ventilator manufacturers and regulators.

Pakistan

This quarter, PQM+ supported DRAP's Medical Device Board to address challenges arising from emergency use authorization (EUA) of devices related to COVID-19 (e.g., ventilators, in-vitro diagnostics [IVD], oxygen systems). PQM+ helped DRAP understand the evaluation criteria and rationale behind them as they relate to type and origin of the equipment or medicine. With this support, DRAP has granted EUA for real-time polymerase chain reaction (PCR) IVDs and an antigen testing kit submitted by Abbott. In addition, PQM+ supported the University of Lahore in an application for EUA for its locally developed PCR diagnostic kit, which was submitted in December. PQM+ also created a focus group with experts and collaborators from around the world to advise on EUA for medical devices and emergency access to indigenously manufactured equipment for COVID-19 and other needs in Pakistan. The focus group consisted of clinical engineering and regulatory experts as well as medical device experts from WHO headquarters.

PQM+ also met with the DRAP CEO and the director of pharmacy services to discuss clinical trial requests related to COVID-19 medicines. PQM+ shared guidelines about regulatory approvals of Phase I and II clinical trials. This quarter, PQM+ also recruited a biostudies consultant to work with CDL.

PPE Testing

This quarter, the University of Lahore (UoL) expressed interest in establishing a PPE testing laboratory and PQM+ started evaluating its eligibility by reviewing its expression of interest. The University of Lahore is a private-sector university with the highest number of pharmaceutical students and faculty members in Pakistan. PQM+ also supported Prime Lab (a private laboratory) in procuring PPE testing equipment. In December, PQM+ supported Tti Lab in submitting its application to DRAP for licensing as a third-party PPE testing laboratory. After the DRAP Medical Devices and Medicated Cosmetics board approves its application, PPE manufacturers will be able to use it for outsourced testing. PQM+ shared the 24-element quality agreement and PPE standards with Tti Lab and the CDL team. PQM+ also guided both labs on DRAP licensing requirements. Once the Tti Lab fulfills the DRAP requirements, another team from DRAP will inspect the lab before granting the license. As part of the private sector

engagement activity, PQM+ and Tti Lab plan to organize a hands-on training for new CDL staff on PPE testing. PQM+ shared international best practices, norms, and guidelines for PPE with the lab. Tti Lab also helped CDL select equipment and shared the market price for essential equipment and its experience using the equipment. Furthermore, the lab is increasing its testing capacity to reduce the wait time for test results.

PPE Manufacturing

Before the pandemic, PPE was imported mainly from China. Now, though many local manufacturers have started producing PPE, none is registered with DRAP. At the beginning of the quarter, PQM+ inspected PPE manufacturer Adsel of Lahore. Adsel is a multisource company, and during the COVID-19 pandemic, started manufacturing surgical masks, multi-sized face shields, goggles, gowns, and bodysuits. PQM+ observed products, manufacturing processes, and quality management, identified the gaps, and shared observations. The CEO expressed his commitment to achieving international certification for his PPE manufacturing facility. PQM+ held similar visits with a sporting goods manufacturer, bottle manufacturer, and other companies throughout Pakistan that are now manufacturing various PPE items.

After these visits, the manufacturers submitted their establishment license applications to DRAP. One major barrier to approval faced by these manufacturers is lack of in-house testing capacity for PPE. Establishing an in-house PPE testing lab requires a huge capital investment that exceeds the cost of PPE production equipment and raw materials. PQM+ met with the DRAP CEO office and the director of the Medical Devices and Medicated Cosmetics Division to discuss international best practices, which do not require that PPE manufacturers have their own testing capacity.

As an alternative, PPE manufacturers can outsource PPE testing to external laboratories and establish a quality control department that conducts basic quality tests based on the external lab results before releasing each batch. PQM+ advised DRAP and the PPE manufacturers on the need for a written agreement with the third-party laboratory and will share a model-quality agreement with them. DRAP agreed with the PQM+ recommendation, and it is expected that the Medical Device Board (MDB) will issue establishment licenses after these requirements are addressed.

Also this quarter, PQM+ team met with the joint secretary (Africa region) of the Ministry of Commerce and her team. PQM+ discussed the work done to ensure quality of local PPE manufacture so the Ministry of Commerce (Africa region) will consider facilitating market access for them in Africa.

Remdesivir Manufacturing

This quarter, the PQM+ team provided technical support to Ferozsons, a manufacturer of remdesivir. PQM+ verified the stability data that will be submitted to DRAP and WHO as a step toward WHO prequalification. Ferozsons has manufactured 70,000 vials of remdesivir for injection. Of this production, 10 percent was used in Pakistan, and the remainder was exported to Indonesia, Ukraine, and several countries in South America. Due to increased demand, Ferozsons is increasing production of both liquid and lyophilized remdesivir. PQM+ supported Ferozsons' successful application for EUA of remdesivir in Indonesia and is helping it seek EUA in the Philippines. With PQM+ support, Ferozsons also has exported 70,000 lyophilized vials to PIC/S countries (Indonesia, Philippines, and Ukraine) as well as South America, with demand for an additional 70,000 vials in the pipeline. In December, PQM+ arranged a virtual training for Ferozsons' quality and regulatory staff on the CTD and eCTD requirements, format, and

numbering system. The training will help Ferozsons file the remdesivir EUA and regular market authorization applications in other countries. Throughout December, Ferozsons continued to manufacture and export vials to Ukraine (30,000) and to meet local demand (which had increased threefold).

In October, PQM+ met with the executive director of the Pakistan Institute of Medical Science (PIMS) to discuss technical assistance to its diagnostic laboratory to achieve ISO 15189 accreditation. PIMS and PQM+ have finalized a MoU that outlines PQM+'s technical assistance related to ISO 15189 accreditation and testing and manufacture of quality-assured alcohol-based hand rub (ABHR). PQM+ started the selection process for an ISO 15189 consultant to support this work.

PQM+ is helping the hospital test and manufacture ABHR. WHO Pakistan has agreed to procure the equipment required for ABHR production. PQM+ shared technical specifications for all needed equipment and approximate cost estimates for upgrading the production facility at PIMS with WHO. Once the equipment is procured and installed, PQM+ will train the staff on QMS development, GMP, and quality control. PQM+ recommended that PIMS include the raw material cost in its regular budget to ensure sustainable funding. By the end of November, WHO had issued a purchase order for the equipment.

This quarter, PQM+ shared the draft RB PMS of COVID-19 products training plan with the DRAP focal person. PQM+ invited 11 national quality control laboratories for a 3-day training on lab techniques for COVID-19 medical products from January 20 to 22, 2021. In addition, the team invited DRAP and the provincial health departments for a consultative meeting on developing a risk-based post-marketing surveillance plan for COVID-19 medical products.

Serbia

In August 2020, PQM+ began working with the Government of Serbia to explore options for external evaluation and market entry of an enzyme-linked immunosorbent assay (ELISA) test kit produced by the Institute for the Application of Nuclear Energy (INEP) at the University of Belgrade. Market authorization will be sought in regional and/or international markets and investing in and expanding manufacturing, if sufficient market opportunities exist. Specifically, PQM+ was tasked with:

- Assisting the INEP on third-party performance validation/evaluation of the ELISA COVID-19 test and
- Implementing a market-demand/competitiveness assessment of the ELISA kit.

PQM+ finalized a nondisclosure agreement between INEP and USP. PQM+ requested USAID approval of a fixed-award agreement with the Global Health Impact Group (GHIG). PQM+ reached out to evaluation sites to confirm if they could evaluate the ELISA test and drafted and finalized a protocol for the evaluation. In December, members from GHIG and the London School of Hygiene and Tropical Medicine's International Diagnostics Centre (LTHSM IDC) sought confirmation from several laboratories that they are available to test the ELISA kit. Due to a recent surge in COVID-19 cases across Europe, several laboratories are no longer available, which has delayed the process. INEP will be ready to send out its ELISA test samples within 10-15 days of selection of a laboratory. Work on this activity has been extended through April 2021.

New Buy-Ins

Table 2. Summary Discussions with USAID for Priority Activities for Future Funding

USAID Team	Summary and Next Steps
Benin	PQM+ submitted a draft work plan and received approval this quarter. As soon as approval was granted, PQM+ was able to identify a local consultant and develop a timeline for implementation.
Cross-Bureau COVID-19	USAID's Office of Health Systems obligated additional cross-bureau funding to PQM+ to support COVID-19 response activities. PQM+ met with the agreement officer's representative (AOR) team to discuss potential activities, based on a scope of work the program submitted in July 2020. The work plan for these activities was submitted in December 2020.
DRC	PQM+ met with the PMI team from the USAID Mission in DRC to discuss priorities. PQM+ will submit a work plan based on these discussions in early 2021.
East Africa/IGAD	After consultations with USAID and relevant regional stakeholders, PQM+ submitted the East Africa work plan this quarter in anticipation of funding in early 2021.
Guinea	PQM+ continued to consult with the USAID/Guinea Mission on priority activities and submitted an initial draft of the work plan at the end of the quarter.
Rwanda	PQM+ provided additional feedback on an initial scope of work for anticipated funding in Rwanda. PQM+ will await further guidance on timing of workplan development next quarter.

Progress by Health Elements

Core Maternal and Child Health (MCH)

PQM+'s support to USAID's core MNCH work focuses on assisting medicine regulatory authorities and manufacturers to improve their systems. PQM+ also supports global leadership efforts in collaboration with other MNCH partners to continue to advance USAID's, global, and country MNCH agendas and to increase access to quality-assured lifesaving medicines for women and children in LMICs.

PQM+'s activities fall under PQM+ objectives 2 and 4. During this quarter, the program:

- Finalized the assessment report on post-marketing surveillance capability, which was conducted in eight PQM+ MNCH countries;
- Completed the guidance document on the risk-based categorization for PMS of MNCH medical products; and

- Finalized the English and French versions of the amoxicillin job aid to assist with dossier preparation and the amoxicillin job aid to assist with laboratory testing.

Progress by PQM+ Objective

Objective 2: Country and regional regulatory systems to assure the quality of medical products in public and private sectors improved

MRAs are responsible for conducting PMS of essential medicines to detect and remove SF medicines from circulation in local markets. Because the PMS process is resource-intensive, the predecessor PQM program developed a risk-based framework and guideline to help regulators streamline the PMS process and focus limited resources on the medical products that present the highest risks to patients.

This quarter, PQM+ finalized a baseline assessment in eight countries where the PQM+ program receives MCH funding (Bangladesh, Ethiopia, Ghana, Kenya, Mali, Mozambique, Nepal, and Nigeria) to determine the PMS status of MNCH products. The assessment included probing into the decision-making process about which MNCH products to include in annual PMS activities. The report was shared with USAID to support future decisions about PMS in countries that receive MCH funding support.

This quarter, PQM+ also completed the English version of the guidance document on risk-based categorization of MNCH products. This guidance document explains how to define probability and impact risks for priority MNCH products and will facilitate the development of sampling plans using the MedRS tool in countries. The MedRS tool assists countries to automate the science and practice of risk-based post-marketing surveillance on a single platform. The tool evaluates three dimensions of risk—medicines, geographic location, and supply chain—to help countries identify the most susceptible medicines, determine the number of samples required, and prioritize sampling to the most vulnerable locations. This guidance document will help countries identify MNCH product-specific risks for input into the MedRS tool.

PQM+ also finalized the English and French versions of the job aids to assist with amoxicillin dossier preparation and job aids to assist with amoxicillin laboratory testing. The job aids were derived from the amoxicillin product information reports (PIRs) developed under the PQM program. They were developed as a quick reference source for regulatory staff that review amoxicillin dossiers for approval and for the laboratory staff on testing, highlighting the core peculiarities for the product to be considered during the review process. The finalized English and French versions of the aids were shared with USAID. PQM+ will work with its countries that receive MNCH funding to adopt them and integrate them into their work processes.

Objective 4: Supply of quality-assured essential medical products of health importance increased

UNICEF is one of the main suppliers of donated MNCH essential products in many LMICs. One of UNICEF's key goals is to increase local sourcing of quality-assured essential medicines for children. PQM+ works collaboratively with UNICEF to support increasing local sources of MNCH products through information sharing sessions. These sessions facilitate collaboration and PQM+ technical assistance efforts to local manufacturers.

This quarter, PQM+ participated in a joint UNICEF-UNFPA-WHO virtual meeting with manufacturers and suppliers. During the series of webinars, participants discussed current challenges affecting product inspections, WHO prequalification approval during the COVID-19

pandemic, steps to ensure that activities continue, and guidelines WHO is developing to provide guidance for countries facing similar challenges. The next PQM+ and UNICEF meetings is scheduled for Q2.

WHO recently issued an expression of interest for manufacturers of amoxicillin dispersible tablets (DT) that want to achieve WHO PQ. Historically, the uptake of amoxicillin DT in countries has been slow, and the local "proximate" supply of quality-assured amoxicillin DT has been inadequate. To increase local supply of quality-assured amoxicillin DT, PQM+ is conducting a landscape analysis of amoxicillin DT manufacturers throughout Africa to identify potential and existing manufacturers for amoxicillin DT. In the previous quarters, PQM+ developed the purpose statement and research questions for this landscape analysis and discussed them with UNICEF supply team and USAID MCH team for their input. This quarter, PQM+ completed the contracting package for a PQM+ Core-FLEX partner, Muhimbili University in Tanzania, to carry out this landscape analysis. This package was submitted to USAID for approval.

PQM+ plans to host a two-day technical consultative meeting to map the challenges around medicines quality assurance for MNCH commodities. The participants in this meeting will include USAID implementing partners, other donors, international agencies, and other organizations working in the quality-assurance space. This meeting was originally planned to be in-person. This quarter, planning discussions commenced for the technical consultative meeting, weighing the feasibility and effectiveness of conducting the meeting virtually, and if it can achieve the planned objectives and outcomes.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Finalize and share the risk-based categorization guidance document for MNCH products;
- Finalize the French versions of the chlorhexidine 7.1 percent gel product job aids to assist dossier preparation and laboratory testing;
- Complete the English and French versions of the oxytocin job aids to assist dossier preparation and laboratory testing;
- Continue planning for a technical consultative meeting on medical quality assurance in LMICs with key MNCH partners;
- Begin, via Muhimbili University, the amoxicillin DT landscape analysis in Africa region and compile preliminary results; and
- Continue technical engagements with UNICEF's supply department for MNCH products.

Core Neglected Tropical Diseases (NTDs)

The recent NTD global roadmap from November 2020, Ending the Neglect to Attain the Sustainable Development Goals: A Roadmap for Neglected Tropical Diseases 2021 – 2030, sets goals for an integrated approach across all NTD diseases with targets to reduce the number of people requiring treatments for NTDs by 90 percent. WHO has been instrumental in coordinating NTD medicine donation from manufacturers for use in affected populations globally. However, shortfalls remain compared to the demand for some medicines. The USAID NTD program targets the most prevalent NTDs that also have proven, cost-effective health interventions—lymphatic filariasis, blinding trachoma, onchocerciasis, schistosomiasis, and soil-

transmitted helminths. The overall goal of the Core NTD program is to ensure the availability of affordable, quality-assured NTD medicines for the patients in need.

PQM+'s activities fall under the program's Objective 4. PQM+ uses a systems strengthening approach to build local organizational and individual capacity of pharmaceutical manufacturers. This quarter, PQM+ continued to work with two manufacturers for albendazole and praziquantel FPP toward achievement of WHO PQ; commenced planning to conduct a market analysis of NTD medical products in Africa and Asia; and began efforts to disseminate and socialize the GMP eLearning training course developed under the PQM program.

Progress by PQM+ Objective

Objective 4: Supply of quality-assured essential medical products of health importance increased

PQM+ continued to support the manufacturer Mepro Pharmaceutical Private Limited, based in India, to manufacture quality-assured albendazole 400 mg chewable tablets for WHO PQ approval. PQM+ is working with the manufacturer to compile the full product dossier for submission for WHO PQ.

PQM+ also continued to support the manufacturer Medopharm Pharmaceutical Private Limited to produce quality-assured praziquantel 600 mg film-coated tablets toward WHO PQ. The manufacturer is still waiting to hear from the WHO PQ team on when the site inspection of the medicine production facility will take place. The WHO PQ team has had delays with in-person site inspections due to COVID-19 restrictions. The PQ team has depended on desk reviews, which has limitations and takes longer. WHO is exploring tools and new technologies for remote inspections to reduce delays with onsite inspections.

PQM+ has engaged two of its partners—Muhimbili University in Tanzania and Mahidol University in Thailand—to conduct a market analysis of NTD medical products to include in the global NTD medicine donation program. The focus regions are Africa and Asia and the analysis will look at APIs and FPPs. PQM+ is in the process of finalizing formal contractual agreements with the two partners and securing USAID approval before the partners commence the market analysis.

This quarter, PQM+ also began efforts to improve uptake of the GMP eLearning training course globally. PQM+ identified areas for improvement to enhance the user experience. PQM+ also assessed the course content to develop a strategy for repackaging the course. Activities planned for next quarter include redesigning the 10 GMP course modules and the website landing page and enhancing functionality. Since the course launched in 2019, more than 5,000 professionals in 91 countries have completed at least one module. Several PQM+ countries are among the top ten to either complete or begin to take the course - Bangladesh, Kenya, India and Pakistan.

Priority Activities for Next Quarter

Next quarter, PQM+ Core NTD plans to:

- Continue to support the manufacturers of albendazole and praziquantel tablets toward achieving WHO PQ;
- Commence the NTD product market analysis landscape activity; and

- Continue efforts to improve the user experience and uptake of the GMP eLearning training course.

Core Tuberculosis (TB)

PQM+ is working toward ensuring uninterrupted supply of lifesaving quality-assured TB medicines by providing direct support to the manufacturers of priority TB products, as well as providing technical leadership by exploring innovative manufacturing processes for priority TB medicines, developing technical documents such as product information reports, and working with partners to ensure the medicines registration processes does not create hurdles for the introduction and scale-up of the new TB medicines.

Objective 2. Country and regional regulatory systems to ensure access to quality-assured TB products improved

In Q1, PQM+ initiated discussions with the U.S. Food and Drug Administration (FDA) to collaborate on an online workshop for medicines regulatory agencies in LMICs to share the FDA's experience with review and approval of new TB medicines (e.g., pretomanid). Discussions and planning of the online workshop will continue in Q2 after the specific contact persons are identified at the FDA.

Objective 4: Supply of quality assured essential medical products of public health importance increased

In Q1, PQM+ continued support to two pharmaceutical manufacturers of first-line, fixed-dose combination (4FDC) TB medicines in Pakistan. One of the manufacturers has ordered the APIs and expected to start a stability study in January. Once the three-month stability data are available, the manufacturer will request a pre-submission meeting with WHO PQT. The BE study, which was supported by the predecessor program PQM, is planned for discussion as well. The second manufacturer also started a stability study for their FLD 4FDC, and they are planning to submit study results to WHO in March. This quarter, PQM+ continued technical assistance in the dossier preparation for this WHO submission as well.

In 2020, the presence of nitrosamine impurities was identified in two key anti-TB medicines, rifapentine and rifampicin, triggering concerns about the global supply. Although manufacturers are responsible for understanding their processes to prevent the presence of unacceptable impurities, the nitrosamine impurity issue caught the industry by surprise. To aid the industry in addressing this challenge, in Q1 of PY2, PQM+ continued the development of analytical methods for the detection of nitrosamines impurities in rifapentine and rifampicin. After completing the validation protocol, efforts to source key materials began but were delayed due to scaled-back production caused by COVID-19 restrictions. Given the sophistication of the methodology required to detect the nitrosamines impurities, quality control laboratories were surveyed to understand their in-house capacity to ensure the methods being developed are suitable for use. In Q2, activities described in the validation protocol will begin with Stage 1 (Equipment Optimization), followed by Stages 2 (Limit of Quantitation Evaluation) and 3 (Evaluation of key validation parameters), all of which are necessary since the nitrosamines impurities are present in very low levels.

This quarter, PQM+ engaged with Virginia Commonwealth University (VCU) in anticipation of a laboratory phase of the subaward (milestones 3 and 4) on optimization of manufacturing process for rifapentine API. Specifically, PQM+ reviewed the budget package and initiated the

compliance due diligence for VCU. The subaward will be finalized in Q2 and VCU will start working on the activity in close collaboration with the PQM+ staff.

PQM+ also worked on analysis of the cost drivers for one of the new TB medicines. The analysis was based on the desk review and information obtained from a patented proprietary database. PQM+ is reviewing the results of the analysis and after its finalization, will present the report to USAID in Q2 for further discussion.

In recent years, pharmaceutical supply chains disruptions have become an increasing issue that the COVID-19 pandemic exacerbated in 2020. Being able to predict such disruptions can be a powerful tool for manufacturers, procurers, and disease programs. To identify supply chain disruptions, PQM+ began to access the potential of using availability and supply chain data for key raw materials, impurities, and active pharmaceutical ingredients as markers for the production and subsequent supply of FPP. In Q1, a concept note was drafted and reviewed internally. After initial review and comments, a second revision is in development to possibly narrow the potential markers to be evaluated. In Q2, the revised concept note will be shared with USAID for review concurrence.

Objective 5: Global medical product quality assurance learning agenda and operational agenda advanced

This quarter, PQM+ started discussions with the USP staff on collaboration for development of the searchable database for PIRs. These PIRs, developed under the PQM program, were organized in the database to facilitate the retrieval of specific priority products information by manufacturers and regulators. In addition, PQM+ will work with its partners, Purdue and Howard universities, on developing new PIRs for anti-TB medicines.

PQM+ staff attended the online "2020 Joint UNICEF–UNFPA–WHO Meeting with Manufacturers and Suppliers of Contraceptive Devices, In Vitro Diagnostics, Vaccines and Immunization Devices, Finished Pharmaceutical Products, Active Pharmaceutical Ingredients and Vector Control Products." PQM+ staff received updates from the WHO PQT about their operations amid pandemic-related restrictions. The WHO PQ process is ongoing, but at a slower pace. Inspections still are risk-based, but their number is low compared to 2019. WHO is developing remote inspections guidelines, and will conduct them as needed. PQM+ discussed potential solutions to expedite the process given the current challenges.

Priority Activities for Next Quarter

Next quarter, PQM+ will:

- Follow up with the manufacturers in Pakistan to ensure that the stability study reports are prepared and submitted to WHO;
- Initiate work with VCU for optimization of manufacturing process for rifapentine for milestones three and four and start working on the laboratory phase for exploring the options for optimization of the manufacturing process for rifapentine API; and
- Follow up with the U.S. FDA to start planning the online workshop with the pharmaceutical regulatory authorities on sharing US FDA's experience on review and registration of new TB medicines.

Program Support

Communications

This quarter, PQM+'s communications activities continued to expand as program activities ramped up. Highlights include:

- Webinar series: In November, PQM+ delivered its first global webinar, entitled "What are regulatory and quality assurance systems and how do they impact health programs?" More than 130 participants joined from around the globe, many from USAID country Missions and USAID/Washington. Planning began for the second webinar, tentatively scheduled for March, drawing on lessons learned from the first one. The proposed topic will be strengthening QC labs.
- PQM+ website: the site map for new program website was developed and submitted to the AOR team for review and feedback.
- Social media: PQM+ shared its activities and progress via Twitter, Facebook, and LinkedIn. Key posts included the PIRIMS launch in Pakistan, the lab reaccreditation in Burma, World Antibiotic Awareness Week, and USAID's Year in Review.
- Fact sheets: The team developed the first draft of the new MCH fact sheet. It is under review by the technical team and will be submitted to the AOR team in Q2.
- New staff: Recruited and hired a new program editor/writer, who will start on January 19, 2021.