Promoting the
QUALITY OF MEDICINES Plus

PQM+ Quarterly Report – Program Year 2, Quarter 3

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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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Contents

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
DT	dispersible tablets (amoxicillin)
EPI	Expanded Program on Immunization
EUA	emergency use authorization
FP	family planning
FPP	finished pharmaceutical product
GBT	Global Benchmarking Tool
GMP	Good Manufacturing Practice
HR	human resources
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

Executive Summary

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). This quarter, the program continued to make significant progress toward its goal of sustainably strengthening medical product quality assurance systems in LMICs.

As part of its effort to improve regulatory system quality assurance at the national and regional levels, the program collaborates closely with country regulatory authorities in all 21 countries where it operates. In Pakistan, PQM+ completed a detailed gap assessment to develop medical device regulations for the **Drug Regulatory Authority of Pakistan** (DRAP). This work reflects international guidance on regulatory structure, device classification, device approval, and post-marketing surveillance (PMS). PQM+ also supported the **Kazakhstan Good Manufacturing Practices Inspectorate** in conducting its first remote assessment, which was of a manufacturer in India. Similarly, the program assisted the **Ethiopian Food and Drug Authority** (EFDA) in establishing a vaccine laboratory, including help developing a draft lab design after discussions with the engineering team at the federal Ministry of Health.

PQM+ collaborates with manufacturers to help increase the supply of quality-assured essential medical products that are important to public health. PQM+ is supporting manufacturers in almost a dozen countries to produce quality-assured medical products for TB, RMNCH, malaria, NTDs, and COVID-19. With PQM+ support, India's Medopharm Private Limited pharmaceutical company this quarter achieved **WHO prequalification** of the NTD drug praziquantel in its 600mg film-coated tablet form. WHO's prequalification of this product will diversify praziquantel's supply sources and increase the security of its global supply. PQM+ and its predecessor, PQM, has worked with Medopharm since 2017 to achieve this milestone.

To optimize financial resources for medical product quality assurance, PQM+ met with the chief executive officer of **Kenya's National Health Insurance Fund** (NHIF) to advocate for inclusion of the medical product quality assurance framework in the country's publicly funded health coverage scheme.

The program's work on improving governance around medical product QA takes many forms. This quarter, PQM+ coordinated with the **Liberia Medicines and Health Products Regulatory Authority (LMHRA)** to complete a five-year strategic plan, securing validation from LMHRA management and board of directors and conducting a human resources assessment at the agency.

This quarter, PQM+'s COVID-19 vaccine-related efforts continued and two important activities commenced: the development of an operational guide on emergency regulatory procedures for COVID-19 medical products and dissemination of the USP's Vaccine Quality Assessment Toolkits for COVID-19 vaccines.

Overview

The PQM+ program is pleased to present this quarterly report for Program Year 2, Quarter 3 (April 1 – June 30, 2021). The report summarizes the activities undertaken during the period and presents cumulative progress by objective and source of funding (USAID country Missions and USAID/Washington). All activities align with at least one of PQM+'s five program objectives, which the Results Framework (Figure 1) details.

Figure 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

Progress by Objective

Objective 1. Improve governance for medical product QA systems.

Regulatory systems play a critical role in any country. These systems are primarily concerned with enabling patient access to quality-assured, safe, and effective medical products as well as preventing proliferation of poor-quality, unsafe products. When appropriately implemented, regulatory systems can ensure the public health benefits of medical products and the safety of patients, health care workers, and the community. *Good governance* refers to "structures and processes that are designed to ensure accountability, transparency, responsiveness, rule of law, stability, equity and inclusiveness, empowerment, and broad-based participation"[1] in developing and implementing regulations.

As the PQM+ team builds capacities within different levels of country governments, the program is seeing encouraging signs that point to longer-term sustainability. PQM+'s governance work highlights this broader engagement and country ownership of governance activities. In

[1] http://www.ibe.unesco.org/en/geqaf/technical-notes/concept-governance

particular, many PQM+ countries have embraced **risk-based post-marketing surveillance (RB-PMS)**. Assuring the quality of medicines is challenging and costly, and it requires close collaboration and coordination among many parties. Risk-based approaches offer an opportunity for countries to channel limited resources toward medicines and locations that present the highest risks to patients. These maximize the likelihood that higher-risk products will be identified and dealt with to protect patient safety and optimizes use of resources, which promotes long-term sustainability of financing for PMS activities.

PQM+ is helping many countries establish **PMS technical working groups** (TWGs) as an important early step in promoting coordination and collaboration among diverse stakeholders with some involvement in medicines quality. These TWGs have ongoing roles in establishing priorities for and reviewing results of PMS, and are building strong, sustainable constituencies for medicines quality. This quarter, PQM+ helped launch new PMS TWGs in **Ghana** and **Guinea**. In Guinea, the government elevated the TWG to the ministerial level. PQM+ also worked with **Bangladesh** and **Kazakhstan** to develop plans for their own PMS TWGs and is collaborating with similar groups in 11 other countries.

Recently in Bamako, the PMS TWG and PQM+ held a dissemination workshop for high-level stakeholders and government officials to share the results from **Mali's** first RB-PMS survey of medical products. The survey found that 69 percent of medical products, many antimalarials, were either unregistered or unapproved. In addition, 4 percent of medicine samples failed quality control tests, indicating they were either substandard—did not include adequate amounts of the active pharmaceutical ingredient (API)—or falsified.

This quarter, PQM+ also noted progress with governance activities in several other countries, including:

- **Bangladesh,** which issued its annual report with a summary of its regulatory activities and achievements;
- **Burkina Faso**, which convened a two-day national workshop on how to coordinate on medicines quality and finalized plans for coordinating between the medicines regulatory authority (MRA) and national quality control laboratory (NQCL); and
- **Liberia**, where the Liberia Medicines and Health Products Regulatory Authority (LMHRA) completed the drafting of its five-year strategic plan.

Objective 2. Improve country and regional regulatory systems to assure the quality of medical products in the public and private sectors.

PQM+ assists countries in improving their regulatory systems, focusing on medical product market authorization, facility inspection, licensing, laboratory testing, and market surveillance. The program is working with 12 countries to strengthen their national quality control laboratories (NQCLs) to meet international standards. Achieving international accreditation is a long process with many stages and important milestones.

PQM+'s lab strengthening work continued around the globe. In **Burma**, PQM+ has been working with the Nay Pyi Taw Pharmaceutical Chemistry Laboratory (PCL). But in June, the Ministry of Health and Sports (MOHS) and DFDA dismissed at least 20 deputy and assistant directors and 125 officers from their posts in Burma's quality control (QC) laboratories for having joined the civil disobedience movement following the military coup. Quality assurance team members and trained analysts from the Nay Pyi Taw PCL were among the dismissed staff.

PQM+ assisted DFDA in forming a new QA team from the existing staff and organized a workshop on QMS to quickly rebuild the new QA team's capacity.

Other lab strengthening highlights include:

- Supporting the establishment of a vaccine laboratory at the **Ethiopian Food and Drug Authority** (EFDA), including helping to develop a draft lab design after discussions with the engineering team at the federal Ministry of Health.
- Engaging third-party testing laboratories in **Pakistan** and **Bangladesh.** National governments will be able to use these labs to test products government labs cannot test, or to meet surges in the demand for testing.
- Conducting peer audits of labs with WHO in both **Pakistan** and **Kazakhstan**. WHO's peer audit system enables quality control labs to detect gaps in technical competence or activities and work to close them.

This quarter, the program expanded its work to include **medical devices**, an important new area.

- PQM+ hosted a medical devices regulatory workshop to provide USAID and field staff with an overview of the regulatory framework and quality system for medical device development and manufacturing. This was followed by a panel discussion on the challenges of interpreting regulations and requirements to gain market authorization for medical devices in LMICs.
- PQM+ completed a detailed gap assessment to develop medical devices regulations for the Drug Regulatory Authority of Pakistan (DRAP). These reflect international regulations on regulatory structure, device classification, device approval, and post-marketing surveillance.

In **Bangladesh,** the PQM+ team provided intense support to the Directorate General of Drug Administration (DGDA) to increase its maturity level, as assessed by the WHO Global Benchmarking Tool (GBT), for its market surveillance and control, laboratory testing, lot release, clinical trial, and marketing authorization regulatory functions. DGDA aspires to achieve WHO Maturity Level 3, which signifies a stable, well-functioning, and integrated regulatory system.

Other significant RSS milestones this quarter include the following:

- **LMHRA** conducted its first medicines registrations dossier evaluations since 2017, with 40 dossiers evaluated from a backlog of more than 150 dossiers.
- In **Ethiopia,** regional inspectors with support from EFDA conducted audit inspections at 258 medicine retail outlets (60 drug stores and 198 pharmacies), which far exceeded the plan for the year of 100 retail outlets.
- **Kazakhstan**'s GMP Inspectorate successfully conducted its first remote assessment of a manufacturer in India. The Inspectorate will share its lessons learned from this experience with colleagues in Kazakhstan and Uzbekistan.

In terms of PMS, several countries made notable progress in their planning and implementation activities. **Bangladesh, Burkina Faso, Ethiopia, and Liberia** all began to collect samples. Unfortunately, as a sign of the extent to which pandemic disruptions to supply chains are

impacting the availability of medicines, in **Ethiopia**, the shortages of medicines were so severe that the teams could not even collect the number of samples targeted in their PMS.

Governments increasingly are recognizing how critical it is to determine medicines quality through PMS. As an example, the PMS TWG of the **Kenya** Pharmacy and Poisons Board (PPB) worked with PQM+ to coordinate the RB-PMS of malaria and reproductive, maternal, newborn, child, and adolescent health (RMNCAH) products. For the first time, PPB will provide human resources, vehicles, and fuel for transporting staff and samples and offered its field offices as MiniLab™ screening sites. This shows increasing ownership of and responsibility for planning, implementing, and funding PMS activities by the Kenyan medicines regulatory body.

The PQM-developed **Medicines Risk-based Surveillance (MedRS) tool** helps MRAs develop risk-based sampling strategies to support national PMS programs. These risk-based strategies maximize available resources by focusing sampling on the medicines and locations that pose the greatest risk. PQM+ finalized version 2 of the MedRS tool and made the revised version available online for country NMRAs that want to use the tool for their PMS. PQM+ also held several discussions with the WHO EMP/ISF team about potential collaboration in the area of RB-PMS.

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

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

PQM+ also supports regulatory authorities and QC laboratories in mobilizing resources to improve their financial sustainability. This quarter, the program team in **Bangladesh** assisted the National Control Laboratory in preparing a cost analysis report. Lab management can periodically review and update their costs and use the report to justify testing fees and budgetary levels.

Similarly, in **Kenya**, PQM+ engaged a consultant to analyze lab services costs. PQM+ also shared a concept note titled “Developing a medicines quality assurance framework for the **Kenya National Hospital Insurance Fund (NHIF)** system” that led to meetings with the NHIF’s chief executive officer, the head of benefits design and claims management, and other officials.

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

In light of the ongoing COVID-19 pandemic, PQM+’s work on strengthening pharmaceutical manufacturers in LMICs has taken on more urgency and importance. 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.

With PQM+ support, manufacturers can obtain marketing authorization or WHO prequalification for quality-assured medicines based on achievement of these standards. PQM+ provides a wide variety of support to manufacturers to help them obtain market authorization, which can take several years. There is a lot of movement in the manufacturing arena, much of it in early stages. Still, these initial steps are promising and bode well for strengthening the manufacturing sector in many PQM+ countries.

This quarter, WHO's Prequalification of Medicines Program approved praziquantel 600mg film-coated tablets, which are manufactured by India's Medopharm Private Limited and used to treat the neglected tropical disease schistosomiasis. PQM+ and its predecessor, PQM, had been working with Medopharm since 2017 to achieve **WHO prequalification** for this drug. Diversifying the supply source and increasing the security of the global supply of this product will benefit the more than 200 million people who need this preventive treatment annually.[2]

Also in Q3, two other manufacturers supported by PQM+ reached the major milestone of submitting dossiers to WHO for prequalification. A **Pakistani** manufacturer submitted its dosser for a first-line TB medicine, and an **Indian** manufacturer submitted its dossier for albendazole, an anti-worm medicine.

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

PQM+ is advancing a global medical products quality assurance (QA) learning and operational agenda that includes evidence-based approaches, research, and advocacy. The program actively **collaborates** with global organizations. This quarter, the Core MNCH team continued coordinating with UNICEF to boost the response rate of amoxicillin manufacturers to an African landscape analysis. PQM+'s NTD program reached out to the WHO NTD team, UNICEF, Drugs for Neglected Diseases Initiative, and UNITAID to obtain data for a new NTD dashboard that is in development. Finally, the PQM+ TB program began collaborating with the U.S. Food and Drug Administration (FDA) to organize an online workshop for MRAs to boost the timely review and approval of TB medicines.

RB Inspection (RBI) of Distribution Chains: Building on Quarter 2 progress, PQM+ continued corresponding with U.S. FDA, Health Canada, Therapeutic Goods Administration (TGA) of Australia, and the PIC/S Secretariat for inputs to revise the concept note for risk-based inspection of distribution chains. Additionally, PQM+ surveyed MRAs in the **Asia Region** (**Bangladesh, Kazakhstan**, and **Pakistan**) and **Africa Region** (**Benin, Ethiopia, Ghana, Kenya, Nigeria**, and **Senegal**) about their use of any risk-based approach to inspect manufacturers for GMP compliance and the pharmaceutical distribution chains. The responses indicated that most countries do not use risk-based approaches to inspecting manufacturers, supply chains, or distribution channels. All countries expressed interest in supporting the introduction and implementation of an RBI approach.

Partners

PQM+ saw an increase in partner engagement, both in direct implementation of activities and partner-led technical discussions. Quarter 3 also marked the first time each type of partner (core, technical resource, and core-FLEX) engaged in direct implementation of PQM+ activities. This included nine partners (three core, four technical resources, and two core-FLEX) actively helping to achieve the goals of the PQM+ program.[3] Examples include IQVIA, a PQM+ core partner, bringing expertise in data analytics and pharmaceutical market intelligence to implement an activity in Nepal; and technical resource partner experts from the University of Washington and Harvard Pilgrim Health Care (an affiliate of Harvard Medical School) supporting cross-bureau work. Muhimbili University of Health and Allied Sciences (MUHAS), a core-FLEX

[2] https://www.who.int/news-room/fact-sheets/detail/schistosomiasis
[3] https://www.usp.org/sites/default/files/usp/document/our-impact/pqm/pqm-plus-brochure-dec-2019.pdf; see p. 5, "Global expertise, local leadership."

partner, advanced from preparing a medical product manufacturer survey in Africa to implementing it with support and oversight from PQM+ technical staff. The engagement with MUHAS is also the program's first opportunity to build the technical capacity of a core-FLEX partner.

PQM+ is ensuring that partners contribute to the success of the program and assist in innovation. To that end, experts from the Centre for Innovation in Regulatory Science (CIRS), a technical resource partner, held a workshop for PQM+ staff on CIRS' Optimizing Efficiencies in Regulatory Agencies (OpERA) program. OpERA combines qualitative (process mapping) and quantitative (performance metrics) information to provide a detailed picture of the regulatory review function of medicine regulatory agencies at any stage of maturity. This program will be implemented in several PQM+ countries in upcoming quarters.

Progress by Health Element

COVID-19

In Quarter 3, PQM+ received approval for work plans on COVID-19 vaccine activities in **Bangladesh, Ghana, Pakistan,** and **Uzbekistan**. In March, approval of the **cross-bureau** COVID-19 work plan enabled activities to commence this quarter. The work plan spells out two main activities: development of an operational guide on emergency regulatory procedures for COVID-19 medical products and dissemination of USP's Vaccine Quality Assessment Toolkits for COVID-19 vaccines. PQM+ is implementing the emergency regulatory procedures with its partners, the University of Washington (UW) and Global Health Impact Group (GHIG)-London School of Hygiene and Tropical Medicine. UW is helping develop an operational guide on emergency use authorization (EUA) of COVID-19 vaccines; GHIG is developing an operational guide on in vitro diagnostic medical devices.

In **Pakistan**, previous COVID-19 program funding remains in use for such activities as facilitating EUAs; fast-tracking quality control testing of personal protective equipment (PPE) and supporting its local manufacture; regulatory support for biostudies related to the virus; and building the capacity of hospitals to manufacture alcohol-based hand rub (sanitizer) in-house, which saves money compared to buying it externally.

Finally, PQM+ closed out its COVID-19 work in **Serbia** this quarter, finalizing and submitting a market assessment and an evaluation of the enzyme-linked immunosorbent assay (ELISA) test kit produced by the Institute for the Application of Nuclear Energy (INEP) at the University of Belgrade.

Other Health Elements

PQM+'s support to USAID's core **maternal, newborn, and child health (MNCH)** work focuses on helping medicine regulatory authorities and manufacturers improve their systems. PQM+, in collaboration with other MNCH partners, supports global leadership efforts to advance USAID's, global, and country MNCH agendas and to increase access to quality-assured lifesaving medicines for women and children in LMICs. In Quarter 3, PQM+ hosted a medical devices regulatory workshop for field office staff and the USAID team based in Washington, D.C. (see above). PQM+ also continued its support to CORE Flex partner Muhimbili University in Tanzania, which is conducting the amoxicillin dispersible tablet (DT) manufacturing landscape analysis in Africa.

Building on Q2 progress, PQM+ continued collaborating closely with Muhimbili University in Tanzania on the **NTD** medical product manufacturer market analysis. Muhimbili University began data collection on the manufacturer bulk procurement analysis for NTD products. The program received approval for the subaward to Mahidol University in Thailand on May 15 for the manufacturer landscape analysis and bulk procurement analysis in Asia. PQM+ and Mahidol finalized the survey questionnaire and the introductory letter for the manufacturers. PQM+ identified a consultant to develop an online NTD dashboard and fully approved a contract with the consultant this quarter. Program staff participated in the Virtual CPhI conference May 17 to 28 to identify NTD manufacturers with a need for WHO PQ support to boost supply. Finally, PQM+ repackaged the GMP e-learning course to make it easier for users to complete, to include offline modules, and to enable collection of more data on user feedback. The revised version is available live and PQM+ disseminated it through several platforms, including the PQM+ website, social media, and the USAID Health Systems Strengthening (HSS) distribution network.

PQM+ is working to ensure an uninterrupted supply of quality lifesaving **tuberculosis (TB)** medicines. The program does this by directly supporting manufacturers of priority TB products, 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 process does not create hurdles for the introduction and scale-up of new TB medicines. This quarter, PQM+ developed a questionnaire and engaged the NMRAs of select high-burden TB countries in identifying topics of interest for a PQM+/U.S. FDA online workshop. During the workshop, the U.S. FDA will share experiences on the regulatory review of new TB medicines. PQM+ also provided ongoing technical guidance and monitoring of the Virginia Commonwealth University (VCU) subaward for the laboratory phase on optimizing the manufacturing process of the rifapentine API.

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 work plan for OHS Cross-Bureau activities was approved in November 2020. During the third quarter, PQM+ completed the activities that follow.

Risk-Based Inspection Methodology Framework

RB Inspection: The risk-based inspection (RBI) methodology framework covers regulatory agencies' inspectorate activities in Good Manufacturing Practice (GMP) and Good Clinical Practice (GCP), as well as inspections for contract research organizations (CROs), bioequivalence (BE) centers, and Good Distribution Practices (GDP). This quarter, PQM+ upgraded the standardized risk-based inspection tool (MS Excel-based) developed in Quarter 2.

The tool computes the risk level across GMP systems and includes the quality management system (QMS); production materials; production; physicochemical properties; microbiology; production water; heating, ventilation, and air conditioning (HVAC); and validation documentation (beta version). PQM+ identified the upgrades after testing the pilot model. With the Excel model finalized, PQM+ began recruitment of a program developer to translate the Excel version into an online tool. The program also began drafting the guidance document on risk-based inspections to complement the tool.

RB Inspection (RBI) of Distribution Chains: Building on Quarter 2 progress, PQM+ continued corresponding with U.S. FDA, Health Canada, Therapeutic Goods Administration (TGA) of Australia, and the PIC/S Secretariat for inputs to revise the concept note. Additionally, PQM+ shared inquiries with MRAs in the Asia Region (Bangladesh, Kazakhstan, and Pakistan) and Africa Region (Benin, Ethiopia, Ghana, Kenya, Nigeria, and Senegal) to assess whether those countries are using any risk-based approach to inspect manufacturers for GMP compliance and the pharmaceutical distribution chains. The responses indicated that most countries do not use manufacturer RBI for GMP, supply chain, or distribution. All countries expressed interest in supporting the introduction and implementation of an RBI approach.

PQM+ began the process of hiring a consultant to develop a web-based interface from the beta (Excel) version of the manufacturer RBI tool.

MedRS Tool

This quarter, PQM+ finalized version 2 of the MedRS tool and made it available online for NMRAs that want to formally subscribe to and use the tool for RB-PMS protocol development and training. PQM+ also created a simplified version to give stakeholders a high-level orientation to the tool. The program has piloted the MedRS tool in Nepal and Ghana and is developing a one-page brief to describe its features and benefits. PQM+'s technical staff has been instructed on the updated MedRS tool and can now use it to train MRA staff. Some key features and functionalities on the revised tool include:

- Embedded PMS protocol and report templates;
- Offline access with the ability to upload data when online;
- Search functionality by product, International Nonproprietary Name (INN) or commercial name, country, year, round, city, region, and pass or fail results;
- Information sharing between MRAs in the region and beyond, such as WHO's Rapid Alert System; and
- Google Maps visualization of the sampling region.

Model to Estimate the Economic and Health Impact of SF Medicines

This quarter, PQM+ organized and facilitated an advisory group meeting to examine the literature review and inventory of existing models completed by the University of North Carolina (UNC) and the conceptual framework drafted by the University of Washington (UW). PQM+ met with program representatives in Bangladesh, Nepal, Nigeria, Ghana, Pakistan, and Kenya to solicit input on the societal dimension of the model for potential uptake. The group identified Kenya as the location to pilot the tool and a case study for the oxytocin injection MNCH product. PQM+ is awaiting USAID Mission concurrence to begin the pilot study in Kenya. The advisory

group also decided to build a generic model for the anti-TB medicine, which the program will pilot at the country level in Year 3.

The next advisory group meeting is planned for July 27 to review the Excel-based SF cost model that UW developed.

Common Standards for Pharmaceutical Information Management

PQM+ continues to coordinate this activity in collaboration with USAID's Medicines, Technologies, and Pharmaceutical Services (MTaPS) program. PQM+ identified the common regulatory standards for the information management system (IMS) of four WHO Global Benchmarking Tool (GBT) regulatory functional areas: national regulatory authority lot release, market surveillance and control, laboratory testing, and clinical trials oversight. This quarter, PQM+ worked with MTaPS to revise the activity implementation plan, identify stakeholders for the planned consultative meeting, and draft a stakeholder engagement letter and terms of reference. The team is working on finalizing the report on identified common standards for all WHO GBT regulatory functions. The stakeholder consultative meeting is planned for Quarter 4.

Pharmaceutical Systems Strengthening Course

PQM+ worked with the USAID MTaPS team to revise and finalize the eLearning course storyline for the quality assurance module it developed. The MTaPS team is adding the storyline content to identified training platforms that will host the full course materials.

Webinar Series

In April, PQM+ delivered its second program webinar, "Strengthening National Quality Control Laboratories (NQCL) to Ensure Quality Medical Products," to 104 people (out of 198 registrants), including 76 USAID staff. PQM+ shared a link to the webinar recording in its May newsletter. The program is planning a third webinar in Quarter 4.

Priority Activities for Next Quarter

Risk-based inspection:

- Finalize the procurement for an application developer.
- Solicit the interest of select MRAs in joining an expert panel/working group to develop the RBI guidance document and an RBI tool for LMICs.

MedRS:

- Continue field testing the enhanced online MedRS in two PQM+ countries.
- Launch the final product for full deployment at the country level.

SF medicines costing model:

- Convene expert advisory panel to review the SF cost model.
- Seek Mission concurrence from Kenya.

Common Standards for Pharmaceutical Information Management Systems:

- Finalize the draft report on identified common standards.
- Plan, coordinate, and deliver the stakeholder consultative meeting.

Webinar series:

- Develop and deliver the next webinar.

Activities and Progress by Country and Regional Buy-Ins

Africa Region

Benin

As is the case in many French-speaking West African countries, the medicines regulatory system in Benin is fragmented. A single agency does not perform all regulatory functions. Moreover, the laws, ordinances, and decrees that make up the regulatory framework are largely outdated. In some cases, important regulatory functions such as post-marketing surveillance of products are lacking, not well defined, and/or not implemented. This allows falsified medical products to enter the supply chain, exposing unsuspecting consumers to illicit, unauthorized, or poor-quality medicines.

The main regulatory body is the Beninois Agency for Pharmaceutical Regulation, *l'Agence Béninoise de Régulation Pharmaceutique* (ABRP), formerly known as the Directorate of Pharmacy, Medicines, and Diagnostics. ABRP develops and implements national pharmaceutical policy and regulations, registers medicines, approves licenses, inspects pharmaceutical establishments, and controls the advertisement and promotion of medicines, including herbal and traditional medicines. The national quality control laboratory, *l'Agence Nationale de Contrôle de la Qualité des Produits de Santé et de l'Eau* (ANCQ), collects and tests medicines at the points of entry into the country (land, sea, and air) or at the request of any national institution.

PQM+ activities in Benin began in PY2, Q2. PQM+ is helping ANCQ strengthen its QMS to achieve international recognition (ISO/IEC 17025 or WHO prequalification). This would assure the reliability of testing and increase the public's confidence in ANCQ's test results.

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.

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

In Q3, as a follow-up to the SATTA training conducted in Q2, ANCQ drafted a standard operating procedure (SOP) to use SATTA to conduct routine internal audits. In addition, ANCQ planned an internal audit, which the quality assurance team conducted using the SATTA tool under the supervision of PQM+. This supervision surpassed ensuring that ANCQ's QA team could use the tool correctly; it provided an opportunity for them to receive feedback on their

internal auditing skills from PQM+ and recommendations on how to improve those skills. This audit also evaluated progress on implementing the CAPA plan developed after the baseline assessment was conducted in Q2. To help ANCQ adequately address audit gaps, PQM+ conducted a training in quality risk management for ANCQ technical staff. This will permit ANCQ's quality team to adopt a risk-based approach to managing quality issues, identify possible risks to their quality system, and implement measures to mitigate these risks (instead of reacting/responding to nonconformities).

This quarter, PQM+ worked with ABRP and ANCQ to identify key stakeholders to include in a national PMS technical working group (TWG). ABRP will invite these agencies to nominate representatives to constitute the TWG, which the ABRP will use to plan and implement post-marketing surveillance activities in the country. PQM+ developed draft terms of reference for the TWG and shared them with both ANCQ and ABRP for review; they were adapted to the country's context.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Inaugurate the national PMS-TWG and orient the group on the principles and benefits of the risk-based approach to post-marketing surveillance, and
- Conduct training for ANCQ on key QMS elements to address gaps identified during the baseline assessment.

Burkina Faso

Malaria is one of Burkina Faso's primary causes of morbidity and mortality. In 2018, the Ministry of Health (MOH) confirmed 12 million cases and 3,974 deaths. The U.S. President's Malaria Initiative (PMI) supported Burkina Faso's National Malaria Control Program's (NMCP) implementation of its Malaria National Strategic Plan 2016–2020, which aimed for a 40 percent reduction in the incidence of and deaths from malaria by 2020.

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 post-marketing surveillance of products. 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.

PQM+ activities kicked off in Q2. The program is working with the main medicines quality stakeholders, ANRP and LNSP, and others to adopt a risk-based, sustainable approach to PMS; strengthening LNSP as it prepares for ISO 17025 accreditation; and assisting 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, 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 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved.

In Q3, after establishing the PMS-TWG, PQM+ facilitated a five-day workshop to train the TWG on the use of the MedRS tool. MedRS helps inform risk assessments by determining which molecules to sample, where to get them, and in what quantities. During the workshop, participants used the MedRS to score various risk dimensions, which later informed Burkina Faso's first risk-based PMS protocol for anti-malaria medicines. The protocol delineated regions and cities for sample collection, facilities from which samples would be collected, and quantities of samples. After ANRP's final review and approval of the PMS protocol, another workshop trained the TWG and medicines samplers on the approved protocol to prepare them for the sampling missions. On June 5, sampling teams deployed to seven regions in Burkina Faso (Central, Central-East, Central-North, East, Haut-Bassins, North, and Plateau Central) for two weeks to sample antimalaria medicines (artesunate injection, artemether injection, quinine injection, and sulfadoxine/pyrimethamine tablets).

One challenge expressed by USAID during the drafting of the work plan was the poor coordination and information-sharing among medicines quality assurance stakeholders in the country. Therefore, in April, PQM+ assisted ANRP in convening a two-day national medicines quality assurance/quality control workshop that drew more than 20 stakeholders from the health ministry and private sector to deliberate and exchange information on medicines QA issues in the country.

Burkina Faso's national quality control laboratory, LNSP, and specifically the DCM, have benefitted from capacity building efforts under the PQM+ program and other projects. The laboratory now requires practical hands-on sessions and advances quality management systems training to build on previous capacity building efforts. As a result, this quarter PQM+ QC experts conducted quality control training on techniques for DCM's desired accreditation scope. The experts routinely apply these techniques in an accredited laboratory (USP-Ghana). The training taught 15 technical personnel (six women, nine men) about six key analytical techniques: pH, loss on drying, dissolution, HPLC, UV-visible spectrophotometry, and titrimetry. PQM+ also conducted advanced quality management systems training on measurement uncertainty for 14 technical staff (six women, eight men). This training will enable the DCM to calculate uncertainties and include them in the results they report, as required by the ISO 17025 standard.

PQM+ helped ANRP convene a two-day workshop to review and validate the memorandum of understanding/agreement framework for collaboration between LNSP and ANRP drafted in Q2. More than 20 managers from both agencies read the draft agreement in plenary and adapted, corrected, formatted, and finalized it. The agreement specifies timelines so each agency can hold the other accountable, commits ANRP to support LNSP in testing medical products, and help the MRA make regulatory decisions.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Review LNSP's draft SOP for the use of SATTA to conduct internal audits;
- Supervise an internal audit of LNSP using SATTA;
- Supervise testing of anti-malaria medicines sampled;
- Support an ANRP workshop to disseminate risk-based PMS results;
- Provide supportive supervision to LNSP for QMS/QC; and
- Collaborate with ANRP and LNSP to organize a second national quality assurance/ quality control stakeholder's workshop built on lessons learned from the Q3 workshop.

Ethiopia

The use of poor-quality medical products can endanger treatment and erode public confidence in health programs, and may contribute to the development of antimicrobial resistance, which leads to more expensive treatment with unpredictable outcomes. The lack of effective regulatory oversight and product quality assurance/quality control systems is putting many lower-and middle-income countries, including Ethiopia, at risk of having substandard and falsified (SF) medical products. Ethiopia still covers more than 85 percent of its demand for essential medicines through imports. Increasingly frequent public health emergencies mean that overdependence on imports for life-saving medicines is a substantial and still-growing threat to public health.

In Ethiopia, authorized bodies at the federal and regional levels regulate medicines. At the federal level, the Ethiopian Food and Drug Authority (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 are not mandated to EFDA fall under the jurisdiction of regional government and city administration regulatory bodies. But the lack of clarity in the mandates of EFDA and the regional regulatory bodies (RRBs), the absence of a formal reporting relationship between them, and the RRBs' poor capacity compromise the proper regulatory oversight of medical products in Ethiopia.

PQM+ contributes to the achievement of Ethiopia's national health targets and goals by supporting efforts to ensure the availability of quality-assured, safe, and efficacious medicines to address Ethiopians' priority health needs. PQM+ has been working with EFDA and the regional regulatory bodies to build capacity to monitor quality in the medical product supply chain and to strengthen their working relationship so they could carry out their respective mandates more efficiently. PQM+ also helps build local manufacturers' capacity to meet international standards, thereby ensuring that locally produced medical products are of good quality and not harmful to end users.

In PY2, PQM+ is working to achieve four high-level objectives:

- 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 the supply of quality-assured essential medical products of public health importance.
- Optimize and increase financial resources for medical products quality assurance.

This quarter, PQM+ provided technical assistance to EFDA and regional regulators to build the capacity of 32 inspectors, which was followed by cascaded training in four regions; conduct audit inspections at 258 medicine retail outlets; develop a roadmap for ISO 17025:2017 accreditation for EFDA's branch laboratories; maintain accreditation of EFDA's central/main laboratory; develop a risk-based PMS protocol, followed by orientation to experts and collection of samples from the field; reinforce the EFDA inspectorate's QMS and prepare it for ISO 17020 accreditation; and strengthen the QMS of the clinical trial regulatory function by developing two directives and 12 SOPs.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved.

To build the capacity of regional inspectors, PQM+ supported a training of trainers (TOT) for 32 inspectors (12 women) from EFDA and the regulatory authority of Addis Ababa. Cascaded trainings to regional inspectors followed at four locations: Amhara, Oromia, Addis Ababa, and the Southern Nation, Nationalities, and Peoples Region (SNNPR). After the training, regional inspectors, supported by EFDA, conducted audit inspections at 258 medicine retail outlets (60 drug stores and 198 pharmacies). This total far exceeded the plan for the year of 100 retail outlets. Inspections took place at medicine retail outlets in Adama, Jimma, Hawassa, Dessie, Debreberhan, and Addis Ababa. PQM+ completed data entry and cleaning this quarter and will conclude report writing and dissemination next quarter. The inspection results will help identify some key downstream supply chain malpractices that facilitate the circulation of substandard and falsified medicines. Accordingly, regulatory authorities can use this information to devise evidence-based strategies to guide regulatory measures in a proactive manner.

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

Repackaging and relabeling medicines are common practices in the manufacturing industry. Inappropriate packaging and labeling can lead to product mix-ups, loss of product identity, and contamination and cross-contamination, which could endanger the safety of the end user. Legislative requirements must support and establish parameters for conducting these manufacturing processes. So far, Ethiopia has not had a regulatory tool to guide such practices.

This quarter, PQM+ provided technical assistance to draft a directive detailing requirements for repackaging and relabeling pharmaceutical products. These requirements cover broad areas, including the manufacture of bulk products, secondary packaging, co-packing, and repacking of returned products. Regulatory inspectors at EFDA will use the requirements to determine manufacturer compliance with standards and grant a certificate of competency to existing or new manufacturing facilities. The draft directive is currently under review by EFDA staff. Once the in-house review is complete, PQM+ and EFDA will co-host a workshop to solicit feedback from relevant stakeholders. The existence and proper implementation of this directive will contribute to the safe use of medicines by patients, caregivers, and consumers by ensuring unambiguous identification of medicines at all levels of the supply chain.

This quarter, PQM+ partnered with EFDA to develop a branch-specific roadmap for ISO/IEC 17025:2017 accreditation of branch laboratories. The roadmap is based on results of the self-assessment branch labs conducted using the SATTA tool. During Q2, EFDA and PQM+ conducted a joint supportive supervision to verify the self-assessment at the three branch labs

(Bahirdar, Jima, and Diredawa). The roadmap is complete, with feedback gathered from relevant experts at EFDA, the content edited, and the final version submitted to EFDA leadership for approval. This roadmap will guide overall support to laboratories, including training, procurement of equipment/supplies, technical assistance, QMS development/ implementation, and more, in their journey toward ISO/IEC 17025 accreditation.

To prepare the EFDA branch laboratories for accreditation, PQM+ procured an ultrasonic sonicator for each laboratory. Sonicators are used for various purposes, including mixing, extraction, and homogenization of samples. After identifying and selecting a suitable vendor, PQM+ procured the equipment for shipment to Ethiopia. The equipment will be delivered soon and is expected to address one of the main challenges the laboratories have experienced in the past (i.e., high-performance liquid chromatography analysis).

In Quarter 3, PQM+ supported the development of a risk-based PMS protocol to guide the collection and testing of product samples for the current year's PMS program. Among the products sampled for this year's PMS were antimalarial medicines and oxytocin. Sampling was based on the MedRS scoring tool and the team completed it following training of relevant staff last quarter. After finalizing the PMS protocol, PQM+ oriented the sample collectors to the protocol prior to field deployment. The team collected samples from the areas and facilities that were selected based on risk scoring/categorization.

The major challenges during sample collection were the inaccessibility of some locations (due to security threats) and a serious shortage of medicines in the country at the time of sample collection. Though the plan was to collect and test 250 product samples per the protocol, the team collected only 70 samples. To compensate for the shortfall, sample collectors redeployed to locations around Addis Ababa, but obtained only about 10 samples—many fewer than expected. This situation is unprecedented among PMS programs. With support from PQM+, procurement of Mini-Labs to test the samples is in progress. The test results of these samples will give the regulatory authority insights into the current situation regarding the circulation of substandard and falsified medicines in the local market.

This quarter, PQM+ provided proficiency test (PT) samples to the EFDA's central laboratory to help it maintain its accreditation status. PQM+ identified two PT providers, procured PT samples, and delivered some of the samples to EFDA's central laboratory. EFDA will submit the PT sample results to the PT provider for evaluation. This is a critical requirement to prove the laboratory's competency.

PQM+ also helped EFDA secure maintenance and calibration services for its condom-testing machine by contracting with Enersol, an Australia-based supplier, per international requirements. Remote technical assistance has already started, and an Enersol technician will visit the lab and provide the remaining services next quarter, if COVID-19 restrictions permit.

PQM+ provided technical assistance to establish a vaccine laboratory at EFDA as a member of the technical working group on this topic. The group developed its terms of reference (TOR) and proposed a draft lab design after discussing it with the engineering team at the federal Ministry of Health. The design is in its final stage of review by the engineering unit of the Ministry of Health.

This quarter, the external accreditation body ANAB audited EFDA's central laboratory to determine if the lab was meeting international requirements. The auditor found that the EFDA lab is compliant with ISO 17025:2017 standards and has fulfilled all the requirements, thereby extending the lab's accreditation for the next two years. In parallel, EFDA is working with the

Ethiopia National Accreditation Office (ENAO) to transition its ANAB accreditation to one from a local accrediting body. However, the progress from ENAO has been slower than expected.

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

PQM+ provided technical assistance to the Food, Beverage, and Pharmaceutical Development Institute (FBPDI) and EFDA to finalize reports on last quarter's assessment to determine local manufacturing industries' implementation of a GMP roadmap. The assessment followed the CAPA submitted during the previous inspection; this inspection sought to determine whether manufacturers were implementing the CAPA as promised, and to understand the extent of manufacturers' compliance with GMP. A team of experts from EFDA, FBPDI, and PQM+ assessed and rated the progress—either "lagging," "in progress," or "on track," and/ or in terms of levels (1-3)—of only six of the nine manufacturers who submitted a CAPA.

The assessment found that, overall, local manufacturers' implementation of CAPA and/or the GMP roadmap was much lower than expected. Only one manufacturer has cleared more than 80 percent of the deficiencies listed in its CAPA plan and received a rating of "on track." Two companies were rated "in progress" for clearing 62 and 68 percent of deficiencies indicated in their respective CAPAs. The rest received a rating of "lagging," scoring below 60 percent of CAPA deficiencies cleared.

Regarding manufacturers' performance, as measured using GMP compliance levels-based rating tools, only one manufacturer received a GMP compliance Level 3 mark, scoring 85 percent. Three companies received a Level 2 rating with scores of 51 percent, 64 percent, and 69 percent. One manufacturer's score of 39 percent translated into a Level 1 rating.

In recent years, the local manufacturing industry has faced several hurdles, as indicated in an assessment PQM+ conducted, titled "Available Capacity and Barriers to Local Production of Pharmaceuticals." These challenges might have contributed to local manufacturers' inability to fulfill the requirements stipulated in the GMP roadmap. Regardless, local manufacturers have considerable work ahead to meet the expected pace toward GMP compliance.

Addressing the gaps identified by WHO's Global Benchmarking Tool (GBT) is a key priority to help EFDA achieve its goal of becoming a WHO-listed authority (Maturity Level 3 or higher). PQM+ is helping EFDA develop and revise relevant QMS documentation in compliance with the GBT requirements. This quarter, PQM+ assisted in preparing the medicine inspection directorate for ISO/IEC 17020 accreditation by participating in a training of inspectors on existing and new SOPs to facilitate their compliance.

In addition, PQM+ aided the inspectorate in conducting an internal audit to determine the status of its compliance with ISO 17020. Development and implementation of corrective and preventive action to rectify the internal audit's findings followed. PQM+ helped the inspectorate identify and create a risk mitigation plan, which is a key requirement for ISO 17020 accreditation; revise/update its quality manual and devise 42 SOPs, assigning numbers per document control requirements; and compile and submit all required documents to ENAO as part of the application for ISO 17020 accreditation. Currently, ENAO is evaluating the documents and EFDA is awaiting the outcome.

ISO accreditation of EFDA's medicine inspection directorate will enhance all its outputs and decisions. This status will not only improve the regulatory services of the inspectorate, but also contribute substantially to EFDA's journey toward becoming a WHO-listed authority.

The proper and timely conduct of clinical trials (CTs) is critical for priority health programs to improve their uptake of new treatments and ensure the safety/efficacy of new and existing products. The national regulatory authority is responsible for authorizing clinical trials, monitoring their adherence to good clinical/laboratory practices, evaluating their results, and authorizing use of their results or publishing them in a way that benefits the public. The national authority can also suspend or withdraw approval for a clinical trial, if necessary. This quarter, PQM+ helped develop tools to guide regulatory oversight of clinical trial applications, reviews, and approval.

PQM+ supported the drafting of two directives: one for good clinical trial practice and another for clinical trial application, review, and authorization. These directives state the regulatory requirements for conducting clinical trials in Ethiopia and ensure that trials on human subjects follow sound scientific and ethical standards within the framework of good clinical practice. Compliance with this standard assures the public that the rights, safety, and well-being of trial subjects are protected and consistent with international best practices, and that the clinical trial data are credible.

As part of strengthening the quality management system of the clinical trial regulatory function, PQM+ assisted in developing 12 SOPs to standardize procedures for the application, review, and approval of clinical trial applications. The SOPs cover screening clinical trial applications, review and authorization of new clinical trial applications, review of informed consent forms, review of amendments (both major and minor) to an approved CT application, importation of investigational medicinal products, evaluation of a reply to a request for further information, consideration of non-clinical data within the CT application review, safety reporting on clinical trials, engagement of relevant stakeholders in clinical trials, communication with clinical trial applicants, conditional approval of a CT application after review by the authority, and conducting Good Clinical Practice (GCP) in trial inspections. Practical implementation of these SOPs will improve the consistency, transparency, accountability, and efficiency of regulatory oversight of clinical trials. This will ultimately enhance uptake of new treatment options and ensure that treatments in Ethiopia are safe and effective.

Priority Activities for Next Quarter

- Complete testing of PMS samples and compile reports;
- Finalize the audit inspection report and disseminate results;
- Provide TA to local pharmaceutical industries based on their needs;
- Consult with stakeholders on the cold chain assessment guidance document and packaging/repackaging directive; and
- Facilitate in-house enrichment and consult with stakeholders on the two clinical trial directives and 12 SOPs.

Ghana

Malaria is endemic to Ghana and a major cause of illness and death in the country, particularly among children and pregnant women. Maternal mortality is another pressing health concern.

Postpartum hemorrhage is the leading cause of maternal death in Ghana, one of 25 countries that account for more than 66 percent of the world's maternal and child deaths.[4]

WHO recommends oxytocin as a first-line treatment for postpartum hemorrhage. With technical assistance from the PQM+ predecessor program, PQM, USAID/Ghana worked on building the capacity of the Ghana Food and Drugs Authority (GFDA) to monitor the quality of maternal and child health commodities such as oxytocin. GFDA, now a WHO Maturity Level 3 medicines regulatory authority, has made great strides in surveying antimalarials, with a failure rate of less than 10 percent in the last survey. However, the challenge of substandard, falsified, and unregistered medicines, including those used to treat postpartum hemorrhage, persists.

PQM+ is working with GFDA and other stakeholders to adopt a risk-based sustainable approach to PMS; helping a local manufacturer achieve WHO prequalification for artemether/lumefantrine tablets to treat malaria; collaborating with GFDA to assess the progress of three other manufacturers audited by PQM in 2019; identifying potential local manufacturers of oxytocin; and collaborating with the Ghana Health Supply Chain-Procurement and Supply Management (GHSC-PSM) to prepare the local pharmaceutical industry and GFDA to adopt 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 the 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.

During Q3, PQM+ helped the GFDA inaugurate its newly established post-marketing surveillance technical working group. This TWG will plan and implement post-marketing surveillance activities in Ghana. The group comprises representatives from GFDA; national control programs on malaria, tuberculosis, and HIV/AIDS; Expanded Program on Immunization; National Health Insurance Agency; Pharmacy Council; and the Ghana Health Service. The TWG's leadership consists of the Pharmacy Council as president, GFDA as vice president, and the National Tuberculosis Control Program (NTCP) as rapporteur. The group reviewed and validated the terms of reference for its establishment and operations, received an orientation on the principles of risk-based PMS, and was introduced to the MedRS tool.

PQM+ experts from Ethiopia and the United States trained the TWG on the online version of the MedRS tool, which was subsequently used to develop Ghana's first risk-based PMS protocol for antimalaria and MCH medicines.

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

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

In Q3, PQM+ finalized and shared three GMP assessment reports with Ernest Chemists (for artemisinin-based combination therapy, or ACT, and oxytocin manufacturing), Amponsah Efah Ltd. (for ACT manufacturing), and Atlantic Life Science Pharmaceutical Ltd. (for oxytocin manufacturing), along with proposed recommendations to close identified gaps. All three local manufacturers have upgraded or built new manufacturing facilities and procured state-of-the-art equipment. However, some do not have a quality management system in place. PQM+ found that each has the potential to manufacture quality-assured medicines and has demonstrated commitment to the process.

PQM+ also conducted a GMP assessment of Entrance Pharmaceuticals Ltd. (EPL), noting progress in the prequalification process. The manufacturer completed bioequivalence studies of the 80/480mg formulation and is analyzing the data. A new heating, ventilation, and air conditioning system has been installed and qualified by engineers brought in from India. This is a significant investment by EPL and a clear testament to its commitment to the prequalification process. Yet, gaps in their GMP implementation remain. The PQM+ chemistry manufacturing and control (CMC) expert also began working with EPL to map out the process of developing their product dossier for the prequalification process.

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

In Q3, PQM+ participated in the second GS1 TWG meeting convened to draft the pharmaceutical traceability strategy for Ghana. The Government of Ghana has issued this document to raise key stakeholders' awareness and advocate for the use of GS1 global standards to support national health care objectives. Adopting GS1 global standards for pharmaceuticals enables the collective use of systems to enhance the quality and amount of data available to support operational processes. In addition to participating in the GS1 TWG meetings, PQM+ developed a questionnaire to assess the readiness of local industry to adopt the standards.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Train the PMS-TWG and medicines samplers on the new RB-PMS protocol;
- Sample antimalaria medicines from five regions in Ghana;
- Provide technical assistance to three local ACT manufacturers, including training and QMS building, to improve implementation of GMP;
- Provide technical assistance to one oxytocin manufacturer to prepare for the manufacture of oxytocin injectables; and
- Deploy the GS1 industry readiness questionnaire and evaluate the survey results.

Guinea

Malaria is the top public health problem in Guinea, taking more lives than any other disease. PMI supports activities in line with the goal of reducing malaria-related mortality by 50 percent.

This is because malaria is the primary cause of medical consultations, hospitalizations, and deaths, particularly for children under 5 years old. The maternal mortality rate in Guinea is one of the highest in the world. Through family planning and reproductive health (FP/RH) funding, USAID aims to integrate family planning services with maternal and neonatal health care, including emergency obstetric and newborn care. Through maternal and child health (MCH) funding, USAID seeks to scale up evidence-based interventions and contribute to a reduction in maternal, newborn, and child mortality.

In collaboration with USAID's Systems for Improved Access to Pharmaceutical Services (SIAPS) program, PQM facilitated the process of revising the pharmaceutical law. Through this effort, Guinea's parliament enacted new legislation in June 2018 and the president signed it into law in July 2018. The National Directorate of Pharmacy and Medicines (DNPM) is installing regulatory provisions related to its mandate while strengthening its technical capacity to carry out regulatory functions.

PQM+ has funding to work in Guinea through September 2021, and will support the following objectives in PY2:

1. Governance for medical product QA systems improved, and
2. Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved.

Progress by PQM+ Objective

Objective 1: Governance for medical product QA systems improved.

This quarter, PQM+ collaborated with DNPM and the national quality control laboratory (*Laboratoire National de Contrôle Qualité des Medicaments*, or LNCQM) to inaugurate a new Post-Marketing Surveillance Technical Working Group (PMS-TWG). The technical advisor to the minister for international cooperation, who is the former head of the medicines' regulatory authority in Guinea, inaugurated the group. The TWG includes representatives from DNPM, LNCQM, the family health and nutrition department, the Health Inspectorate, the National Public Health Institute, University of Conakry, central medical stores, the National Order of Pharmacists, public and private wholesalers, and national programs on malaria control, tuberculosis, AIDS, hepatitis control, the fight against noncommunicable diseases, and neglected tropical diseases.

The TWG elected its leadership, with DNPM's deputy director general serving as president. During a five-day workshop, the group reviewed the draft terms of reference developed by PQM+ in plenary, adapted it to the context of Guinea, and validated it to demonstrate acceptance. The TWG also agreed to advocate for the adoption of the terms of reference as a ministerial decree. PQM+ oriented the TWG on the principles of risk-based PMS and introduced it to the MedRS tool.

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

In Q3, PQM+ developed a training curriculum to build LNCQM capacity to apply good practices in the quality control of medicines. The training incorporated PowerPoint presentations and discussion to ensure trainees' full understanding and appreciation of these best practices. Courses included Basic Laboratory Safety, Good Practices for Pharmaceutical QC Labs, Good

Documentation Practices, Proper Use of Pharmacopoeia, and Good Weighing Practices. Participants completed course evaluations and pre- and post-knowledge checks. Training sessions took place in-country in English, with a professional language consultant present for the entire training to provide translation. French versions of all training materials, including the PowerPoint presentations, were available to the trainees. This training will prepare the laboratory for advanced training and supportive assistance in quality control and quality assurance. One woman and 12 men attended the training.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Train the PMS-TWG on the use of the online version of the MedRS tool;
- Support the PMS-TWG in developing a protocol for antimalaria, MNCH, and family planning medicines;
- Evaluate equipment needs for LNCQM to help prioritize procurement of needed equipment in subsequent program years;
- Conduct quality control training for technical staff at LNCQM; and
- Conduct training on SATTA and CAPA for technical staff at LNCQM.

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), NQCL, Division of National Malaria Program (DNMP), Department of Family Health (DFH), MOH's Division of Health Products and Technologies (HPT), and the counties to further strengthen stakeholders' capacity to ensure citizens' access to quality-assured medical products.

In PY2, PQM+ is working to:

- Improve governance for medical product QA systems;
- Strengthen regulatory systems for assuring quality of medical products;
- Optimize and increase financial resources for medical product QA systems;
- Increase supply of quality-assured essential medical products of public health importance; and
- Advance the global medical product QA learning and operational agenda.

During Q3, PQM+ focused on improving governance for medical product QA systems and strengthening regulatory systems to assure the quality of medical products in Kenya.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved.

Quality assurance framework for malaria commodities: During Q3, PQM+ worked with Kenya's DNMP to edit, design graphics for, lay out and format, and print the QA Framework for Malaria Products. This framework outlines the institutional stakeholders involved in quality

assurance of essential health commodities for malaria treatment and prevention in the country, as well as their respective roles. In preparation for disseminating the framework, PQM+ participated in the quarterly DNMP malaria commodities review meeting, a multi-stakeholder forum that discusses critical issues affecting malaria commodities' supply and quality. The forum also shares updates from the DNMP and implementing partners with county health teams. The counties use it to share best practices and the challenges they face with malaria commodities. The meetings helped PQM+ understand the needs of the DNMP and counties. The program team made attendees aware of PQM+'s contribution, especially in supporting the upcoming RB-PMS activity and QA framework on malaria commodities.

Malaria Commodities Management Committee of Experts meeting: PQM+ participated in the Division of National Malaria Program's Procurement and Supply Management (PSM)/ Commodities Management Committee of Experts (COE) virtual meeting on May 4. This multi-stakeholder forum discusses critical issues affecting malaria commodities' quality, procurement, and supplies. PQM+ will deliver a presentation on RB-PMS at the next PSM/COE meeting.

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

Developing a PPB online platform for self-directed learning: PQM+ continued supporting the PPB to set up an online platform for self-directed learning. PQM+ technical advisors and consultants began designing and customizing the open-source Moodle platform for online learning for the PPB and presented updates to PPB for their review and input. The consultants shared a prototype of the platform with PPB for review and input. In parallel, a second team of PQM+ consultants continued helping PPB determine training needs and develop content and materials for learning. To identify training needs, the consultants completed key informant interviews and focus group discussions (FGDs) with PPB personnel. PQM+ later facilitated a workshop for the PPB team to validate the training needs identified. The workshop also initiated the process of content development for PPB's self-directed learning. Consultants and subject matter experts are now creating content for selected regulatory functions, including medicines post-marketing surveillance, quality control, product evaluation, and registration. As part of this process, PQM+ identified reference materials to use in developing content for the courses.

Human resource capacity development at the NQCL: In Q2, PQM+ conducted an HR capacity assessment of the NQCL, identifying the strengths and weaknesses of the laboratory's workforce on four capacity dimensions, namely NQCL's staffing level, skills mix, staff motivation, and working conditions. NQCL scored 65 percent on staffing level, 62 percent on skills mix, 63 percent on staff motivation, and 60 percent on working conditions. This represented an overall workforce capacity maturity level of 2.5 (emergent) on a scale of 1 (foundation) to 4 (advanced). As a follow-up to the assessment findings, PQM+ facilitated a workshop with NQCL in Q3 to plan for implementation of the HR assessment recommendations. The workshop developed a detailed implementation plan for improving the HR function, as recommended in the workforce capacity assessment report.

Karl Fischer titration equipment for the NQCL: PQM+ procured and delivered a specialized laboratory tool, the Karl Fisher titrator, for the NQCL. A Karl Fischer titrator is the standard equipment for determining the water content of medicines, especially those that are sensitive to moisture; and provides accurate results within minutes. Program medicines for which the titrator is crucial include artemisinin-based antimalarials like artesunate and dihydroartemisinin and reproductive, maternal, neonatal, child, and adolescent health (RMNCAH) medical products like amoxicillin dispersible tablets, oxytocin, and medroxyprogesterone, which require careful control

of moisture content. As part of the installation and set-up, the supplier conducted equipment calibration and qualification at the NQCL premises. PQM+ and NQCL continued preparing to hand over the equipment, which will include a ceremony by USAID and Ministry of Health representatives.

Risk-Based Post-Marketing Surveillance of Product Quality: This quarter, PQM+ provided technical assistance to members of the joint pharmacovigilance and post-marketing surveillance technical working group (PV/PMS TWG) of the PPB to build the board's capacity to lead and coordinate RB-PMS of quality of malaria and RMNCAH products. The PQM+ team met with and advised the PPB technical team on how to strategically engage other stakeholders to strengthen pharmaceutical product quality in the country. Among the issues agreed upon was consideration of a quarterly PV/PMS TWG stakeholder meeting with updates by PPB and partners on strengthening PMS systems and implementing PMS activities, including achievements, challenges, and planned activities.

To prepare for the upcoming RB-PMS fieldwork activity, the PPB technical team compiled an inventory of crucial reagents for the MiniLab kits to test the quality of medicines during field-based sampling and screening. A report of the inventory exercise informed procurement of the depleted MiniLab kit reagents and equipment. PQM+ is procuring these reagents, equipment, and stationery to support the RB-PMS activity planned for Q4. As part of cost-sharing, PPB will contribute to the activity by providing human resources, vehicles, and fuel for transporting staff and samples. In addition, PPB will offer its field offices to be used as the MiniLab screening sites. Finally, PQM+ assisted the PPB in adapting, domesticating, and harmonizing implementation of a regional cross-border PMS protocol for RMNCAH products, given PPB's role as the PMS lead agency for the Intergovernmental Authority on Development (IGAD).

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

Rationalizing fees for medicines quality testing: PQM+ supports the NQCL in analyzing costing of its medicines quality testing services to identify ways to make the laboratory financially sustainable. To this end, PQM+ initiated procurement of a consultant to perform this task. The process is ongoing, and the program anticipates having the consultant onboard in July. PQM+ met with the chief executive officer (CEO) of Kenya's National Health Insurance Fund (NHIF) to advocate for inclusion of the medical product QA framework in this publicly funded health coverage scheme in Kenya.

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

Local supply of essential medicines for childhood pneumonia: PQM+ collaborated with its regional partner, the Muhimbili University of Health and Allied Sciences (MUHAS), to coordinate a survey on the local supply of amoxicillin dispersible tablets (amoxicillin DT) in Kenya. The objective of the assessment is to identify local pharmaceutical manufacturers who can potentially increase the local supply of quality-assured amoxicillin DT in Kenya. Amoxicillin DT treats pneumonia in children. This is part of a wider assessment by PQM+ on identifying opportunities to scale up the local supply of quality-assured amoxicillin DT on the African continent. Data compilation is ongoing.

Furthermore, PQM+ is collaborating with the PPB to strengthen its regulatory capacity for overseeing GMP and promoting GMP compliance by local manufacturers. During the quarter, PQM+ contracted a consultant to ensure that local manufacturers are producing antimalarials and RMNCH products according to acceptable quality standards.

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

Analysis and synthesis of local data from previous PMS activities to inform policy: PQM+ supported PPB in early analysis of previous PMS data and review of PMS reports; the goal is to draft a manuscript for publication in a scientific journal. PQM+ had discussions with PPB and the NQCL staff and agreed on the indicators to analyze.

Priority Activities for Next Quarter

Next quarter, Kenya plans to:

- Help the DNMP disseminate and implement the QA framework for malaria commodities;
- Support the PPB in implementing a PMS survey based on the RB-PMS protocol developed for antimalarials and RMNCAH products;
- Assist the PPB in finalizing the online platform for self-directed learning;
- Strengthen the technical capacity of PPB and local pharmaceutical manufacturers in GMP to increase the supply of quality-assured antimalarial and RMNCAH commodities;
- Advocate for inclusion of a medical product QA framework in select health coverage schemes in Kenya;
- Analyze and synthesize local data from previous PMS activities to inform policy direction for QA of malaria and RMNCAH products; and
- Continue helping PPB integrate their PMS into the PV system to create a medicines safety and quality dashboard.

Liberia

PQM+ sustainably strengthens medical product quality assurance (QA) systems in 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).

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

This quarter, PQM+ coordinated with the Liberia Medicines and Health Products Regulatory Authority (LMHRA) to complete a five-year strategic plan. PQM+ technical support enabled the

LMHRA to perform its first dossier evaluation since 2017. In June, PQM+ also delivered hands-on dossier evaluation training to nine senior dossier assessors at LMHRA. As a result of PQM+'s technical assistance, LMHRA was able to assess a local pharmaceutical manufacturing plant. This quarter, PQM+ coordinated with LMHRA to validate guidelines for RB-PMS and sampling and testing protocols, and completed collection of antimalarial and MNCH medicines samples in Nimba, Lofa, Gbapolu, Sinoe, and Grand Geddeh.

Objective 1: Governance for medical product quality assurance systems improved.

PQM+ helped LMHRA complete a draft of a five-year strategic plan. On April 28 in Monrovia, LMHRA management and its board of directors, representing the Ministry of Health, School of Pharmacy, Ministry of Justice, Ministry of Commerce, and the Consumers Groups Association, validated the strategic plan. In May, PQM+ submitted the final copy of the strategic plan to LMHRA. In June, PQM+ conducted a human resources assessment at LMHRA, which included interviewing 15 employees, including the managing director. Results from this exercise will help LMHRA address its human resource capacity challenges.

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

Medicines' registration is one of LMHRA's key regulatory functions. As a result of PQM+'s technical assistance, in April and May, LMHRA conducted its first dossier evaluations since 2017; 40 dossiers from a backlog of more than 150 were evaluated. In June, PQM+ delivered a 10-day hands-on dossier evaluation training for nine LMHRA senior dossier assessors. The PQM+ activity manager at USAID's Liberia Mission visited the training site and issued certificates of achievement to participants.

The lack of a complete and effective QMS in the LMHRA QC lab is adversely affecting LMHRA's capacity to ensure that only safe medicines reach the Liberian people. In April, PQM+ reviewed the status of the lab's QMS documentation and agreed with LMHRA on a plan for document development. PQM+ also delivered a three-day ISO/IEC 17025:2017 QMS awareness training to 34 LMHRA employees in April. Participants included staff from LMHRA's administration, human resources, internal auditing, finance, and QC lab. This quarter, PQM+ inspected key equipment at the LMHRA lab and trained two staff in equipment preventive maintenance, then trained nine analysts on measurement uncertainty and internal auditing.

The supply of quality assured essential medical products is important to public health. This quarter, PQM+ helped LMHRA conduct a one-day gap analysis of Global Pharmaceutical's facility in Monrovia. PQM+ released the findings of the assessment to LMHRA. In addition to lauding PQM+'s report, LMHRA's managing director has said it will inform the agency's decision on Global Pharmaceutical's operation in Liberia.

In June, PQM+ coordinated with LMHRA to validate guidelines on RB-PMS and the sampling and testing protocol. The validation meeting was attended by 23 people from LMHRA, the Pharmacy Board, Ministry of Health disease control programs, and the Central Medical Store. PQM+ also trained 18 sample collectors from the national disease control programs and LMHRA. Later, sample collectors spent eight days collecting 303 antimalarial and MNCH medicines samples in Nimba, Lofa, Gbapolu, Sinoe, and Grand Geddeh.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Assist the LMHRA in resuming laboratory testing activities;
- Complete the drafting of regulations;
- Support the LMHRA in implementing regulatory actions based on the outcome of the PMS;
- Support the LMHRA in hosting a PMS results dissemination meeting;
- Continue supporting workforce development at LMHRA; and
- Conduct a stakeholder forum on the deployment of priority regulations.

Mali

Over the past decade, the Government of Mali has engaged in widespread institutional reform. In 2019, however, the *Cellule de Développement Institutionnelle* (Institutional Development Unit, or IDU) rejected regulatory provisions for the creation of a national pharmaceutical regulatory agency, as proposed by the Directorate of Pharmacy and Medicines (DPM). According to the IDU, the provisions needed major revision. The DPM has yet to submit a revised proposal and is working to mobilize national support for the initiative. DPM hopes to share case studies of successful precedents in francophone Africa to convince the IDU of the need to establish a national pharmaceutical regulatory agency.

In PY1, PQM+ Mali supported *Laboratoire National de la Santé* (LNS, the National Health Laboratory) and DPM in establishing a PMS-TWG. The TWG includes representatives from the LNS, DPM, disease programs, *Pharmacie Populaire du Mali* (Popular Pharmacy of Mali), and private wholesalers' association. This was to address the lack of coordination in PMS activities. The working group adapted the *Guidance for Implementing Risk-Based Post-Marketing Quality Surveillance in Low- and Middle-Income Countries* to the Mali context and developed a risk-based PMS protocol for antimalarial and MCH medicines.

PQM+ Mali also continued strengthening LNS's QC processes so the laboratory could achieve ISO/IEC 17025 accreditation. Thus, PQM+ implemented SATTA at LNS to help laboratory staff identify areas for improvement as they pursue accreditation and prequalification. PQM+ Mali trained staff on the techniques for its proposed accreditation scope in preparation for accreditation.

In PY2, PQM+ Mali is building the capacity of DPM's dossier evaluation committee to assess CTD dossiers, establishing a metrology team within LNS, and supporting implementation of PMS activities planned by the PMS-TWG.

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; and
- Increase financial resources for medical product QA optimization.

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+ reviewed the risk-based PMS report for the protocol implemented earlier this year. The results indicated that 69 percent of products sampled from four "at-risk" regions (Kayes, Sikasso, Koulikoro, and Segou) were unregistered, 4 percent of antimalarials did not conform to pharmacopeial specifications, and 2 percent of the MNCH molecules also did not conform to specifications. The nonconformity observed resulted from either a lack of active ingredients or substandard quantity.

A workshop to disseminate the results of this first risk-based approach to post-marketing surveillance adopted by Mali's LNS and DPM took place in Bamako at Azalai Salam Hotel. It was the fruit of months of technical assistance from PQM+ with USAID PMI and MCH funding and strong collaboration among various stakeholders who work to assure the quality of medicine in the country. The workshop opened with remarks from the technical advisor to the minister for health and social development, Dr Sekou Oumar Dembélé, representing the honorable minister. More than 40 participants from the Laboratoire National de la Santé (LNS), Direction de la Pharmacie et du Médicament, la Pharmacie Populaire du Mali, Inspection National de la Santé, Institut National de la Santé Public, health programs, and other technical and financial partners, such as United Nations Population Fund (UNFPA), Medicines, Technologies, and Pharmaceutical Services (MTaPS), and Procurement and Supply Management attended. Health sector stakeholders made strong recommendations for corrective and preventive regulatory actions, and the group delineated clear next steps and assigned responsibilities.

In Q3, PQM+ also supported the PMS-TWG in developing a second RB-PMS protocol for antimalaria and MCH medicines and helped identify and train three TWG members on training medicines samplers. These members will now serve as technical resources to train sample collectors before they go into the field for sampling. Further, the TWG reviewed and validated three SOPs for conducting risk-based PMS; their aim is to help the TWG sustain operations.

During the quarter, PQM+ in-country RSS consultants followed up closely with the laboratory on implementing the corrective action plan developed in Q2, providing weekly updates to the program's management and technical teams. A biweekly quality/management meeting was also instituted and chaired by the Director General of LNS to discuss quality issues and motivate personnel to support the drive to attain ISO/IEC 17025 accreditation. With support from PQM+, LNS identified qualified (ISO 17025-accredited) metrology service providers in the region and selected the vendor with the largest accreditation scope. The vendor was then recruited, with support from PQM+, to calibrate all equipment and measurement devices within the LNCM to solve a major gap in the laboratory's QMS. LNS management now has the actual cost of this service and all contact details of this vendor, whom they plan to include in their approved vendor's list. Also, to improve equipment management at LNCM, an equipment maintenance consultant provided technical assistance for equipment preventive and breakdown maintenance and worked with the internal metrology team to develop protocols for basic equipment preventive maintenance. This will foster sustainability, and this metrology team will have the capacity to conduct preventive maintenance of basic equipment.

To improve the capacity of the DPM to evaluate technical dossiers, PQM+ RSS experts worked with IntraHealth and DPM focal points to design a CTD dossier evaluation training curriculum to address the specific needs of the DPM identified by a training needs assessment.

To improve the motivation of LNS personnel and possibly reduce high staff turnover, IntraHealth used a local consultant to work through a series of workshops at LNS's premises and develop performance management SOPs and staff development plans. These SOPs and development plans will be implemented in 2021 and PQM+ will closely monitor their impact on staff motivation.

Next quarter, PQM+ plans to:

- Supervise sampling for 2021 risk-based PMS activity;
- Supervise testing of samples;
- Conduct dossier evaluation training (implementation of dossier evaluation curriculum developed);
- Provide technical assistance to LNS to review its testing/analysis cost; and
- Support LNS and DPM in developing a framework for collaboration.

Mozambique

Mozambique established its National Directorate of Pharmacy (DNF) in 2017 as a transitional organization; the goal is to become an autonomous National Medicines Regulatory Authority (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 DNF to attain Maturity Level 3 in the WHO GBT program and ISO/IEC 9001:2015 accreditation.

In PY2, PQM+ is working 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.

In Q1, PQM+ reviewed and provided commentary to the DCQ on the existing regulation for the medicines quality control laboratory, which is now obsolete. In Q3, PQM+ continued following up for feedback from DCQ in the quest to develop an updated, robust regulation for DCQ that will support and facilitate its implementation of Good Laboratory Practices.

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

A major activity on the updated ISO 17025 accreditation roadmap is for PQM+ to assist DCQ to develop, revise, and update key QMS documents. To achieve this milestone, PQM+ has started helping DCQ evaluate both the status of its QMS documents and CAPAs raised after the last audit and revise the quality risk management SOP.

DCQ, the national quality control lab of Mozambique, requires internet connection to communicate with its customers and access essential information available online for its operation, as well as technical support from PQM+ during COVID-19. This quarter, PQM+ procured and installed high-quality internet bandwidth for the lab.

The availability of supplies and reagents is pivotal to DCQ's operation. PQM+ continues to support procurement of key reagents and supplies for DCQ. This quarter, the first set of procured proficiency test samples was delivered to the lab. DCQ received two U.S. Pharmacopeia (USP-NF 2021) hard copy references with PQM+ support. These important pharmaceutical reference books are vital for the quality control laboratory to accurately and consistently test the quality of essential medicines used in MNCH and other priority public health programs in Mozambique. To ensure that DCQ's laboratory equipment is qualified and functional, PQM+ completed the procurement process for external vendors to provide equipment calibration or performance verification services. However, ongoing COVID-19 travel restriction is causing delays in obtaining an invitation letter.

To build capacity of the DNF Department of Evaluation of Medicines, Vaccines, and Biological Health Products on dossier evaluation of medical devices, PQM+ is designing and developing a course curriculum for evaluation of dossiers on condoms. Weekly meetings are ongoing, as is interaction with DNF's Evaluation Department for information exchange.

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

This quarter, PQM+ spoke with lab officials and staff about the need for DCQ to generate revenue to enable procurement of supplies and services required for its operation.

Priority Activities for Next Quarter

Next quarter, PQM+ Mozambique plans to:

- Calibrate DCQ's lab equipment and performance qualification of instruments using an external vendor, and
- Help with DCQ's participation in proficiency testing for selected test methods under the proposed scope of accreditation.

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 is a serious problem in Nigeria. Malaria remains the country's leading public health problem, disproportionately affecting children younger than 5

years and pregnant women. Furthermore, Nigeria has a high incidence of communicable and non-communicable diseases.

PQM+ is focused on helping ensure the quality of medicines and other medical products with an emphasis on USAID and Government of Nigeria priorities, namely, malaria and MNCH medicines and family planning commodities. PQM+ collaborates with stakeholders in the public and private sectors to increase local pharmaceutical manufacturing capacity and sustainably strengthen regulatory systems at the national and state levels. PQM+ also strengthens quality management systems (QMS) and builds laboratory capacity in quality control testing in compliance with international 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;
- Optimize and increase financial resources for medical product quality assurance; and
- Increase the 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.

PQM+ collaborated with the Pharmacists Council of Nigeria (PCN) to implement activities from the action plans to strengthen state-level regulatory and quality assurance systems. The target beneficiaries are for-profit retail outlets (community pharmacies [CPs] and proprietary patent medicine vendors [PPMVs]) involved in the sale of medicines and consumables and provision of essential primary health care services. PQM+ implemented the following activities:

- Capacity building sessions on communication and people management for members of the pharmaceutical inspection committees (PICs) in the three states (Sokoto, Ebonyi, and Bauchi). The sessions sought to improve the relationship between PICs and operators of retail outlets to improve the latter's registration with PCN.
- Capacity building sessions on QA topics and good practices in supply chain management for registered CPs and PPMVs in the three states. In addition to helping improve the quality of care and availability of medical products at these outlets, the sessions provided incentives for unregistered outlets to benefit from future workshops by registering with PCN.
- Content development for job aids (infographic guidelines on sourcing, procurement, storage, etc.) on medical products for CPs and PMSs. This was done to further assure the quality of medical products at outlets.

PQM+ conducted a gap assessment of PCN headquarters using the ISO 9001:2015 checklist in continued efforts to institutionalize a QMS at the council. The report from the gap assessment led to development of an ISO 9001:2015 roadmap for the council. This assessment will help the PCN address actions recommended in their institutional development plan (IDP) and facilitate the joint attainment of the desired Maturity Level 3 with the National Agency for Food Drug Administration and Control (NAFDAC).

The gap assessment identified 72 nonconformities (19 major, 33 minor, and 20 observations) at PCN. PQM+ subsequently conducted a capacity building workshop to help close the immediate knowledge gaps identified and to assist PCN in addressing the 29 CAPA issues arising from a previous WHO GBT assessment conducted in conjunction with NAFDAC.

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

PQM+ assisted manufacturers of malaria and MNCH medical products in compiling medical product dossiers and upgrading production facilities. A summary of the tasks, by manufacturer, completed in Q3 include:

Swipha – Commenced the review of the dossier for zinc sulfate 20mg dispersible tablets in preparation for pre-submission to the WHO prequalification team.

Emzor – Prepared the technical team for NAFDAC's advisory inspection of its ready-to-use therapeutic food (RUTF). This included reviewing the QMS document for the RUTF plant.

Emzor – Reviewed the validation report on the upgrade of the heating, ventilation, and air conditioning (HVAC) system of Emzor's upgraded beta lactam plant to produce amoxicillin (125 & 250) mg dispersible tablets. The upgrade is due to high humidity levels at the plant which could impact the quality of the moisture-sensitive active pharmaceutical ingredient (API).

Emzor – Reviewed the API section of the sulfadoxine + pyrimethamine SP (500+25) mg tablet dossier as part of the ongoing compilation for submission to WHO's PQ team. PQM+ also followed up with the contracted research organization on the progress of the bioequivalence study of the product. The Jordan-based research organization has obtained approval from the institutional review board of the Jordanian Food and Drug Administration Authority to commence the study.

Juhel – Magnesium sulfate 50%w/v injection – PQM+ helped the manufacturer address additional product data related to the primary product's packaging, adhesive for the product label, and ink migration from label to product. As result of QMS strengthening, Juhel supplied 84,000 does of oxytocin injection to the Bauchi state government for its Drug Revolving Fund (DRF) scheme.

Capacity Building – PQM+ conducted online workshops on data integrity in pharmaceutical manufacturing and good practices for pharmaceutical quality control laboratories for professionals in the pharmaceutical industry. About 200 participants attended the workshops.

Priority Activities for Next Quarter

Next quarter, PQM+ Nigeria plans to:

- Finalize and print the job aids for CPs and PPMVs;
- Help PCN conduct a zonal inspectors' workshop to discuss gaps in the quality assurance and regulatory systems with the intent of improving these systems;
- Provide technical assistance to Juhel to address observations from the WHO PQ team on its magnesium sulfate 50%m/v injection labels;

- Review and monitor progress on product data for compilation of product dossier for oxytocin 10iu/1mL injection;
- Finalize the review of Swipha's zinc sulfate 20 mg dispersible tablet dossier for submission to WHO PQ;
- Provide technical support to Emzor on its compilation of the SP dossier, production of scale-up batches of artemether lumefantrine (20/120) mg with API from a WHO PQ manufacturer, and commence dossier compilation for the AL; and
- Conclude the pharmaceutical manufacturing sector stakeholder survey and update the GMP roadmap report with inputs from stakeholders.

Senegal

The Government of Senegal has developed a five-year (2019–2023) integrated strategic plan for the DPM and the *Laboratoire National de Contrôle des Medicament* (LNCM, the National Medicines Control Laboratory). 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 of the DPM and LNCM. These 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, "Establish an appropriate institutional framework for the optimal implementation of pharmaceutical regulatory and control functions," and the third, "Evaluate and control the quality of drugs." PQM+ is also addressing two sub-objectives 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, LNCM, 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 for RB-PMS for antimalarial medicines using the MedRS tool. During PY2, PQM+ continues to build on this progress.

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.

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+ reviewed the report for the first risk-based PMS implemented in Senegal. The results show that 2 percent of the molecules (artemether/lumefantrine, artesunate, sulfadoxine/ pyrimethamine and sulfadoxine/ pyrimethamine/ amodiaquine) sampled from five regions—Dakar, Kolda, Djourbel, Kaolack, Kedougou, and Tambacounda—did not conform to specifications. In addition, PQM+ assisted the national PMS Unit in reviewing and validating five

SOPs for conducting risk-based PMS. The SOPs are designed to foster sustainability of the PMS Unit by enabling unit staff to carry out key functions with minimum assistance from PQM+.

During the quarter, with support from PQM+, LNCM identified qualified (ISO 17025-accredited) metrology service providers in the region and selected the vendor with the largest accreditation scope. The vendor was then recruited, with support from PQM+, to calibrate all equipment and measurement devices within the LNCM to solve a major gap in the laboratory's QMS. To improve equipment management at LNCM, an equipment maintenance consultant (based in Dakar) provided technical assistance for equipment preventive and breakdown maintenance and worked with the internal metrology team to develop protocols for preventive maintenance of basic equipment.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Participate in the workshop to disseminate results from PMS antimalaria samples collected in 2020, and
- Build the capacity of LNCM in key advanced quality management system elements: measurement uncertainty and analytical method validation.

Asia Region

Asia Bureau

PQM+'s technical assistance funded by USAID's Asia Bureau aims to promote regional regulatory convergence and reliance. PQM+ is working 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 plan builds on support provided through the PQM program and leverages current PQM+ work in Southeast and Central Asia.

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

The Asia Bureau work builds on harnessing regional collaboration, often managed by the regional economic communities' medicines regulatory harmonization (MRH) efforts. This quarter, PQM+ followed up with members from SEARN to inquire about PQM+ participation in the network's annual meetings to introduce the PQM+ program as well as Asia Bureau activities. SEARN is finalizing the date and agenda and confirming if the meeting will be virtual or in-person, in light of COVID-19 breakouts in Asia. PQM+ continues to engage USP India in coordination with SEARN.

After receiving formal feedback from the ASEAN PPWG on the concept note regarding areas of potential support that PQM+ and MTaPS jointly proposed last November through the ASEAN Secretariat and USAID's Asia Bureau, PQM+ has been revising its technical assistance areas to reflect the priorities that PPWG requested.

PQM+ signed the subaward agreement with Mahidol University in Thailand to conduct a regulatory landscape analysis of the medical product quality assurance system for SEARN and ASEAN member countries. The survey questionnaire is under internal review board review before finalization and beginning data collection. PQM+ has provided country contacts in SEARN and ASEAN to Mahidol and has reached out to the university to introduce the project activity and request support for and participation in the landscape analysis.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Continue the landscape analysis of medical products quality assurance systems for SEARN and ASEAN member countries;
- Collaborate with SEARN (ASEAN) to strengthen PMS systems and improve reliance and information sharing for GMP inspections; and
- Collaborate with MTaPS to finalize key technical areas of support to ASEAN PPWG.

Bangladesh

In Q3, PQM+ focused on implementing activities under four of five program objectives in the PY2 approved work plan and on 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 systems focusing on vaccines; and manufacturers to increase production of quality-assured first-line anti-TB medicines.

In PY2, PQM+ in Bangladesh 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 and optimize financial resources for medical product quality assurance;
- Increase the supply of quality-assured essential medical products of health importance; and
- Advance the global medical product quality assurance learning and operational agenda.

Objective 1: Governance for medical product quality assurance systems improved.

Activity 1.1: Support the institutionalization of good governance practices related to transparency, accountability, and stakeholders' communications at DGDA: The annual performance report is one of the DGDA's best channels to ensure transparency and accountability for dissemination of regulatory activities. In Q3, PQM+ provided support to DGDA to develop its 2019-2020 annual report, incorporating key achievements of DGDA and NCL that PQM+ supported, along with the forecast for each of the functional activities. PQM+ provided guidance to the report development committee to acquire information and data that reflects DGDA's overall performance throughout the year. In June, PQM+ supported DGDA to publish the report, which initiated the process of information dissemination with stakeholders and the public. This report will help DGDA ensure accountability and transparency in providing quality-assured services, regulations, and enforcement activities throughout a medicine's lifecycle, starting from production through patient intake. To sustain this reporting system, PQM+ started working with the committee to develop an SOP including terms of reference for institutionalizing the reporting system as a routine process.

Annual report handover to DG and DGDA by PQM+ representatives.

Activity 1.2: Evaluate the feasibility and capacity of private laboratories to provide quality testing services of MNCH, TB, and FP medical products, including vaccines to the DGDA: On June 16, the PQM+ team visited the Independent University Bangladesh (IUB) Plasma Plus Research and Testing Laboratory (PPL) to gain an idea of services the lab is offering and the feasibility of providing services as a third-party laboratory for DGDA's NCL. The visit covered the quality system, materials management, the equipment and facilities system, and the laboratory system overall. The team also gathered information about the present organogram, staff competency, and budgetary provisions. The IUB lab has filled out and returned a questionnaire that PQM+ sent after the visit.

PQM+ visited the IUB Plasma Plus lab in June.

The PQM+ team has observed the IUB facility, trained staff, assessed the availability

and number of equipment, the quality manual, laboratory safety policy, emergency eye wash station, emergency shower, and emergency exit plan in place. A gap assessment can identify opportunities for improvement and develop a roadmap for standardization.

The PQM+ visiting team recommends supporting the IUB PPL as a third-party lab in Bangladesh toward achieving international standardization (WHO-PQ, ISO/IEC-ANAB, etc.).

Activity 1.3: Support DGDA to establish Good Review Practice (GRP) to improve and ensure consistency, transparency, timeliness, and process predictability in the regulatory review process: The major function of DGDA is to conduct registration and marketing authorization (MA) of medical products, including active pharmaceutical ingredients (APIs), medicines, vaccines, biologicals, medical devices, and diagnostics. DGDA is increasingly seeking ways to improve its performance and ensure the quality of its regulatory systems. GRPs are an integral part of overall good regulatory practices and focus on the medical product review aspect of regulatory work.

Medical product review is a highly complex, multidisciplinary assessment of the medical product applications to ensure that they meet the scientific and evidentiary standards for safety, efficacy, and quality. It forms the scientific foundation for regulatory decisions. Implementation of GRPs helps achieve these outcomes by ensuring that those involved in the review process have the critical thinking skills and tools needed to optimize scientifically sound, evidence-based decisions. It also facilitates progress toward regulatory convergence through the exchange of review reports and the enhancement of mutual understanding among regulatory authorities. For strengthening the registration and MA function of DGDA, PQM+ provided extensive technical support to develop standard procedures, guidelines, manuals, protocols, checklists, and more. With PQM+ technical support, DGDA developed the following SOPs for MA functions:

1. Procedure for registration of pharmaceutical products (SOP: NRA-MA-001)
2. Procedure for marketing authorization of drug products (SOP: NRA-MA-002)
3. Procedure for management of post-marketing authorization variations (SOP: NRA-MA-003)
4. Procedure for renewal of product registration (SOP: NRA-MA-004)
5. Procedure for regular updating of registered product list along with Summary of Product Characteristics (SPC) (SOP: NRA-MA-005)
6. Procedure for marketing authorization review activities by advisory or scientific committee (SOP: NRA-MA-006)
7. Procedure to withhold, suspend, withdraw, or cancel a registration/ marketing authorization in the event of an adverse finding related to quality, safety, and efficacy of medical products (SOP: NRA-MA-007)
8. Standard procedure for renewal of marketing authorization (MA) (SOP: NRA-MA-008)
9. SOP of internal tracking system for product registration procedure (SOP: NRA-MA-009)
10. Procedure for issuance of no-objection certificate (NOC) in case of need in the interest of public health (SOP: NRA-MA-010)
11. SOP for the procedure of fast-track evaluation and issuing emergency use authorization (EUA) for imported COVID-19 vaccine (SOP: NRA-MA-011)

12. Procedure of dossier evaluation for vaccine and biological product registration (SOP: NRA-MA-012)
13. Procedure for registration of vaccine and biological products (SOP: NRA-MA-013)
14. SOP on training effectiveness evaluation (SOP: NRA-MA-014)
15. SOP on donation of vaccine and other pharmaceutical products (SOP: NRA-MA-015)
16. Procedure for acceptance of certificate of analysis or lot release certificate of foreign vaccine products from foreign NCL/NRA (SOP: NRA-MA-016)
17. Procedure for renewal of marketing authorization of vaccine and biosimilar products (SOP: NRA-MA-017)
18. Procedure for the evaluation of summary product characteristics (SOP: NRA-MA-018)
19. Procedure for monitoring, maintaining, and updating database (SOP: NRA-MA-019)

PQM+ provided training on SOP NRA-RS-002 to the DGDA inspectors.

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

Activity 2.1.1. Continue support to DGDA for attaining WHO Maturity Level 3 of its market surveillance and control, laboratory testing, lot release, clinical trial, and marketing authorization: Regulators are an essential part of the health workforce, and effective regulatory systems are an essential component of health systems that contribute to better public health outcomes. Inefficient regulatory systems can be a barrier to accessing safe, effective, and quality medical products. The DGDA is the only regulatory authority responsible for controlling the quality, safety, and efficacy of medicines in Bangladesh. DGDA, with technical support from WHO and other development partners, has established a coalition of interested partners (CIP), and the taskforce aims to coordinate activities with partners supporting regulatory strengthening efforts for medical products. A roadmap was prepared in March 2016, followed by an institutional development plan (IDP) that is continuously updated according to the WHO GBT and emerging needs. Since then, DGDA has made remarkable progress, including several self-assessments using the WHO GBT. The Drug Testing Laboratory (DTL) /National Control Laboratory (NCL) achieved Bangladesh Accreditation Board (BAB) Accreditation (DTL) in 2017, ISO 17025 accreditation 2018, and WHO PQ in 2020.

Benchmarking, a method of identifying and importing best practices to improve performance in line with quality, includes the process of learning, adapting, and measuring outstanding practices and processes from any organization to improve performance. Under regulatory systems strengthening (RSS), DGDA has conducted three self-assessments and one interim assessment and made remarkable progress that includes development of several SOPs, guidelines, manuals, plans, frameworks, matrices, and more. WHO GBT is an instrument for self-assessment, internal audit, and formal assessment and benchmarking. Using the GBT, PQM+ has continuously supported DGDA to monitor its progress and update the 206 IDP recommendations. These 206 IDP recommendations came from the interim assessment of WHO HQ and self-assessment of DGDA using WHO GBT, which has nine specific functions, 62 indicators, and 268 sub-indicators. For Maturity Level 3, DGDA needs to comply with a minimum of 210 sub-indicators; 58 sub-indicators are under Maturity Level 4. At present, DGDA is moving forward to achieve Maturity Level 3 for the vaccine scope only.

In line with updating the IDP, PQM+ has supported a gap analysis, development of documents, and compliance with observations. DGDA is using a systematic approach to comply with all 210 sub-indicators under Maturity Levels 1-3. The directorate has a well-established legal framework, albeit with some gaps following previous acts and rules. DGDA arranged a gazette notice, policies, and guidelines to comply with all legislative requirements. PQM+ provided technical support for a legislative gap analysis, regulatory gap analysis, input to the new drug act, development of the official notification and gazette placement, development of guidelines, SOP, manuals, procedures, protocols, a record log, registrars, checklists, forms, presentations, and reports. The program also provided technical support for training plan development, monitoring, and evaluation, as well as abundant training during the quarter, including a training evaluation to update the compliance level following the IDP. PQM+ fully supported DGDA to conduct an internal audit, a mock-audit, and a self-assessment and extended technical support for national regulatory authority (NRA) input, assessor input, IDP update, evidence documents generation, evidence documents uploading into SharePoint, and linking with the GBT tool.

Following the latest self-assessment, the compliance level is 100 percent for all functions and DGDA is now ready for formal assessment. This assessment is targeted to vaccine scope only. Table 1 summarizes compliance levels.

Table 1: DGDA Compliance Levels

Sl. No.	Name of Function	Sub-Indicator % Met from Interim Assessment, September 2018	Sub-Indicator % Met from Self-Assessment, June 2021
01	National Regulatory System (RS)	88%	100%
02	Registration and Marketing Authorization (MA)	91%	100%
03	Vigilance (VL)	75%	100%
04	Market Surveillance and Control (MC)	89%	100%
05	Licensing Premises (LI)	66%	100%
06	Regulatory Inspection (RI)	63%	100%
07	Laboratory Access and Testing (LT)	82%	100%
08	Clinical Trial Oversight (CT)	74%	100%
09	NRA Lot Release (LR)	58%	100%

PQM+ is providing continuous technical support in the following ten areas to comply with all requirements for WHO Maturity Level 3:

1. Legal provisions, regulations, and guidelines (Complied)
2. Organizational structure and good governance (Complied)
3. Strategic plan, objectives, and procedures (Complied)
4. Leadership and crisis management (Complied)
5. Quality management systems (Complied)
6. Sustainable human resources (Complied)
7. Sustainable financial resources (Complied)
8. Infrastructure (Complied)
9. Transparency, accountability, and communication (Complied)
10. Monitoring and evaluation of regulatory performance and output (Complied)

PQM+ is now leading the support to all nine DGDA functions for strengthening national regulatory system for medical products, including vaccines, biologicals, medical devices, and in-vitro diagnostics. DGDA is moving forward to achieve Maturity Level 3. To accomplish this goal, DGDA will undergo WHO formal assessment in July. DGDA officials and staff are fully engaged to update their legal provisions, regulations, guidelines, protocols, manuals, working procedures forms, checklists, and records to generate evidence for the formal audit. PQM+ is now fully engaged on a daily basis. DGDA officials and staff have received PQM+-supported training on updating the WHO GBT. DGDA is ready to receive observations and indications of further action needed and will make plan to comply within the stipulated time. Afterward, DGDA will comply with all actions in the CAPA plan. Now DGDA is fully optimistic about achieving Maturity Level 3 in terms of vaccine regulation.

To accomplish WHO ML3 of DGDA, PQM+ supported development of the following key documents focusing on regulatory, QMS, and QA/QC.

Table 2: Documents Developed with PQM+ Support

Functional Areas	Documents (Regulatory & QMS)
Regulatory Inspection (RI)	• SOP: Procedure for Inspection Planning Based on Quality Risk Management (NRA-RI-14) • SOP: Conducting GXP inspection with performance monitoring (NRA-RI-15) • SOP: Procedure for Competency Assessment of DGDA Inspectors (NRA-RI-16) • Functional organogram of RI department • Flow chart of GMP Inspection Process • Flow chart of Good Distribution Practice (GDP) of wholesale depot & retail drug shop inspection process • Updated six job descriptions of the RI team members. • Developed Inspection Plan based on Quality Risk Assessment (QRM) regarding vaccines and biologics.
Market Surveillance and Control (MC)	• Yearly Plan for Risk-based Sampling-2021 for generic medicines. • Yearly Plan for vaccines sampling-2021. • Updated four job descriptions of the MC team members • Minilab™ reports register

Functional Areas	Documents (Regulatory & QMS)
National Regulatory System (RS)	• QMS action plan 2021 • Functional organogram of QMS department • Updated five job descriptions of the QMS team members • Process flow of PMS

Table 3: Training Conducted in Q3

Topics	Number of Participants
Internal audit	5 (3 M, 2 F)
CAPA management	5 (3M, 2 F)

Areas for further improvement and development:

- Improve the National Regulatory Framework and develop regulatory framework documents.
- Develop and/or improve a risk-management plan for regulatory action.
- Improve the monitoring and evaluation (M&E) framework, implementation, and output measurement.
- Develop a competency framework and competency matrix.
- Continuously improve QMS and information management systems (IMS) to ensure sustainable implementation of regulatory activities.
- Develop risk-based regulatory inspection planning, conducting, monitoring, and reporting.
- Develop and/or improve good governance system.
- Improve good review practice.
- Improve transparency, accountability, reproducibility, and monitoring.
- Improve the IT-based database/platform/software for HR, products and service management, asset management, records management, process implementation, monitoring, etc.
- Secure approval of the Drug Act 2021.
- Improve human resource mobilization and optimization through an online application and evaluation system (to minimize workload).

Activity 2.1.6. Facilitate the implementation of RB-PMS: In Q3, PQM+ continued to support DGDA and NCL to improve their capacity to implement effective RB-PMS. Following are the key accomplishments this quarter.

- To sustain effective RB-PMS, DGDA established a functional committee for coordination, planning, and follow-up to the surveillance activities. In April, a seven-member RB-PMS committee formed, headed by DGDA's director of the Market Surveillance and Control Department, with clear TORs set forth.

- On the same day, DGDA sent an official notification to all headquarters and field officials with clear instructions and guidance to conduct sampling and testing of selected samples and send a report to the committee members. The notification assigned two committee members to continuously follow up on the implementation.

MiniLab™ demonstration at the drug administration office in Chattogram

- In May, at its first meeting, the RB-PMS committee developed a yearly plan of RB-PMS sampling. Based on the plan, field inspectors performed sampling and testing of five medicines: azithromycin, moxifloxacin, dexamethasone, doxycycline, and metronidazole during May. Including a few other medicines, field inspectors tested 94 total samples at MiniLab™ sites. Among the samples, two (one omeprazole and one azithromycin) were found suspicious and are undergoing NCL confirmatory testing. Another five samples—cefuroxime, cetirizine HCL, fluconazole, ciprofloxacin, and cefixime—are under surveillance for June.
- This quarter, the PMS unit started vaccine sampling and testing, with seven samples withdrawn from the market. After conducting a visual inspection, the field inspectors sent samples to the NCL vaccine lab for confirmatory testing. PQM+ assisted DGDA and NCL with the testing. Among the samples, two have already undergone testing and passed. The other four are still under confirmatory testing at the vaccine lab.

Activity 2.2.2. Provide technical assistance to NCL to increase the vaccine laboratory's capacity for testing: To achieve Maturity Level 3 and as part of capacity building for NCL's vaccine laboratory, PQM+ provided guidance and training to improve the staff's competency on the following topics.

- Provided hands-on training on vaccine testing to the vaccine lab analysts.
- Provided support on laboratory access and testing (LT) and NRA lot release (LR) functions to prepare and review SOPs/documents/job descriptions/ analytical methods, etc., per GBT to achieve Maturity Level 3.
- Conducted two mock audits on laboratory testing and NRA lot release function to identify gaps and helped prepare SOPs/documents based on the assessment.

PQM+ assisted vaccine analysts to perform vaccine testing using ELISA on April 6.

- Gave hands-on training to new staff of the vaccine lab on: Good Laboratory Practice, Good Documentation Practice, the quality manual, quality policy, internal auditing, etc.
- Assisted with preparing job descriptions.

- Reviewed the standard testing procedures (STPs) and specifications of vaccine chemical tests and prepared the list of test parameters they can perform in their laboratory.
- Helped vaccine lab analysts prepare a trend card using the test result of vaccines.
- Assisted vaccine lab analysts to prepare protocol analytical method validation of the meningococcal vaccine. Guided them in analysis and generation of the validation report after completion of analysis.
- Assisted vaccine lab to maintain calibration and qualification status and prepare calibration report.
- Assisted vaccine lab staff to implement equipment maintenance recordkeeping system and provided training on how to maintain this system.
- Helped vaccine lab prepare third-party laboratory audit report to test some parameters of vaccines using their laboratory facility.
- Reviewed SOPs for the internal audit, CAPA, document control, calibration, qualification, procedure for operation of water distiller, communication with stakeholder etc., and assisted with preparing a training needs assessment of vaccine staff.
- Assisted with the system suitability for sterility test (draft stage).
- Assisted with installation of the chemical storage cabinet in the vaccine laboratory.
- Assisted with closing WHO CAPA, which has remained open as long-term action.

Activity 2.2.3. Continue support to increase the capacity for compendial testing of priority medicines (e.g., TB, MNCH, FP) in the NCL: PQM+ assisted NCL to expand its testing scopes for the next ANSI National Accreditation Board (ANAB) re-audit, as well as strengthen its capacity for a new testing area and sustain its achievements against international standards. This quarter, PQM+ assisted NCL to arrange the PTs from the provider on time and helped the physicochemical lab's staff analyze the PT samples within the scheduled time.

PQM+ assisted NCL analysts to perform four proficiency tests (PTs): gas chromatography, acid/base titration as new scope expansion, dissolution, basic chemical testing (density, refractive index, melting point, acid/base titration) as new PT, and UV-VIS spectroscopy as reschedule, per NCL's PT plan.

PQM+ provided guidance and assistance on the following activities:

- Assisted with review of the SOP for procedure of deviation/incident, chemical reagent management SOP.
- Supported testing PMS samples in the physicochemical laboratory.
- Assisted the physicochemical lab's staff to test the PT sample from the External Quality Assurance Assessment Scheme at WHO to show its commitment to performance maintenance and improvement.
- Helped NCL to raise change request form for new equipment and electronic data storage center.
- Assisted with the review of the calibration and qualification SOPs and compilation of the status report.

Activity 2.2.4. Provide support to DGDA to assess the progress on previous gap assessment report on Chattogram Drug Testing Laboratory (CDTL) and to prepare a roadmap for addressing the remaining gaps: Director General Rahman chaired a March consultative meeting in the CDTL's meeting room. All CDTL staff, senior DGDA officials, the director of the Maa-o-Shishu Hospital, and the PQM+ team attended. Meeting participants agreed to prepare a roadmap/strategic plan for the lab to achieve ISO 17025:2017 accreditation or WHO PQ as the deputy lab of NCL Dhaka. In April, PQM+ supported DGDA to develop a "Roadmap 2025" with the goal of "full functioning of CDTL as a modern regional drug testing laboratory to achieve ISO 17025 accreditation or WHO PQ by 2025." The roadmap focuses on the following key decisions:

- The Chattogram Drug Administration Office will receive at least 30 samples per month for testing at CDTL.
- The NCL deputy chief in Dhaka will arrange quarterly visits to CDTL in collaboration with PQM+ to plan testing of RB-PMS samples and support lab functioning.
- Procurement of equipment for CDTL is in process by the Central Medical Stores Depot (CMSD). CDTL needs to complete proper electric connection and other required arrangements for this equipment. Mapping for installation space also needs to occur as soon as possible.

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

Activity 3.1: Support NCL to adopt an in-house costing tool and prepare a proposal for the Ministry of Health and Family Welfare (MoHFW) to rationalize fees for medicines quality testing: PQM+ worked with NCL to prepare a cost analysis report so that lab management can periodically review and rationalize the testing fee rate and submit a proposal to the MoHFW through DGDA to revise testing fees. This will help NCL sustain achieved international standards and ensure continued smooth operations to certify safe medicinal products.

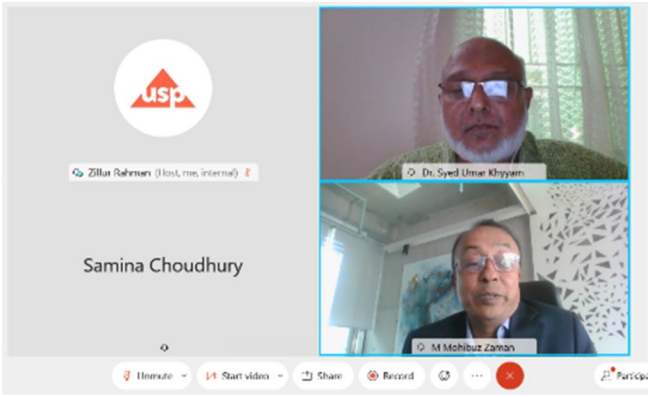
Objective 4: Supply of quality-assured essential medical products of health importance increased.

Activity 4.1: Continue to provide technical support to a local manufacturer of priority first-line TB medicines to progress toward achieving WHO PQ: In Q3, PQM+ experts continued providing technical guidance and recommendations to ACI Pharmaceutical in its manufacture of quality-assured, first-line, fixed-dose combination anti-TB medicines. In May, PQM+ organized an online technical discussion session with ACI technical staff involved in the TB project. PQM+ GMP experts attended the session to answer technical questions from ACI colleagues about producing bio-batches. PQM+ inform ACI that PQM+ is willing to conduct remote inspection using the Avatour tool. ACI agreed to remote inspection. In June, PQM+ Bangladesh received the Avatour tool from PQM+ headquarters. PQM+ Bangladesh staff will

conduct a GMP inspection at ACI's new site in July to confirm its readiness and compliance to WHO GMP standards.

Avatour remote inspection tool onboarding

In April, PQM+ arranged a meeting between USAID, PQM+, and ACI. The meeting focused on ACI's progress and USAID's future support to ACI. The chief executive officer (CEO) of ACI described the progression of the TB medicine bioequivalence (BE) batch production and clinical research organizations (CROs) bioavailability / bioequivalence (BA/BE) study process. The CEO stated that production of the BE batch of anti-TB medicine will occur in June for submission to the CRO for BE study. They also expected support from USAID; Dr. Samina Chowdhury is willing to provide the support and plans to visit the ACI site, along with the Mission director.



PQM+ arranged a coordination meeting in April between USAID, ACI, and PQM+

On April 26, PQM+ conducted an online technical discussion session with ACI technical staff focusing on GMP compliance for APIs and FPPs toward BE batches production and discussed on the planned inspection to ACI new facility that develop the BE batches. In total, 15 participants joined the technical session from ACI and PQM+.

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

Collaborative training program with PQM+, USP, and Bangladesh Aushad Shilpa Samity (BAPI): On June 7, PQM+ met with the Bangladesh CEO, Aushad Shilpa Samity, at BAPI's office to collaborate on an online GMP training program between PQM+, USP Education, and BAPI. The GMP training program will ensure medical and API product quality.

As the CEO of BAPI showed tremendous interest, PQM+ will arrange an online meeting with the existing interested and potential owner of an API manufacturer in Bangladesh. BAPI will dedicate its conference hall for the online and offline meetings for participants. The follow-up discussions will help BAPI and USP create a long-term memorandum of understanding to start selected training programs for the target participants, as proposed and desired by BAPI Secretary General Mr. Md. Shafiuzzaman during the visit of USP Senior Vice President Emily Kaine in 2019.

Priority Activities for Next Quarter

In Q4 of PY2, PQM+ will continue efforts to accomplish remaining activities, including the following:

- Organize a dissemination workshop for National Quality Assurance Guideline (NQAG) in Dhaka either onsite or online involving all relevant stakeholders;
- Conduct a gap analysis on Good Review Practices (GRP) of DGDA and develop an action plan based on the analysis;
- Continue support to DGDA's nine functions to achieve WHO GBT Maturity Level 3;
- Organize a training on the MedRS tool for DGDA staff;
- Conduct GMP inspection of ACI's new facility and develop CAPA plan;
- Support vaccine lab to conduct analyst validation of its staff; and
- Provide support to vaccine lab to perform measurement uncertainty of equipment and reagent stability.

Burma

PQM+ in Burma is working to build the capacity of the country'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 a focus on antimalarials, and thereby contribute to the National Malaria Control Program's effort to eliminate malaria by 2030.

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.

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 Q3, PQM+ provided technical assistance to DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory (PCL) to resume its QMS functions and maintain a stable output of medicine quality testing. By the end of June, the Ministry of Health and Sports (MOHS) and DFDA had dismissed at least 20 deputy and assistant directors and 125 officers who joined the civil disobedience movement following the country's military coup. Quality assurance (QA) team members and trained analysts from the Nay Pyi Taw PCL were among the dismissed staff.

PQM+ assisted DFDA in the formation of the new QA team from the existing staff, while DFDA transferred trained analysts from the Yangon PCL and Nay Pyi Taw bio-standardization laboratory to Nay Pyi Taw PCL. Currently, Nay Pyi Taw PCL is operating with 15 staff, down from its original 33. PQM+ also assisted DFDA in recovering electronic documents from the document control system and enabled the laboratory to produce and record analytical data systematically.

To build the new QA team's capacity, PQM+ plans to organize a workshop on the QMS. PQM+ began preparations for workshop in April and engaged with IntraHealth to design a system to deliver the coursework in a remote setting. The QMS workshop will help the new QA team better understand the ISO 17025:2017 standards and internal audit procedures so they will be ready for the ANAB's annual surveillance, which is due in September 2021.

PQM+ is also engaged with IntraHealth and USP Ghana to produce materials for the metrology training, which PQM+ expects to deliver in the first quarter of Program Year 3.

Priority Activities for Next Quarter

Next quarter, PQM+ Burma plans to:

- Organize a QMS workshop at Nay Pyi Taw PCL;
- Organize a technical webinar on the general impurity testing; and
- Continue the development of training materials for the metrology training.

Nepal

PQM+ provides technical assistance to Nepal's Department of Drug Administration (DDA) to strengthen medical product QA and QC systems at the central and branch offices at province levels. In addition, PQM+ is strengthening the capacity of laboratories to conduct quality testing at the National Medicines Laboratory (NML). PQM+ is strengthening private medicine testing laboratories and local medicine manufacturers, including 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 Ministry of Health and Population [MoHP], the Association of Pharmaceutical Producers of Nepal [APPON], 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+ is working to:

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

PQM+ continued to work in various areas to strengthen the institutional capacity of the DDA and NML. Introducing risk-based approaches within DDA's PMS function was a key activity in the quarter. With the support from the RB-PMS TWG, PQM+ conducted a workshop that helped DDA understand the steps and requirements for RB-PMS. PQM+ also organized a training workshop on the MedRS tool for DDA and NML staff, with the help of USP experts. In addition, PQM+ separately trained a DDA staff member to act as the focal person for MedRS.

Table 4: Training and Workshops for Regulatory Bodies

Dates	Training and workshops for regulatory bodies	Participants
May 3-7, 2021	GMP training (remote)	DDA: 16; NML: 18 MTaPS: 1
April 16, 2021	RB-PMS kick off meeting (in-person)	DDA: 7; NML: 1 PQM+ (Nepal): 5
May 17-18, 2021	Med-RS focal person training (remote)	DDA: 1 PQM+ (Nepal): 1
May 24-27, 2021	Med-RS workshop (remote)	DDA: 18; NML: 9

PQM+ conducted a remote GMP training to DDA and NML staff to enhance inspection capacities in the regulatory bodies, coinciding with the start of a nationwide lockdown due to the second wave of the COVID-19 pandemic. Participants said they found the training useful, especially in the areas of cleaning validation, water purification, HVAC system, and premises maintenance. PQM+ supported the drafting of a complaint-handling SOP for the DDA's Inspection Division. The inspection TWG is reviewing the SOP. The SOP will help formalize and enhance the complaint-handling process in line with international best practices.

On the laboratory side, PQM+ mostly focused on finalizing the SATTA assessment report and the IDP that lays their path for ISO accreditation. The NML sees the report and the IDP as a suitable medium to advocate to MOHP for more resources for its under-funded laboratory activities; hence, the program has put meticulous effort into these documents. PQM+ also supported NML to draft a quality manual and upgrade its internal communication system.

PQM+ conducted a virtual discussion on the workforce assessment report and the IDP, with participation from both DDA and NML officials. Participants called for linking the assessment report, the IDP, and the DDA's annual work plan to enable implementation of the IDP. With this feedback, PQM+ is finalizing the report and the IDP; similarly, the IDP will feed into PQM+ workforce activities for the next fiscal year.

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

PQM+ invited local manufacturers to submit expressions of interest for technical assistance for WHO prequalification. A committee consisting of DDA and PQM+ staff reviewed the documents and provisionally short-listed six companies for the next step of rapid assessment.

PQM+ conducted a training needs assessment to get insight for a training curriculum to support private manufacturers' GMP compliance. The program will conduct the training using local and international experts. Senior technical staff from 40 industries have shown interest in participating.

PQM+ is working to develop the Nepal Pharmaceutical Strategy. With input from DDA, it has listed stakeholders to form a working group to develop the strategy. The working group includes representatives of professional councils, professional associations, and academia, as well as former government officials and subject matter experts. PQM+ also finalized contract details with its consortium partner IQVIA to conduct a landscape analysis of the Nepali medicines market to inform the pharmaceutical strategy.

To assure the quality of medicines in the public medicine supply chain, PQM+ is reviewing current public procurement practices and policies at the federal, provincial, and local levels. Similarly, PQM+ has planned to work with the National Health Insurance Board (NHIB) on the supply of quality medicines that are procured through universal health coverage. The work with NHIB will begin next year; NHIB and PQM+ are considering a memorandum of understanding (MOU).

PQM+ Nepal and the Nepal Health Research Council (NHRC) are in the final stages of reaching an MOU to jointly work on documenting research-based evidence related to quality medicines and advocating for policy change to promote quality medicines. To prevent the public from accessing SF medicines, PQM+ and DDA collaborated to design messages to print on posters that will, following the approval process for communication materials, be disseminated to retail pharmacies in the major cities of Nepal.

Priority Activities for Next Quarter

PQM+ plans to:

- Conduct GMP training for industries;
- Disseminate the workforce assessment report and finalize the IDP to lay the groundwork for workforce development activities next year;
- Finalize and endorse a complaint-handling system mechanism;
- Conduct a rapid assessment of industries for WHO prequalification technical assistance;
- Commence a landscape analysis of the Nepali medicines market when travel restrictions ease; and
- Finalize the IDP for the National Medicines Laboratory to support the path toward ISO accreditation.

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. 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 PY2, PQM+ Pakistan is working to:

1. Improve governance of medical product QA systems;
2. Strengthen medical product regulations;
3. Enhance private sector engagement; and
4. Reduce the availability of SF medical products.

Progress by PQM+ Objective

In Q3 of PY2, PQM+ Pakistan's program activities focused on using an integrated approach to improve the quality of medical products and systems through the following areas.

Objective 1: Governance for medical product quality assurance systems improved

Develop risk-based regulations for market authorization of high-risk medical devices: PQM+ is supporting DRAP in drafting revisions to regulations regarding medical devices (e.g., diagnostic kits or in-vitro diagnostic devices to identify communicable diseases and antimicrobial discs for culture sensitivity) to address refurbished medical devices and formulate a risk-based approach for improving regulatory compliance of new and refurbished medical devices.

PQM+ experts discuss medical devices with the CEO of DRAP and other officials.

For this purpose, PQM+ completed a detailed gap assessment to develop medical devices regulations for DRAP, reflecting international regulations on aspects including regulatory structure, device classification, device approval, and post-marketing surveillance. The PQM+ team used the GBT to conduct the assessment and provided DRAP with a rating of medical devices according to WHO GBT performance maturity levels. PQM+ assistance helped lay out short-, medium-, and long-term recommendations for DRAP based on the assessment, including HR capacity related to medical equipment and devices, development of integrated information management systems, establishment of conformity assessment bodies (CABs) to evaluate medical devices, planning for high-priority equipment protocols, and protocols for refurbished and remanufactured equipment.

PQM+ has finalized the procedures and guidelines for refurbished equipment after the incorporation of the feedback from the stakeholders including manufacturers, importers from pharmaceutical industry etc. and is submitted for approval by DRAP.

Appellate Lab, NIH, Islamabad

Development of ISO 17025:2017 QMS system SOPs of the National Appellate Laboratory, Islamabad: In Q2, PQM+ completed the gap assessment of the Appellate Laboratory at the National Institute of Health (NIH) in Islamabad against the ISO 17025:2017 standard, followed by the development of a CAPA plan. PQM+ also developed the quality manual, which NIH will sign after receiving proficiency test (PT) samples. (PT results for pH are already in hand). As a result of PQM+ assistance, all QMS documents are in the final execution stage. Lab staff conducted final uncertainty measurement calculations for HPLC and pH on their internal control templates and have issued the method verification protocol for execution. PT samples are still pending.

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

Improve the laboratory quality system by preparing additional laboratories for international certification: Following last quarter's completion of the gap assessment of the Public Health Laboratory (PHL) at the Institute of Public Health (IPH) in Lahore for the achievement of ISO 15189 accreditation (an international standard for QMS at Medical Diagnostic Laboratories), PQM+ developed a list of procedures and two policy documents on quality and ethical policy.

PHL at IPH, Lahore

As a result of PQM+ assistance, PHL's application is ready to submit for accreditation to the Pakistan National Accreditation Council (PNAC).

PQM+ and the WHO Prequalification Team established a partnership for peer audits to strengthen the quality control lab system in Pakistan. PQM+ visited the Drug Testing Laboratory (DTL) in Multan to prepare peer audits and helped address queries on the laboratory information file (LIF) against ISO 17043 standards on proficiency testing[5] from the Pakistan National Accreditation Council (PNAC). Attainment of ISO 17043 by DTL Multan will ensure proficiency testing services to other quality control labs within and outside Pakistan. This intervention, through USAID support, will help build the capacity of external quality assurance schemes, which are mandatory to maintain accreditations. At this moment, quality control laboratories depend on international resources for proficiency testing, which are both expensive and time-consuming. With support from PQM+, Multan Drug Testing Laboratory will be in the position to offer this to other quality control laboratories nationally and internationally.

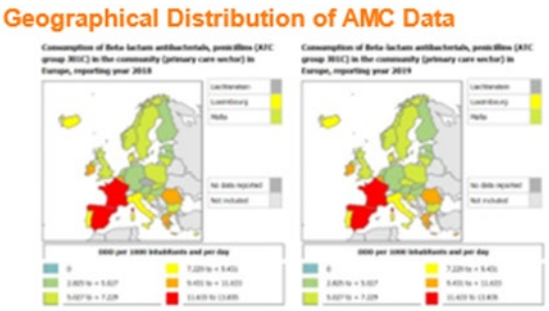

During WHO PQ audit visit at DTL, Rawalpindi

With PQM+ assistance, DTL Bahawalpur submitted an LIF for WHO PQ. Prior to that, PQM+ aided in reviewing the LIF and shared observations with the staff. The LIF is now approved.

PQM+ provided technical assistance to DTL Rawalpindi during the WHO PQ audit in April. As a follow-up, PQM+ assisted DTL Rawalpindi for CAPA preparation and submission to WHO, which is now reviewing the CAPA plan.

[5] Proficiency testing (PT) is interlaboratory comparisons that are organized regularly to assess the performance of analytical laboratories and the competence of the analytical personnel.

Development of antimicrobial consumption (AMC) dashboard in the Pakistan Integrated Regulatory Information Management System (PIRIMS): In collaboration with DRAP, PQM+ developed an AMC dashboard to link to the PIRIMS portal, which will help pharmaceutical industry users submit data relating to production/batch, sales, distributors, resellers, and patients through PIRIMS.



Through this representation, DRAP can easily assess the geographical distribution of consumers' antimicrobials consumption in Pakistan.

AMC quantifies the consumption of antimicrobial agents, conducts comparative analysis at the country level, and evaluates the impact of regulatory interventions, thus playing a key role in anti-microbial resistance (AMR) surveillance. Access to AMC data, however, remains challenging in Pakistan.

Private sector engagement to increase the supply of quality-assured priority medical products: PQM+ developed a concept note to formulate a national pharmaceutical development strategy for Pakistan. PQM+ conducted several meetings with the chairman of the Board of Investment (BOI) and officials from the Prime Minister's Office to discuss ways to attract new investment, bringing about industrial reforms for realizing greater export potential, diversification into knowledge-based sectors, and a new level of global economic connectivity. Stakeholders also mutually agreed to develop a 10-year National Pharmaceutical Development Strategy.

For this, PQM+ developed and shared detailed terms of reference (TOR) for the proposed technical working group (including the Ministry of National Health Services, Regulation, and Coordination (MONHR&C) to drive the formulation of the strategy with the BOI. PQM+ has started work on the strategy development process led by an internal strategy working group. The preliminary desk review focused on gathering key data points around the current state of the pharmaceutical industry, mapping key stakeholders, lessons from other countries, key challenges to the growth of the industry and consolidating recommendations to promote investment and ease of doing business in the pharmaceutical sector from secondary literature.

PQM+ briefed the DRAP CEO regarding the need for and the objectives of the strategy-building exercise. The DRAP CEO expressed appreciation for the initiative and its need for the industry. This was an important step to ensure buy-in from the regulator for the process and the final recommendations, which will contain proposals for further regulatory reforms. In addition, PQM+ has initiated awareness-raising for the strategy development exercise with key stakeholders, such as business associations and other development partners working on public health-related initiatives in the country.

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

Support the adoption of data standards, including the Common Technical Document format, to facilitate dossier review and information management with manufacturers: The ISO Identification of Medicinal Products (IDMP) standards specify the use of standardized

definitions to identify and describe medicinal products for human use. The purpose of these standards is to facilitate the reliable and consistent exchange of medicinal product information by providing a common product language for stakeholders to use in their interactions.

PQM+ is providing technical assistance to DRAP to adopt and implement IDMP standards. Last quarter, PQM+ shared the five IDMP ISO standards and the draft roadmap with DRAP for the implementation of these standards, including:

1) Drug substances (ISO 11238);
2) Pharmaceutical dose forms, units of presentation, routes of administration, and packaging (ISO 11239);
3) Units of measurement (ISO 11240);
4) Regulated pharmaceutical product information (ISO 11616); and
5) Regulated medicinal product information (ISO 11615).

With the support of PQM+, DRAP has adopted two ISO standards—11239 for pharmaceutical dose forms, units of presentation, routes of administration, and packaging; and 11240 for units of measurement. These ISO standards have been incorporated in the PIRIMS portal.

Europe and Eurasia Region

Central Asia/Kazakhstan

PQM+ is strengthening the medicines regulatory system in Kazakhstan by providing technical assistance to the National Center for Expertise of Medicines and Medical Devices (NCEM). The main objectives are to improve the medicines registration system; support medicines quality control laboratories (MQCLs) so they can test the quality of medicines reliably and accurately according to international standards; strengthen the GMP inspectorate; and prepare the country for accession to the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S).

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

In Q3, PQM+ continued technical assistance to the Almaty and Karaganda MQCLs to help them achieve and maintain WHO prequalification. In Q3, PQM+ coordinated with the Almaty laboratory and WHO to complete a virtual assessment of the laboratory. As agreed with the WHO PQ team, WHO will accept the PQM+ assessment as a peer review audit. PQM+ prepared a draft assessment report for submission to WHO. After reviewing the peer audit report, WHO will assign a date for the lab's WHO PQ audit. Meanwhile, PQM+ has started working with the laboratory on implementation of CAPAs following the virtual assessment.

In Q3, PQM+ completed the procurement of three analytical instruments (pH meter, conductometer, and Karl Fischer titrator) for the Karaganda laboratory and safety showers for

the Almaty laboratory to improve the compliance of each with WHO guidelines. PQM+ also completed procurement of services on training on computerized system validation (CSV) for Karaganda and Almaty laboratories.

PQM+ is supporting Kazakhstan in strengthening the pharmaceutical inspectorate and preparing for ascension to PIC/S membership. This will facilitate reliance and open access to the GMP inspection mechanism with other PIC/S member countries, resources for further capacity development, and eventually quality-assured medicines in country. Kazakhstan's PIC/S membership and the application of the PIC/S GMP guidelines in local industry inspection will also facilitate the export of medicines. In Q3, PQM+ provided technical assistance to the Pharmaceutical Inspectorate to successfully conduct the first distant GMP assessment of a pharmaceutical manufacturer. Due to COVID-19 travel restrictions, conducting on-site GMP inspections of some manufacturers in foreign countries was not possible, leading to delays in the market authorization of some products. PQM+ provided extensive support to the GMP inspectorate to prepare, which included training on the principles of distant GMP assessment, detailed planning of each day of the inspection, and developing corresponding questionnaires and checklists. As a result, the GMP Inspectorate successfully conducted its first distant assessment of a manufacturer based in India from May 11 to 14, then developed an assessment report.

The GMP inspectors expressed that it was a valuable experience they could use in future distant assessments. As a cross-country collaboration effort, PQM+ and the Kazakh inspection group arranged a webinar to share the first-hand experience of Kazakhstan GMP Inspectorate on the distant assessment of foreign manufacturers, with 22 participants from Kazakh and Uzbek pharmaceutical inspectorates. PQM+ presented general approaches to distant assessments, and representatives of the Kazakh inspectorate shared their experiences in preparing for, performing, and reporting on the distant assessment. They also described the main challenges they faced during the assessment.

In Q3, PQM+ provided a two-day training for the inspectorate on deficiencies classification, with. 61 participants from the Committee for Medical and Pharmaceutical Control and NCEM in attendance. The training covered the main principles of classifying GMP deficiencies, the structure of SOPs, the details of the PIC/S document on the classification of deficiencies, and practical examples of GMP deficiencies.

The WHO GBT assessment of Kazakhstan identified gaps in market surveillance and control. In Q3, PQM+ had a follow-up meeting with NCEM and discussed further assistance in implementing RB-PMS in Kazakhstan. PQM+ recommended arranging a technical working group under the regulatory authority, to include RB-PMS stakeholders. Kazakhstan established a commission with functions like the TWG; identification of stakeholders to join the commission is under discussion. PQM+ also assisted in developing the terms of reference, which describes stakeholders' functions and responsibilities as well as a sample of the RB-PMS protocol. These documents are finalized and NCEM is now planning the sampling of products from the market.

NCEM requested PQM+ assistance in improving the medical devices (MD) inspectorate. In Q3, PQM+ arranged the first meeting between the medical devices inspection group and PQM+ technical experts. PQM+ discussed the current situation with MD inspections, the legislative framework, the system for MD classification, and the inspection system. PQM+ will help the MD inspection group develop the relevant quality management system, work on training inspectors, and evaluate MD dossier applications.

PQM+ continued work with NCEM's scientific educational center (SEC). The center is important to ensure the sustainability of PQM+'s efforts to build the capacity of the medicines regulatory workforce in Kazakhstan. In Q3, PQM+ held meetings with SEC to discuss technical assistance. PQM+ delivered a presentation on workforce development and instructional design to demonstrate potential areas of technical assistance (TA). The SEC identified priority areas for PQM+ TA, including obtaining accreditation from a local accreditation body as an education institution and training SEC's staff in adult teaching techniques. PQM+ developed a questionnaire to assess the center's status to plan for any needed TA. Based on the questionnaire and conference calls, PQM+ drafted an outline of a competency-based learning and adult learning workshop for Q4. PQM+ reviewed accreditation requirements and will assist SEC with preparation for local accreditation as an educational entity.

In Q3, NCEM continued work on transition from the national registration regulations to those of the Eurasian Economic Union (EAEU). PQM+ met with NCEM to understand the implication of the transition, which is still in process. The future of WHO collaborative registration, a fast-track process for registering quality-assured medicine, remains uncertain after July 1, when Kazakhstan activates the EAEU registration procedure. EAEU members are considering proposals to keep the WHO Collaborative Registration Procedure (CRP) as part of the EAEU registration procedure.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Address findings related to good regulatory practices from the GBT assessment in collaboration with NCEM;
- Continue technical assistance to the NCEM on developing approaches and procedures for RB-PMS;
- Assist in implementation of CAPAs resulting from the virtual audit of the Almaty MQCL to prepare the laboratory for WHO PQ;
- Continue technical assistance to the PIC/S working group in the areas outlined in the PIC/S accession roadmap;
- Provide technical assistance to the medical devices inspection group to become operational and compliant with international standards; and
- Continue technical assistance to the scientific educational center to ensure its development as a main element of the system for continuous education of NCEM staff.

Uzbekistan

Uzbekistan is graduating from the Global Fund-supported procurement of TB medicines to domestically funded procurement, and the country plans to gradually increase the funding it allocates to procure 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 the quality of medicines on the local market, PQM+ is assisting 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.

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

In Q3, PQM+ initiated technical assistance to the Agency on the ongoing development of an integrated electronic information system for registering medicines. With PQM+'s advocacy, the Agency created a working group consisting of representatives from the information technology (IT) department, the medicines registration department of the State Center, and the IT company that is directly engaged in developing the information system. Prior to that, the IT and medicines registration specialists had only sporadic interaction. Meetings with the working group now occur on a weekly basis. In Q3, PQM+ supported the working group to develop a plan to create the information system. PQM+ also provided technical assistance in updating the SOPs related to the registration process, reflecting the staff's actions and responsibilities related to the information system.

In Q3, PQM+ continued to provide technical assistance to strengthen the medicines registration system. At this point, the priority is to develop appropriate SOPs that will meet international standards. PQM+ is providing guidance to develop 47 relevant SOPs; the program assisted in reviewing the SOPs and provided recommendations to the members of the working group for finalization. In Q3, the working group finalized four SOPs.

PQM+ continued facilitating coordination between the State Center, Global Fund (GF), National Tuberculosis Program (NTP), and the Global Drug Facility (GDF) to advance the process of registering WHO-prequalified TB medicines in Uzbekistan through WHO CRP. Daily coordination takes place between PQM+, GDF, and NTP to prepare a package of documents to submit for registration through the WHO CRP mechanism. PQM+ and GDF held meetings with all manufacturers—suppliers of WHO-prequalified TB medicines—to identify each one's authorized persons and companies. The list of authorized persons is now compiled. In addition, PQM+ organized a training for manufacturers' authorized persons on requirements to apply for registration of WHO-prequalified and stringent regulatory authority (SRA) approved medicines through WHO CRP in Uzbekistan. State Center registration department specialists conducted the training with PQM+ technical assistance. The authorized persons have started preparing the applications to register the corresponding medicines through WHO's CRP procedure.

In Q3, PQM+ continued technical assistance to the Agency in strengthening the pharmaceutical inspection system and preparing the GMP inspectorate for meeting the PIC/S accession requirements. After PQM+ advocated for the organizational structure of the pharmaceutical inspectorate, provided corresponding technical assistance, and collaborated closely with Agency leadership, the Agency developed a draft resolution of the Cabinet of Ministers on establishing an independent center for various good practices, the GxP Center (inspectorate), as a separate unit of the Agency. No clear structure or responsibilities of the inspectorate are

currently in place. All interested parties have agreed to the resolution and submitted it to the Cabinet of Ministers for final approval. Once approved, it will be an important milestone for establishing a functioning inspectorate with a clear organizational structure and responsibilities.

In addition, with PQM+ technical assistance, the Agency's PIC/S working group finalized the SOP for the consideration of complaints and appeals, the annual work plan for the GxP inspectorate, and the matrix of inspectors. PQM+ also supported the Agency in preparing updated versions of the SOP for inspections.

From April 20 to 22, PQM+ conducted an online training called "Classification of Deficiencies" for the State Center's GMP Inspectorate staff and all branches of the Agency. During the training, 28 GMP inspectors and experts learned the principles of the Classification of Deficiencies and the structure of the related SOP, as well as about follow-up activities. The training included practical tasks for participants. On June 9 and 10, PQM+ conducted an online training titled "Data Integrity" for the GMP Inspectorate staff. During this training, 18 GMP inspectors and experts learned about data integrity principles, the structure of the related SOP, and follow-up activities, as well as participated in practical tasks.

PQM+ has been providing technical assistance to strengthen the quality management system of the Andijan MQCL to ensure laboratory operations are in accordance with Good Laboratory Practice (GLP) standards to meet requirements for WHO prequalification. A significant deficiency that the PQM+ assessment of the Andijan MQCL identified was the lack of a quality assurance department and dedicated staff responsible for overseeing the laboratory's QMS. After visiting the Andijan MQCL, PQM+ advocated for enhancing the organizational structure by creating a qualified QA team. Based on the recommendations, the Andijan MQCL collaborated with PQM+ to develop a new organizational structure and two job descriptions: head of the QA Department and QA manager. Both positions will oversee activities in the laboratories to ensure that the QMS is implemented and functions appropriately. In May, the new organizational structure, which includes the QA department and job descriptions, received official approval and corresponding allotment of funding. The Andijan MQCL selected staff for these positions. PQM+ is now working with the Andijan MQCL to equip the QA staff with the necessary capabilities to lead the laboratory's QA activities.

PQM+ has continued to provide technical assistance to laboratories in preparation for accreditation. In June, local accreditation of all MQCLs is planned. PQM+ conducted the following trainings, requested by the laboratories' staff:

- Verification of Analytical Methods,
- Decision Rule, and
- Principles of the Calculation of Uncertainty.

The trainings were important for not only staff of the Tashkent and Andijan laboratories to attend, but also staff from other regional laboratories (Samarkand, Karshi, and Urgench). Outputs of the trainings included development of some specific SOPs.

A high-performance liquid chromatography (HPLC) machine for the Andijan MQCL procured by PQM+ has arrived in Tashkent. It is undergoing a customs clearance prior to its delivery to the laboratory. The machine will provide important support to the laboratory by helping strengthen the infrastructure to test the quality of medicines.

PQM+ has also worked to provide technical assistance to Tashkent and Andijan laboratories in strengthening their QMS for WHO prequalification. In Q3, PQM+ updated the implementation plan for Tashkent and Andijan MQCLs, which the counterparts discussed and agreed to. Correspondingly, PQM+ recorded the following progress on its recommendations:

- Following PQM+ recommendations, the Andijan MQCL has changed its organizational structure and approved a QA department with two staff units, and the laboratory developed a job description for a QA manager based on PQM+ recommendations.
- The Tashkent laboratory reviewed and updated the implementation plan and the catalog of reference standards; PQM+ is reviewing these documents.

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

In Q3, based on PQM+ recommendations, Nobel Pharmasanoat has developed an implementation plan to purchase a new WHO-prequalified API to produce levofloxacin. PQM+ has reviewed the plan and delivered the comments.

During the reporting period, studies by Nobel on the possibility of penicillin cross-contamination eventually detected none. This is an important milestone because cross-contamination risk management, which includes an ability to test air samples, was an issue that prevented the project from moving forward. Now the manufacturer can focus on product development and PQM+ can provide continued support in that regard.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Review the newly developed SOPs to support strengthening of the medicines registration system;
- Provide technical assistance to develop the integrated information management system for medicines registration;
- Facilitate registration of WHO-prequalified TB medicines through the WHO CRP mechanism;
- Conduct an assessment of the three additional regional MQCLs (Samarkand, Karshi, and Urgench);
- Continue technical assistance to the PIC/S working group in its preparation for the PIC/S accession, including strengthening QMS and building the GxP inspectorate staff's capacity;
- Complete delivery of HPLCs to the Andijan MQCL;
- Provide technical assistance to MQCLs as they prepare for local ISO 17025 accreditation;
- Start technical assistance on strengthening the post-marketing surveillance system; and
- Continue technical assistance to Nobel Pharmsanoatin its preparation for WHO PQ for levofloxacin production.

COVID-19 Response Activities

Bangladesh

As part of USAID's COVID-19 response efforts in Bangladesh, PQM+ received funding to support the DGDA, Bangladesh's national regulatory authority, in policy, planning, and coordination. The program has been providing technical support to DGDA, its NCL, and other relevant stakeholders to (i) strengthen safety surveillance systems in support of COVID-19 vaccine introduction and ensure patient safety; and (ii) revise and adopt expedited market authorization procedures, such as EUA/no-objection certificate (NOC) with appropriate requirements for product safety, efficacy, and quality monitoring through the following activities:

Bangladesh started vaccination against COVID-19 in February with targeted high-risk groups using the Oxford-AstraZeneca vaccine. Since then, more vaccines have been added to the COVID-19 vaccination program. Due to the pandemic, the DGDA must release the deployed vaccines to the immunization program in the shortest possible time. The routine immunization program in Bangladesh currently uses passive/voluntary surveillance through a paper-based system with both facility-based and community-based surveillance. Following the introduction of COVID-19 vaccines, officials expect higher reporting rates for suspected adverse events following immunization (AEFI) and adverse events of special interest (AESI) and efforts to determine causality and reassure the public of the vaccine's safety. Generally, the priorities focus on ensuring the availability of and access to vaccines, but often are not targeted to maintain the efficacy, safety, and quality of those vaccines. Quality is one cause of safety issues in vaccines or any medical product.

After the work plan was approved in April, PQM+ started working to understand the status of the Bangladesh systems for post-marketing surveillance (PMS) of COVID-19 vaccine quality, identify different stakeholders, and update the COVID-19 vaccine deployment plan including the surveillance system to better monitor the quality of vaccines in Bangladesh. This quarter, PQM+ held introductory meetings/consultations with key stakeholders to discuss the needs and scope of activities, including:

Consultation with DGHS line director

- The director general and other DGDA senior officials;
- Line director, Directorate General of Health Services (DGHS) (key stakeholder for routine EPI activities and COVID-19 vaccination program);
- Dr. Selina Ahmed, national program officer (vaccine safety and quality), WHO Bangladesh;
- Mr. Md. Ashraf Hossain, deputy director, market surveillance and control, DGDA; and
- Dr. Md. Harun-Or-Rashid, deputy chief and Dr. Nasima Pervin, bacteriologist, National Control Laboratory.

In these stakeholder interviews/consultations, PQM+ focused on understanding the current views on PMS; the COVID-19 vaccine deployment plan, supplies, and distribution chains; and AEFI surveillance for routine expanded program on immunization (EPI) and the COVID-19 safety surveillance mechanism. PQM+ also completed desk reviews of relevant documents

prepared by DGDA, WHO, and others. Key findings from the consultations and desk review will guide the RB-PMS plan for COVID-19 vaccines that the team is drafting.

Vaccine wing of DGDA's National Control Laboratory in Dhaka

In addition to working with the DGDA on its RB-PMS plan, the PQM+ team has been supporting the DGDA toward achieving WHO Maturity Level 3 and for the vaccine wing of the NCL to sustain its achieved standards and safety surveillance system in support of COVID-19 vaccine introduction and ensuring patient safety. For this activity, PQM+ will find a mechanism that can regularly map NCL's need to carry out testing of COVID-19 vaccines.

DGDA recently conducted an assessment of the vaccine regulatory system and vaccine laboratory with support from development partners to strengthen the NCL for vaccines quality control and lot release in compliance with WHO prequalification at a Maturity Level 3. The DGHS sent the proposal for necessary support (equipment, human resources, technical support, operational costs, etc.) to the World Bank and plans to have technical support implemented by WHO and PQM+. In addition, in Q3, the PQM+ team mapped the standard testing procedure for vaccines, which is crucial to establish robust monitoring systems in settings with varying capacities to identify, report, investigate, analyze, and determine the cause of and respond to AEFI due to COVID-19 vaccines.

In addition to supporting the DGDA in monitoring AEFI from the COVID-19 vaccine rollout, PQM+ Bangladesh is **reviewing existing DGDA EUA/NOC guidelines and alignment of vaccine marketing authorization process in response to the COVID-19 vaccine introduction.** The DGDA is responsible for EUA of medical products, including vaccines, and ensuring equitable access. As part of its goal to strengthen regulatory preparedness, DGDA is working for transitioning regulatory pathways and practices from a traditional, reactive control system to a proactive, risk-based approach. EUA is a special authorization procedure, usually granted for vaccines in the case of a public health emergency when less certainty about the efficacy and safety of products is tolerated. The PQM+ review of DGDA's existing EUA/NOC process will help identify and prioritize the required data for obtaining EUA to strengthen regulatory decision-making and align the DGDA's EUA procedures with global standard practices. This quarter, PQM+ reviewed the existing legislations/provisions, standard operating procedures, and essential documents regarding EUA in Bangladesh, along with international guidelines for EUA of COVID-19 vaccines. The team conducted a face-to-face meeting with DGDA officers and designed a checklist for a gap analysis of existing EUA procedures.

The gap assessment is now in process. It includes both a quantitative and qualitative assessment using the developed gap assessment tool. PQM+ is also forming a task force to develop an EUA guideline for COVID-19 vaccines and scheduling a stakeholder's consultation meeting. The EUA guideline for COVID-19 vaccines will improve the efficiency of DGDA's assessment, review, and authorization of proposed vaccines.

Cross-Bureau

PQM+ received funds from the Office of Health Systems (OHS) to support COVID-19 pandemic-related activities that contribute to Objective 2 of the PQM+ results framework: Improve country and regional regulatory systems to assure the quality of medical products in the public and private sectors. USAID approved the work plan in March 2021, with two main activities to implement:

- Develop an operational guide on emergency regulatory procedures for COVID-19 medical products and
- Disseminate the USP quality control toolkit for COVID-19 vaccines.

PQM+ is implementing the two activities with its partners, the University of Washington and the Global Health Impact Group (GHIG)-London School of Hygiene and Tropical Medicine (LSHTM). Activity updates for this quarter are:

Emergency Regulatory Procedures for COVID-19 Medical Products: PQM+ engaged two technical partners: UW to support the development of an operational guide on EUA for vaccines and GHIG to develop an in vitro diagnostic medical devices guide.

The task order for UW received full approval this quarter. PQM+ held a kick-off meeting to go over the programmatic and administrative aspects of the subaward contract management with UW. The university achieved two of its deliverables this quarter: 1) methodology for the desktop research and implementation plan and 2) the country MRA assessment questionnaire. PQM+ is reviewing the questionnaire and coordinating with GHIG and PQM+ field offices on data collection.

The fixed-price award to GHIG also received full approval in June. PQM+ facilitated a meeting between the two technical partners to map out timelines and coordinate country MRA data collection tools and approaches. GHIG completed its first deliverable: an activity implementation plan and a desk review summary of EUA programs for in vitro diagnostics (IVDs), including COVID antigen rapid tests. PQM+ reviewed both documents. GHIG is developing the MRA country assessment questionnaire, with both partners planning data collection in Quarter 4. PQM+ also compiled a list of program country focal points to facilitate the MRA assessment data collection process.

Dissemination of the USP quality control toolkit for COVID-19 vaccines: PQM+ is collaborating with USP and African Medicines Regulatory Harmonization (AMRH) to plan and execute two webinar sessions on July 27 and August 3.

This quarter, PQM+ identified the target audiences and webinar presenters and began developing presentation materials. PQM+ will disseminate four toolkits from USP documentary resources to support the development and validation of analytical assays for testing and release of vaccines products to safeguard populations. The four toolkits will focus on the following topics:

- Introduction to the toolkits and general vaccine chapters and compendial methods;
- Assessing the quality attributes of mRNA vaccines;
- Assessing the quality attributes of viral vector vaccines; and
- Assessing the quality attributes of inactivated vaccines.

PQM+ will introduce two toolkits each day of the webinar series. USP will offer complimentary access to the select USP-National Formulary (USP-NF) chapters associated with the four toolkits. Webinars will be available in English, French, and Portuguese simultaneously. PQM+ is in the final stages of developing the draft webinar concept note and invitation and will translate them into French and Portuguese. The program is working with USP resources on the webinar registration site and webinar delivery platform.

Ghana

To enable FDA Ghana to conduct all quality control tests required for COVID-19 vaccines—both universal tests required for parenteral drug products and specific product quality tests—PQM+ will provide training for analysts at the FDA Ghana Laboratory and procure needed consumables to conduct these tests. Though FDA Ghana is a Maturity Level 3 authority, the potency assay for the COVID-19 vaccine is unique and the analysts at FDA Ghana do not have experience conducting this test. They will therefore require capacity building to enable them to adhere to manufacturer testing requirements. The FDA Ghana microbiology laboratory is currently at Biosafety Level 2 (biosafety levels are on a scale of 1 to 4, with 4 being the highest level of containment); however, COVID-19 vaccine testing should occur in a Biosafety Level 3 environment to ensure adequate containment and protection of the analysts. While supporting FDA Ghana to test in the current conditions, PQM+ will assess existing FDA facilities to identify requirements to achieve Biosafety Level 3 in the future.

PQM+ received approval to start work with the Ghana FDA in mid-May. Since then, the team has strategized with PQM+ counterparts in Asia on the approach to train the FDA Ghana lab on the potency assay for COVID-19 vaccines. Since the potency assay method differs for each vaccine, the training curriculum will have to cover all vaccines granted EUA in Ghana, including Astra Zeneca, Sputnik V, and Johnson & Johnson. Pfizer vaccines will follow soon. PQM+ also hired a consultant to train the local senior microbiologist at USP-Ghana and another PQM+ microbiologist in Asia with vaccine testing experience. FDA Ghana lab analysts will be trained, with a few selected for a follow-on in-depth training of trainers program to take ownership of building capacity for vaccines testing internally. Finally, PQM+ created a list of accessories/ consumables required for vaccines testing to prioritize them based on available budget.

As part of its work plan, PQM+ is also supporting FDA Ghana to enhance its COVID-19 vaccine safety monitoring and supportive supervision. FDA Ghana has designed cohort event monitoring (CEM) as a prospective COVID-19 active safety surveillance study in 16 sentinel sites across Ghana, including one site in each region. Approximately 10,000 participants are expected to enroll, with follow-up on predetermined days after each of the two doses; 2,500 people have already enrolled. The study team will require training and will receive the needed logistics to manage the study, including tablets for data entry, airtime for follow-up, and periodic allowances. A monitoring team of officers from FDA Ghana and the EPI will undertake supportive supervisory visits to ensure implementation of the cohort event monitoring according to the protocol and data collection as planned. The study started in March and is expected to last eight months; given the lack of available vaccines to enable deployment, it may extend beyond October. PQM+ will support FDA Ghana to implement this study by assisting with enrolling at least 3,000 additional participants; developing and implementing training programs for site coordinators and the study team; developing job aids; and participating in the supportive supervisory visits. PQM+ will also assist FDA Ghana with the logistics to facilitate the study for its duration.

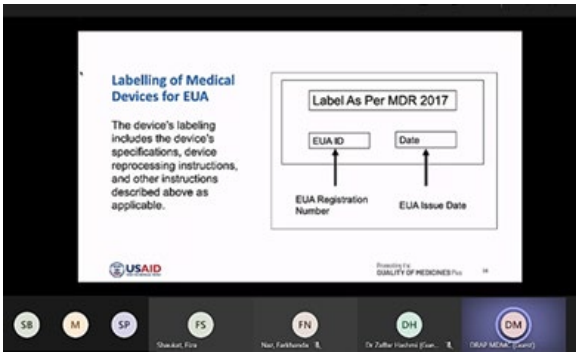
As part of this activity, PQM+ has:

- Received the CEM study protocol and progress updates:
  - CEM study is ongoing in three regions: Central (one facility), Greater Accra (two facilities), and Ashanti (two facilities).
  - So far, data has not been entered via electronic tablets (so PQM+ will procure the first 10 tablets—two per region—for this study.
  - Job aids have yet to be developed.
  - No training materials (beyond the protocol) were used for previous training, which was virtual.
- Agreed with FDA Ghana to discuss with the Expanded Program on Immunization and prioritize the next five regions for the CEM.
- Received specifications for tablets to be used for data entry for the CEM and initiated the procurement process.
- Started development of job aids and the training curriculum for training of the study team based on the CEM study protocol provided by FDA Ghana.
- Recruited a pharmacovigilance consultant. The contract has been signed and PQM+ is issuing a work order for Ghana-specific activities.

Pakistan

The PQM+ COVID-19 program supported DRAP and the pharmaceutical industry through the following major activities:

Improving access to new treatments, medical products, and technologies through risk-based emergency use authorization (EUA) regulatory approvals from DRAP reference countries: During the pandemic, the Drug Regulatory Authority of Pakistan (DRAP) was unable to grant emergency approvals or implement EUA due to a lack of legal provisions and procedures, especially regarding medical devices — such as personal protective equipment (PPE) — and pharmaceuticals (remdesivir). USAID's PQM+ Pakistan COVID-19 program has developed draft EUA guidelines in line with international best practices to strengthen DRAP's regulatory systems and enable Pakistan to respond to the COVID-19 pandemic and future public health emergencies.



PQM+ Pakistan conducted a virtual consultative meeting with stakeholders and DRAP on EUA draft guidelines in May.

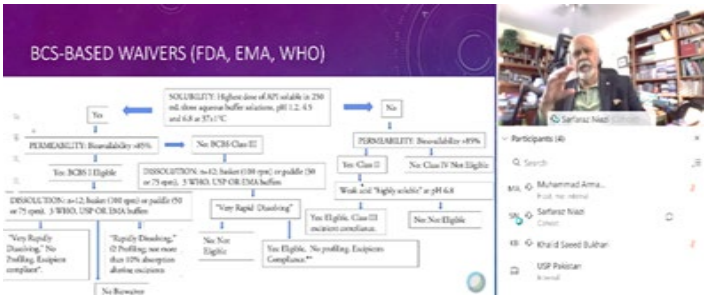
PQM+ held a virtual consultative meeting with various stakeholders on draft EUA guidelines for medical devices on May 6. Participants from the Pakistan Pharmaceutical Manufacturing Association (PPMA), Pharma Bureau, chairman of the Healthcare Devices Association of Pakistan, president of the Federation of Pakistan Chambers of Commerce and Industry (FPCCI), regulatory affairs managers from Abbott and Roche pharmaceutical companies, and the director of medical devices and DRAP staff attended. PQM+ has updated the draft EUA guidelines to include stakeholder feedback and has shared them with DRAP for final approval.

DRAP also shared draft national PPE standards with the PQM+ team for review and feedback. PQM+ is planning to conduct a consultative meeting with relevant stakeholders to obtain feedback on the draft standards. Once finalized, PQM+ will work with DRAP to implement these national PPE standards in Pakistan, ensuring that all PPE products available in the market are safe and quality-assured, to help the government adequately contain and respond to the COVID-19 pandemic. PQM+ is also planning to conduct a training on dossier assessment of medical devices (especially in-vitro diagnostics) and other medical products relevant to COVID-19 for DRAP staff, which will help them regulate and ensure that all medical devices being used under EUA are of acceptable quality and safe for use in Pakistan.

Conduct fast-track quality control testing of priority medical products for COVID-19: The pandemic has created a greater demand for masks and other PPE in Pakistan. Because of the increase in demand, the risk of poor-quality PPE circulating in the local market is also rising. As the public sector lacks the capacity to conduct quality testing and PMS of PPE, PQM+ is working to strengthen public sector laboratories, such as DRAP's Central Drug Laboratory (CDL) in Karachi, by providing CDL with PPE testing equipment according to international standards to ensure PMS of PPE in Pakistan. The procurement of testing equipment is approaching its final stages, with PQM+ coordinating with vendors and customs clearing agents for shipment and payment details for 11 instruments. The provision of this equipment to CDL Karachi will enable the government to conduct PMS of PPE in Pakistan, helping to ensure access to safe PPE, while working toward infection prevention and control during the pandemic.

Personal protective equipment (PPE)

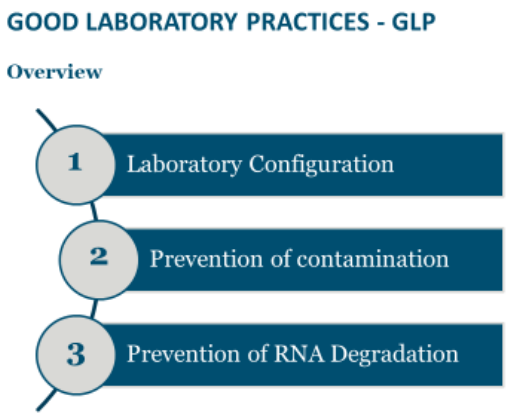
Provide regulatory support to DRAP and contract research organizations (CROs) on COVID-19 related biostudies (clinical studies): COVID-19 has led to many new medical products being introduced internationally. However, because some are still under review, and data on safety and quality is under investigation; this development stage requires extra vigilance and expertise to review before DRAP can allow market authorization in Pakistan. Bioequivalence studies are essential for developing preparations in the pharmaceutical industry. The objective of such studies is to evaluate the therapeutic equivalence of tested medicines. Through USAID funding, PQM+ is working on strengthening DRAP by developing guidance documents on conducting biostudies (clinical studies/trials). This intervention will build the capacity of DRAP staff on biostudies and help DRAP develop and implement national biostudies guidelines to ensure reliable, evidence-based clinical data on new treatments during the pandemic. PQM+ is coordinating with DRAP to implement the project-developed biostudies guidance documents, for which several consultative meetings and trainings are planned for Q4.



A virtual meeting in May covered implementation of the biostudies guidance document. Attendees included the DRAP CEO, DRAP staff, PQM+ staff, and the PQM+ biostudies consultant.

Provide regulatory support to reduce the risk of shortages of quality-assured and evidence-based COVID-19 medical products and supplies: Public health emergencies such as the COVID-19 pandemic often result in medicines and their ingredients being in short supply. Thus, it is necessary to identify and arrange for alternative sources of active pharmaceutical ingredients (APIs) and finished pharmaceutical products (FPPs) to prevent drug shortages and guarantee timely access to both COVID-19 medicines and regular supplies of essential medicines. PQM+ is assisting DRAP to develop/integrate a database to monitor and act on API and FPP shortages. PQM+ has initiated the procurement process for online API and FPP database subscriptions and has requested that DRAP provide a list of required APIs for inclusion in the database. PQM+ has also developed a draft guidance document for monitoring API shortages and shared it with DRAP for review. The document will help build DRAP's staff's capacity to prepare for implementation of the API and FPP monitoring system.

Engage the private sector to build the capacity of public and private sector diagnostic laboratories to use new COVID-19 diagnostic technologies: COVID-19 has created an urgent need to build the capacity of public and private sector laboratory staff on COVID-19 laboratory techniques. PQM+ conducted a one-day virtual training for public sector laboratory staff in Pakistan on COVID-19 in-vitro diagnostic technologies and Good Laboratory Practices (GLP) on May 27 in collaboration with a U.S.-based diagnostic equipment provider. The training included sessions on GLP, pre-analytical errors in COVID-19 testing, COVID-19 application training, and environmental cleaning and waste disposal, in addition to an overview of biosafety levels (BSL) 2 and 3. This training will enable public sector hospital laboratory staff to conduct accurate and quality COVID-19 tests according to international best practices, in compliance with biosafety and biosecurity.



PQM+ hosted a virtual one-day training on COVID-19 in-vitro diagnostic technologies and Good Laboratory Practices (GLP) in collaboration with a U.S.-based diagnostic equipment provider in May.

Engage local private sector laboratories to test PPE: As part of its PSE strategy, PQM+ is engaging private sector PPE testing laboratories in Pakistan. To facilitate and improve the regulatory environment for PPE manufacturers, PQM+ is working with DRAP to develop and implement a guidance document that lays out required conditions and accountability criteria for private sector testing labs to qualify as independent testing laboratories for PPE manufacturers. This guidance document will help define prerequisites for PPE third-party labs to submit applications for the license and will also assist in setting standards for evaluating the license applications, based on international best practices. This activity will help ensure consistency and quality of PPE testing in Pakistan. PQM+ presented the criteria for selecting outsourced PPE testing labs to the DRAP Medical Device Board (MDB) on April 20. The DRAP MDB has approved the criteria and will issue an official notification after completion of administrative procedures.

In addition, Tti Testing Lab (PQM+'s partner laboratory for PPE testing in the private sector) conducted an extensive onsite training for three PQM+ consultants based at the CDL in Karachi from May 31 to June 11 at the Tti facility in Lahore. The hands-on training covered bacterial filtration tests, particle filtration tests, blood penetration tests, wet and dry penetration tests, flammability tests, and more. The PQM+ team also visited the newly established microbiology lab at the Tti Lab and provided technical inputs to the Tti team on QMS documentation, validation, and calibration. The PQM+ team will train the lab staff at the CDL in Karachi on PPE standards, testing, material identification, and other topics to increase the lab staff's capacity to conduct these tests independently in future.

PQM+ seconded staff from CDL, Karachi during an extensive on-site training on PPE testing and standards at Tti Testing Lab, Lahore (PQM+ private sector partner lab for PPE testing) in May and June.

Engage the local private sector to manufacture quality-assured PPE: PQM+ is assisting PPE manufacturers to produce high-quality PPE per international standards, for both local use and exports. The program advertised an EOI for PPE manufacturers to receive support on ISO 13485 accreditation and the *Conformité Européenne* (CE) mark for one product (which signifies that the product can be sold in the European Union). This accreditation will allow PPE manufacturers in Pakistan to design quality management systems and maintain the effectiveness of their processes according to international standards, as well as export PPEs globally. PQM+ Pakistan is recruiting consultants to provide ISO 13485 and CE mark trainings and certification services to targeted PPE manufacturers.


PQM+ conducted an onsite gap assessment visit to the BF Biosciences Ltd. (Ferozsons) facility in Lahore in June.

Engage the local private sector to manufacture quality-assured remdesivir: PQM+ is engaging Pakistani manufacturer BF Biosciences Ltd. (Ferozsons) to produce remdesivir under the brand name Remidia, according to GMP and other international standards. With PQM+ support Ferozsons increased its production and is supplying remdesivir to local markets in Pakistan and globally through exports.

Table 5: Production of Remidia

Product	Standard Batch Size	# Batches Produced (April 9, 2021)	# Vials Produced (April 9, 2021)
Remidia Liquid for Infusion 100mg/20ml	3780	13	48,169
Remidia Lyophilized powder for Infusion 100mg	4800	32	147,795

PQM+ is also guiding Ferozsons to achieve compliance with GMP under PIC/s standards. In June, PQM+ led a detailed five-day on-site visit to Ferozsons to conduct a gap assessment of

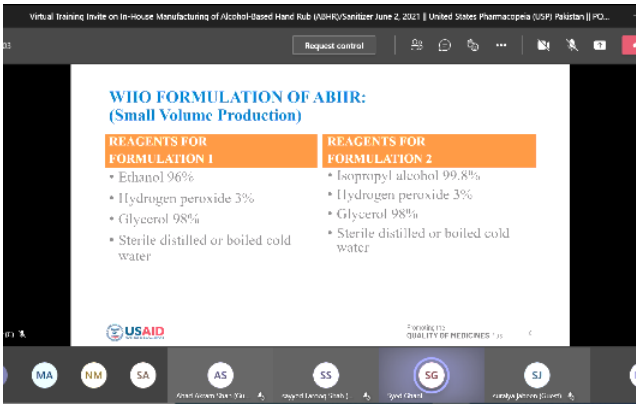
the facility in Lahore. The PQM+ team conducted an assessment of the manufacturing site, its ancillary areas, and the pharmaceutical QMS against PIC/s standards and is compiling a detailed gap assessment report. The team will share key observations and findings from the visit with the Ferozsons management team.

Introduce and implement a QMS in the Pakistan Institute of Medical Science (PIMS) public diagnostic laboratory: PQM+ is strengthening the testing quality of public sector hospitals' diagnostic laboratories by implementing a QMS at PIMS for ISO 15189 accreditation. This accreditation will help ensure quality-assured and accurate testing for the PIMS hospital laboratory and aid the Pakistan government in effectively managing COVID-19 cases. PQM+ conducted a gap assessment of the PIMS lab, along with development of SOPs and lab quality procedures, job descriptions for lab staff according to ISO 15189 standards, and CAPA implementation. PQM+ is filing an application for ISO 15189 accreditation from the Pakistan National Accreditation Council (PNAC) on behalf of PIMS's laboratory.

PQM+ provided on-site training to Pakistan Institute of Medical Sciences (PIMS) laboratory staff on ISO 15189 requirements in April.

Conduct consultative meeting to develop an RB-PMS plan for COVID-19 products based on the existing RB-PMS framework with DRAP and regions: To protect patients from SF medical products, PQM+ is working with regulators to implement risk-based quality surveillance and inspection by developing and implementing a National Action Plan for RB-PMS for COVID-19 supplies. DRAP has issued an official notification for provincial implementation of the National Action Plan on RB-PMS for COVID-19 products. PQM+ will disseminate the surveillance plan after receiving approvals from all provinces. Implementation of this PMS plan for COVID-19 medical products by provinces would help ensure a supply of quality medical supplies in Pakistan during the COVID-19 pandemic.

Build capacity of public sector tertiary care hospitals for in-house manufacturing of alcohol-based hand rub (ABHR): Local consumption of ABHR, also called hand sanitizer, has increased significantly due to the COVID-19 pandemic. This is particularly the case in tertiary care hospitals, where daily utilization totals hundreds of liters. As costs increase, so does a pressing need for public sector hospitals in Pakistan to sustainably produce quality ABHR. PQM+ hosted a virtual training for public sector hospital staff across Pakistan on in-facility production of ABHR on June 2. Topics included key recommendations by the WHO and USP, formulations, manufacturing steps, labeling, and quality control testing. This training will help build the capacity of public sector tertiary care hospitals in Pakistan to manufacture sanitizer in-house and help them improve the prevention and control of COVID-19 infection.



PQM+ hosted a virtual training on in-house manufacturing of alcohol-based hand rub (sanitizer) in June for public sector hospitals across Pakistan.

Support the provincial health care commissions to ensure that private sector health care facilities engage in vaccine vigilance and AEFI surveillance reporting: DRAP has issued EUA for COVID-19 vaccines in response to applications from importers in Pakistan, albeit with limited clinical trial data. The chance of adverse events following immunization (AEFI) is more likely when safety data is limited. It is imperative to monitor and record all adverse events, in addition to creating a system to reduce such events. Moreover, coordination with both the private and public sectors is necessary to develop a comprehensive system of AEFI reporting for effective use of data in decision-making. PQM+ held an inception meeting with the CEO of the Punjab Healthcare Commission (PHC) to share proposed COVID-19 AEFI activities to develop an AEFI reporting system. Establishment of an AEFI reporting system for public and private sector hospitals will enable the Pakistan government to effectively conduct vaccine vigilance and take necessary actions in case of any side effects experienced as a result of the COVID-19 vaccine, in addition to ensuring vaccine safety and acceptance in Pakistan.

Serbia

In August 2020, PQM+ began working with the Government of Serbia (GOS) to respond to the COVID-19 pandemic. The program is helping the GOS explore options for external evaluation and market entry of the enzyme-linked immunosorbent assay (ELISA) test kit produced by the Institute for the Application of Nuclear Energy (INEP) at the University of Belgrade to regional and/or international markets and investing in and expanding manufacturing when sufficient market opportunities exist. Specifically, PQM+ was tasked with:

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

This quarter, PQM+ worked with *Institut Pasteur Dakar* (IPD), the third-party lab in Senegal, to complete the independent evaluation of INEP's ELISA kit. IPD is part of a network of highly qualified labs curated by two PQM+ sub-partners, the Global Health Impact Group (GHIG) and London School of Health and Tropical Medicine (LSHTM). In March, IPD performed the evaluation of INEP's ELISA kits. During this time, PQM+ finalized contract and payment details, held calls with GHIG to discuss timelines, and generally facilitated information-sharing between INEP and IPD. IPD completed the evaluation in late March and submitted the evaluation report to GHIG for review on April 7.

After GHIG reviewed the report in April, PQM+ hosted calls with all involved parties on May 5 and May 17 to present preliminary results to INEP. Overall, the results found that INEP's ELISA kit met the acceptable sensitivity thresholds set by WHO, but the specificity of kits needed improvement, specifically if INEP wanted to market the kits in Africa.

Based on feedback, IPD and GHIG worked to prepare the final report with clarifications from INEP and submitted the final report to PQM+ on May 25. PQM+, GHIG, and LSHTM presented these results to USAID on June 2. Based on that meeting, IPD performed an additional relative operating characteristic (ROC) analysis, understanding that adjusting for specificity will affect sensitivity. Because of the high number of invalids, IPD also had additional results on the analytical specificity from the immunoglobulin G (IgG) plates and ran the plate from a different lot, enabling lot-to-lot comparison. These results are in the final deliverable.

Finally, PQM+ also worked on finalizing the market assessment drafted the previous quarter. PQM+ completed a technical review of GHIG's first draft of the market demand/ competitiveness assessment and sent its comments to GHIG to review. In early March, PQM+ held calls with GHIG to discuss the market demand/ competitiveness assessment and any lasting questions before finalization. During these calls, the parties decided that it would be useful for GHIG to provide a deeper analysis of costs and costs margins for the ELISA kit, scale-up, uptake, and competition. These are important drivers to bring INEP's ELISA kits to market. GHIG reached out to INEP to obtain more information relating to this and worked to incorporate INEP's feedback, as well as any information from IPD's performance and feasibility study. After incorporating the feedback, the team finalized the assessment report. In the report, PQM+ suggests potential pricing strategies, the importance of WHO prequalification, potential market entrances, and ways to market ELISA to the most relevant audiences. Both INEP and the USAID/Serbia Mission said they were satisfied with the findings and recommendations in this report. With both deliverables completed, PQM+ submitted a final project report to USAID and closed out program activities in early June.

Uzbekistan

COVID-19 cases continue to rise in Uzbekistan, making it critical to ensure that COVID-19 vaccine(s) are available faster for the country's population. Facilitating the establishment of EUA for COVID-19 vaccine(s) provides an expedited regulatory approval pathway allowing health authorities to make the product available for medical use. PQM+ is providing technical assistance to the Development of the Pharmaceutical Industry (the Agency), including the State Center on Expertise and Standardization of Medicines, Medical Equipment, and Medical Devices (the State Center) in developing a system for EUA by conducting a preliminary assessment of existing in-country guidelines and procedures, developing SOPs and guidelines, and providing trainings to Agency staff. The guidelines will be regulatory tools to prepare the Agency for future public health emergencies as part of Uzbekistan's plan to ensure access to quality, safe, and effective medical products during emergencies. Under this activity, PQM+ is tasked with the following sub-activities:

1.1 Conduct a desk review of existing in-country guidelines and documentation of best practices (in-country, regional, and international) for COVID-19 vaccine(s) EUA.
1.2 Support the Agency to develop/update guidelines for EUA and corresponding SOPs, including public-facing information and guidance to industry.
1.3 Train Agency staff on the guidelines and SOPs for EUA of COVID-19 vaccines, including EUA review and oversight of EUA conditions.

PQM+ received USAID approval to move forward with activities in early May and met with the Agency's registration department and management to present an overview of EUA. The discussions confirmed the country currently has no EUA system. The COVID-19 vaccines that are currently present (ZF-UZ-VAC-2001, AstraZeneca, and Sputnik V) were authorized by waiving the registration requirement. Following the presentation, PQM+ shared a summary document explaining the concept of EUA and provided corresponding WHO and U.S. FDA resources. Afterward, PQM+ conducted a virtual training for the registration specialists on EUA. A formal working group has been established at the MRA and will begin work to draft the specific SOPs, as well as explore what changes are needed in the Resolution of Cabinet of Ministers #213 document.

With the increasing availability of COVID-19 vaccines in Uzbekistan, it is critical to monitor them through an active safety surveillance system. PQM+ is supporting the Agency in strengthening

vaccine surveillance systems to ensure the system can detect, investigate, and analyze AEFIs and AESIs to ensure an appropriate and rapid response. According to an assessment, collaboration between the National Immunization Program (NIP) and the MRA is weak on AEFI surveillance and a need for clear definition of roles and responsibilities exists to avoid duplication of efforts or gaps in AEFI information for regulatory decisions from the MRA. Under this activity, PQM+ will review the current processes and procedures in place for coordination between the NIP and the MRA on AEFI surveillance through document review and consultation with stakeholders to identify gaps that will help in developing targeted interventions. Also, in consultation with national stakeholders, PQM+ will support the Agency to define roles and responsibilities and information flow and to develop procedures for coordination between MRA, NIP, and other institutions involved in AEFI surveillance. In addition, PQM+ will provide technical assistance to the MRA to secure mechanisms to share COVID-19 vaccine safety data with the relevant international partners (e.g., WHO). This quarter, PQM+ identified a pharmacovigilance consultant on a competitive basis. The consultant will begin work in July.

New Buy-Ins

Table 6: Summary Discussions with USAID for Priority Activities for Future Funding

USAID Team	Summary and Next Steps
Kazakhstan COVID-19 Vaccine Activity	Discussions with the Mission point of contact are ongoing to finalize the scope for the COVID funding. A consultant was identified, but the procurement is on hold pending finalization of the project scope.
Madagascar	PQM+ received work approval and funding in late-May 2021. Once approval was received, the team worked on hiring in-country consultants and conducting introductory calls with stakeholders.
Rwanda	PQM+ received work plan approval in June 2021. Once approval was received, the team worked on hiring in-country consultants and conducting introductory calls with stakeholders.
Tajikistan	PQM+ received funding for Tajikistan in June 2021 and is drafting a work plan for activities.

Progress by Health Elements

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.

In Q3, PQM+ hosted a medical devices regulatory workshop for field office staff and the USAID team based in Washington, D.C., on May 25 and 26. The workshop delivered an overview of the regulatory framework and quality system for medical device development and manufacturing, followed by a panel discussion with medical device innovators that uncovered challenges in interpreting regulations and requirements to gain market authorization in LMICs. The panel

participants included Sisu Global Health, PATH, Equalize Health, Monash University, and Rice University.

PQM+ continued support to Core Flex partner Muhimbili University in Tanzania, which is conducting the amoxicillin dispersible tablet (DT) manufacturing landscape analysis in Africa. The overall response rate remains low at 27 percent, even after five follow-ups with manufacturers as well as leveraging PQM+ in-country staff. The low response rate can be attributed to generalized versus specific contact information accessed from the company websites, staffing shortages, lack of interest, business closures, company focus on high-volume products, and acquisitions. PQM+ is leveraging USAID MNCH and UNICEF contacts from the list of manufacturers identified to boost survey uptake. In the interim, Muhimbili University is working on data analysis and writing the report to be sure to meet the subaward deadlines.

PQM+ continued to engage with the UNICEF supply team this quarter. The teams met June 14 to provide updates on their priority activities. PQM+ shared the list of manufacturers and countries identified for the amoxicillin DT manufacturer landscape analysis with UNICEF to validate the contact list and address the low response rate. PQM+ also shared the list of companies currently receiving PQM+ support with UNICEF to support manufacturers for tender purposes. UNICEF agreed to share an updated tender calendar for PQM+ to explore joint audits as an observer for the manufacturers supported by PQM+. The parties agreed that a memorandum of understanding (MOU) is needed for information-sharing of sensitive data. PQM+ began drafting the MOU to share with UNICEF for review, discussion, and finalization. The next meeting is planned for Quarter 4.

On its website, PQM+ posted the English and French versions of the documents developed to support MRAs to strengthen PMS, dossier preparation, and laboratory quality control activities for MNCH products. These included a guidance document on the risk-based categorization of MNCH products and aids to assist with dossier preparation and laboratory testing for amoxicillin, chlorhexidine 7.1% gel, and oxytocin injection.

Neglected Tropical Diseases (NTDs)

Building on Q2 progress, PQM+ continued collaborating closely with Muhimbili University in Tanzania on the NTD medical product manufacturer market analysis. Muhimbili University began data collection on the manufacturer bulk procurement analysis for NTD products, but the survey response rate remains low due to the lack of incentives for manufacturers to participate. For the manufacturer landscape analysis, PQM+ revised the survey methods based on the lesson learned from the bulk procurement survey to boost survey uptake by validating contacts, redesigning the questionnaire, and tracking views. The data collection is planned to start in Quarter 4.

The subaward for Mahidol University in Thailand was approved on May 15 for the manufacturer landscape analysis and bulk procurement analysis in Asia. PQM+ and Mahidol finalized the survey questionnaire and the introductory letter for the manufacturers. Mahidol has also identified local manufactures in the countries of interest. Mahidol did not identify any manufacturers of NTD medical products in Brunei or Bhutan. The survey is awaiting internal review board (IRB) approval before data collection can begin.

PQM+ identified a consultant to develop the NTD dashboard and fully approved a contract with the consultant this quarter. The tool is in the design phase before proceeding to development. PQM+ continues to be in communications with the WHO NTD team, UNICEF, Drugs for Neglected Diseases Initiative (DNDi), and UNITAID for potential dashboard data.

PQM+ participated in the Virtual CPhI conference May 17 through 28 to identify NTD manufacturers with a need for WHO PQ support to boost supply. PQM+ identified two potential manufacturers for ivermectin and will invite them to respond to an expression of interest to manufacture specific NTD products in Quarter 4.

PQM+ repackaged the GMP e-learning course to make it easier for users to complete, to include offline modules, and to enable collection of more data on user feedback. The revised version is available live and PQM+ disseminated it through several platforms, including the PQM+ website, social media, and the USAID Health Systems Strengthening (HSS) distribution network.

Tuberculosis (TB)

PQM+ is working to ensure an 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

The development and introduction of new TB medicines and novel TB treatment regimens are essential for achieving the Sustainable Development Goals and ending the TB epidemic. In recent years, three new TB medicines (bedaquiline, delamanid, and pretomanid) were introduced, and a large pipeline of new TB medicines and regimens are in varying stages of clinical research. In this evolving situation, it is important that national medicines regulatory agencies (NMRAs) stay engaged and ensure timely review and approval of the new TB medicines to ensure access to these life-saving products. In recent years, NMRAs in some countries at times have faced challenges in timely reviews and approval of new products due a lack of corresponding experience and procedures.

To address this challenge, PQM+ started collaboration with the U.S. Food and Drug Administration (U.S. FDA) to organize an online workshop for representatives of MRAs from high-burden TB countries, at which the U.S. FDA will share experiences on the regulatory review of the new TB medicines. In Q3, PQM+ developed a questionnaire and engaged the NMRAs of select low- and middle-income countries (LMICs) to identify topics of interest for the workshop. As a result, PQM+ compiled topics and developed a draft program. In Q4, PQM+ will work with U.S. FDA on organizing a workshop.

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

In Q3, PQM+ continued to support to the two pharmaceutical manufacturers of first-line, fixed-dose combination (4FDC) TB medicines in Pakistan. In Q3, PQM+'s technical assistance to one manufacturer enabled the finalized compilation of a dossier, including the report on a completed stability study. The dossier was submitted to the WHO PQ team, which accepted it. This is an important milestone toward prequalification of the product and ensuring that TB patients in Pakistan have access to quality-assured TB medicines. PQM+ will continue to provide

assistance through full prequalification of the product. In addition, with approval from USAID, PQM+ is working toward supporting the manufacturer to pay for the WHO dossier review fee.

Further development of the analytical methods to detect nitrosamine impurities in two priority anti-TB medicines, rifapentine and rifampicin continued in Q3. The results of this work will be of assistance to manufacturers and regulators especially in LMICs. Following the validation protocol developed in Q2, PQM+ was able to show the gas chromatography-mass spectroscopy/mass spectroscopy method was able to selectively detect individual nitrosamines impurity standards at the required detection and quantitation levels. However, when applying the method to an actual rifapentine tablet, the nitrosamine impurity co-eluted with an ingredient in the tablet thereby making the nitrosamine impurity undetectable. In Q4, PQM+ will make modifications to the method conditions to resolve the co-elution issue in rifapentine tablets. Subsequent work will then move forward with the nitrosamine impurity in rifampicin tablets. If efforts using the gas chromatography-mass spectroscopy/mass spectroscopy method is unsuccessful, a liquid chromatography-mass spectroscopy/mass spectroscopy method will be applied. In Q3, PQM+ provided ongoing technical guidance and monitoring of the Virginia Commonwealth University (VCU) subaward for the laboratory phase on optimizing the rifapentine API manufacturing process. It is expected that the laboratory phase will be completed in Q4. PQM+ developed a concept note and budgetary need for the next phase, which includes scaling up the synthesis process. The program submitted the concept note to USAID for approval.

Priority Activities for Next Quarter

Next quarter, PQM+ will:

- Follow up with the manufacturer in Pakistan to ensure the finalization of the stability study reports and the submission to WHO;
- Follow up with the manufacturer in Pakistan to ensure initiation of the WHO dossier review and adequate support to the manufacturer to respond to WHO questions and queries;
- Continue to refine the proposal for Phase 2 of the optimization of manufacturing process for rifapentine, on scaling up the proposed synthetic process and technology transfer; and
- Prepare for the U.S. FDA workshop with the pharmaceutical regulatory authorities on sharing U.S. FDA's experience on the review and registration of new TB medicines.

Program Support

Communications

This quarter, PQM+'s communications activities grew considerably, particularly in the areas of social media, country communications support, and website development. The two-person communications team supports all editorial and communications efforts of the program, which now includes 20 countries as well as an extensive COVID-19 portfolio. This quarter, PQM+ leadership approved the hiring of a communications specialist and recruitment will begin in Q4.

- In April, PQM+ held its second **webinar** on Strengthening NQCLs. PQM+ experts explained NQCLs and unpacked their critical, central role in helping countries' regulatory authorities ensure the safety and efficacy of medical products circulating in their

markets. A total of 198 people registered for the webinar and 102 attended, many of them from USAID missions. HQ also supported PQM+'s Kenya team as they developed a joint webinar on generic medicines with EPN.

- PQM+ disseminated its third program **newsletter** in late May, featuring Bangladesh's PPE activities, the WHO PQ of the NTD medicine praziquantel 600mg film-coated tablets, the updated online GMP course, and a link to the NQCL webinar. The newsletter continues to perform extremely well, with a 46 percent open rate and a 16 percent click rate. The next newsletter will be sent in August.
- PQM+ continued to share its activities and progress via three **social media** platforms - Twitter, LinkedIn, and Facebook. This quarter, the program shared 40 posts highlighting a wide variety of countries and activities, including the WHO PQ of the NTD medicine, Pakistan's COVID-19 work, and Uzbekistan engagement with the private sector. When hired, the new communications specialist will assist in increasing the program's social media engagement.
- The new MNCH **factsheet** was posted to the PQM+ page this quarter along with the new MNCH job aids, which are available in French and English, and are designed to support MRAs to strengthen PMS, dossier preparation, and laboratory quality control activities for MNCH products. All products were disseminated via social media and will be shared in the next newsletter and via email to specific MNCH contacts.
- The senior communications manager has been regularly attending USAID's NTD team meetings to support the dissemination of the **GMP online course**. The link to the new course was shared via the newsletter, social media, the HSS network, targeted emails to Nepal and Nigeria contacts, and inclusion in webinar materials.
- The senior communications manager also supported several **country teams** with their communications efforts, including Central Asia, Kenya, Mali, Liberia, and Pakistan. She drafted or rewrote success stories for the Kenya, Mali, and Pakistan teams and continues to work with them to confirm facts and revise language before submitting to USAID for review. She also trained the new Central Asia program associate in how to identify and develop social media posts for their USAID client and is working with the Liberia team to screen candidates to fill a new communications consultant position to support LMRHA.
- The senior communications manager coordinated with USP's **website** manager to revamp the existing PQM+ page on the USP corporate website to make it easier to find resources, particularly the Guidance on Development and Manufacture of Chlorhexidine Digluconate (7.1%) Gel, the updated GMP online course, and the new MNCH resources. In addition, she liaised and coordinated with USP's IT, Website and Design teams to determine next steps on the new PQM+ website and develop a timeline.