

Promoting the
QUALITY OF MEDICINES Plus

PQM+ Quarterly Report – Program Year 3, Quarter 1



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About PQM+

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

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Acronyms

AEFI	adverse events following immunization
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	WHO Global Benchmarking Tool for evaluation of national regulatory systems
GMP	Good Manufacturing Practice
HPLC	high-performance liquid chromatography
HR	human resources
ISO/IEC	International Organization for Standardization/ International Electrotechnical Commission
LIF	laboratory information file
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
MSP	model strategic plan
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
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

Letter from the Director



At the time of award in September 2019, the Promoting the Quality of Medicines Plus (PQM+) program had a mandate to increase the supply of quality-assured essential medical products of public health importance. The COVID-19 pandemic has highlighted the importance of building local manufacturing capacity in low- and middle-income countries (LMICs), given the health dangers of depending on imported medicine.

This Program Year 3, Quarter 1 report highlights efforts by PQM+ to collaborate with public and private stakeholders to stimulate local production. Innovatively, PQM+ performed the first fully remote Good Manufacturing Practices (GMP) inspection at ACI Healthcare Ltd. in Bangladesh in October. With PQM+ technical support, Pakistan manufacturer Ferozsons increased local production of the COVID-19 treatment remdesivir and expanded exports to several countries, adding to earlier successes in Pakistan with personal protective equipment production and export.

Additional quarter highlights are the program's technical assistance to PT Sanbe in Indonesia to receive WHO prequalification (WHO-PQ) for levofloxacin, and support to Medopharm Pvt. Ltd. in Chennai, India, for praziquantel, which led to a successful WHO-PQ site inspection in November.

These successes are a testimony of our commitment to respond to emerging global health priorities through innovative support to local manufacturers. In the coming quarter, PQM+ will continue to support local production of COVID-19 medical products through technical discussions with other key stakeholders. The second part of our webinar series titled "Playing the Long Game: How Can Strengthening Medical Product Regulatory and Manufacturing Systems Help Countries Respond to COVID-19 and Future Health Crises?" will occur in March and we look forward to collaborating with our technical partner Howard University to co-host a West African regional webinar aimed at capacitating manufacturers in key areas.

This quarter, our team expanded to ensure technical and operational excellence to implement activities related to COVID-19 and other areas. **Dr. Joel Keravac** joins us as technical director for PQM+. He has held management and technical leadership positions at the Brazilian medicines regulatory agency (ANVISA), Management Sciences for Health (MSH), the Global Drug Facility, the Drugs for Neglected Diseases initiative (DNDi), and the Pan-American Health Organization (PAHO). He brings expertise in laboratory services, product development, product supply, and regulatory systems. Additionally, he has experience implementing USAID cooperative agreements and managing donor support to low- and middle-income countries (LMICs). In December, **Dr. Sameh Saleeb** joined as director of technical process quality. A public health physician with 30 years of experience, he has supported global health programs aimed at strengthening national pharmaceutical systems in LMICs to address global health priorities. He has held leadership positions at MSH, Chemonics International, and Africare. Quality assurance and compliance expert **Angela Oliver** also joined the program to lead the operational implementation and continuous improvement activities of PQM+ laboratory programs technical deliverables across core and country portfolios. Finally, strategy expert **Ian Warthin** joined as a senior advisor to lead our work in pharmaceutical sector strategic planning.

Our partnerships remain our cornerstone as we continue in our mission to ensure that quality-assured medical products are available to those who need them most. As always, we invite you to follow our progress.

Jude I. Nwokike
Director, Promoting the Quality of Medicines Plus

Executive Summary

At the start of Program Year 3, the Promoting the Quality of Medicines Plus (PQM+) program is working with 21 low- and middle-income countries (LMICs) to sustainably strengthen their medical product quality assurance (QA) systems. PQM+ helps ensure access to quality-assured essential medicines for HIV/AIDS, tuberculosis (TB), malaria, neglected tropical diseases (NTDs), COVID-19 and other infectious diseases as well as for maternal, newborn, and child health (MNCH).

The report that follows summarizes activities during Quarter 1 (October 1 to December 31, 2021) by objective and funding source (USAID country Missions and USAID/Washington). All activities align with at least one of PQM+'s five program objectives detailed in the Results Framework (Figure 1).

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

Governance. The PQM+ program has engaged in governance-strengthening activities in many of the countries. Our work has included the development, dissemination, and implementation of strategic plans, quality assurance policies, and legal frameworks and/or regulations to increase the availability of and access to quality-assured medicines. The program is helping countries develop **pharmaceutical sector development strategic plans** in Burkina Faso, Kenya, Liberia, Mali, Nigeria, and Nepal. We are providing technical assistance to the Ministry of Health (MoH) of Uzbekistan in developing the “pharmaceuticals and medical devices” strategic block of the MoH’s Health Strategy 2030, while Bangladesh is assessing and refining its regulatory framework to address recommendations in its **Global Benchmarking Tool (GBT) institutional development plan (IDP)**. These types of activities and progress illustrate that many countries supported by PQM+ are advancing plans to define the future state of their regulatory and quality assurance systems and assume long-term ownership and ability to sustain them over time.

Similarly, we worked with the Drug Regulatory Authority of Pakistan (DRAP) to revise that agency’s five-year strategic objectives with the goal of promoting **transparency and consistency in regulatory processes**. This document will foster improvement in DRAP’s operations and performance, which are essential for it to be considered fully functional and stable per the World Health Organization’s GBT.

Regulatory systems strengthening. PQM+ supports countries to improve their regulatory systems as assessed by the WHO GBT, which identifies gaps and weaknesses in a country’s regulatory system. During the quarter under review, we supported six regulatory functional areas in Bangladesh, Ethiopia, Kazakhstan, Nigeria, Pakistan, and Rwanda to facilitate their progress toward achieving WHO Maturity Level 3. While the majority of our support is in the area of laboratory testing, many PQM+ countries continue to show strong interest in market surveillance and control (MC) through establishing or strengthening risk-based post-marketing surveillance (PMS) systems to help monitor the quality of medicines circulated in their markets. PQM+ is building the capacity of PMS technical working groups in nine countries.

We are supporting risk-based PMS (RB-PMS) of medical products in the following countries:

- Antimalarials: Benin, Burkina Faso, DRC, Ethiopia, Ghana, Guinea, Kenya, Liberia, Madagascar, Mali, Nigeria, and Senegal.
- Family planning/reproductive health: Bangladesh, Ethiopia, Madagascar, Nepal, and Rwanda.
- HIV and AIDS: Mozambique.
- Maternal and child health: Bangladesh, Ethiopia, Ghana, Guinea, Kenya, Liberia, Madagascar, Mali, Nepal, Nigeria, and Rwanda.
- Tuberculosis: Bangladesh, Kazakhstan, and Uzbekistan.

In Ethiopia, PQM+ provided technical assistance to the Medicine Registration and Licensing Directorate in developing post-approval variation guidelines for registered vaccines. This marks the first time PQM+ is supporting a regulatory agency to develop post-approval variation guidelines. Post-approval variations are common in the pharmaceutical industry; changes related to manufacturing sites, manufacturing processes, specifications, sourcing of active pharmaceutical ingredients (APIs), and container closure systems account for the majority. Some of these changes may require prior approval by the regulator, as they may have significant impact on the quality of the product.

PQM+ continued working with several countries to implement RB-PMS activities to optimize limited resources while continuing to monitor the quality of medical products in local markets. We continue to deploy our MedRS tool, which helps MRAs develop risk-based sampling strategies to support national PMS programs, in more countries that we support. To date, 11 PQM+ countries have requested access to this tool and have used or are now using the tool to develop an RB-PMS protocol. Interest in MedRS is high, with four countries that do not receive support from PQM+ also seeking to use the tool.

As part of USAID's **ongoing response to COVID-19**, PQM+ finalized and widely disseminated two practical guidance documents on emergency use authorization (EUA) for [vaccines](#) and [in vitro diagnostics \(IVDs\)](#). Countries can learn from our examples of Pakistan and Uzbekistan, where authorities used global regulatory reliance pathways to expedite the availability of and access to lifesaving COVID-19 medical products, and Bangladesh, which is conducting risk-based PMS for COVID-19 products.

In other efforts to **promote regulatory reliance**, we are helping medicines regulatory authorities (MRAs) develop and strengthen frameworks they can use to expedite the availability of and access to life-saving medicines and vaccines. In Uzbekistan, PQM+ advocated and provided technical assistance for the adoption and use of the WHO Collaborative Registration Procedure (CRP) for accelerated registration of WHO-prequalified (WHO-PQ) medicines. Uzbekistan successfully used CRP to approve two TB medicines, cycloserine and protionamide. This time-saving and cost-reducing approach can serve as a model for other countries.

Our program objectives include a focus on workforce development. This quarter, PQM+ incorporated the draft WHO global competency framework for regulators into two training needs assessments, as well as added some elements pertaining to the quality of labs. Implementation took place at the Rwanda Food and Drug Administration (FDA) and in Nepal at the Department of Drug Administration's inspection and post-marketing surveillance units and at the Nepal Medicines Library. PQM+ works collaboratively with its country partners, empowering them to articulate, refine, and document practices and tools that will strengthen and sustain their workforces.

National quality control laboratories (NQCLs) play a critical function in the regulatory quality assurance system, as testing results inform decision-making across multiple areas. From market authorization to investigation of product complaints, the NQCLs provide vital data needed to enforce regulatory actions. This quarter, PQM+ equipped staff in 11 countries to enhance and broaden their understanding and skills in performing physical-chemical and microbiological testing to assure medicines quality. Ethiopia is leveraging its quality system development knowledge gained under PQM+ to build capacity in three of its branch laboratories, extending its ability to confirm the quality of medicines in remote areas. In Pakistan, we are working to create a network of accredited entities to support NQCLs. To increase efficiency and reduce costs, our team is working toward accreditation of a proficiency testing provider and certification body to provide services to the NQCLs.

PQM+ is also building momentum in its efforts to strengthen medical laboratories. This quarter, we helped the Public Health Laboratory (PHL) in Lahore, Pakistan, take additional steps toward ISO 15189 accreditation, the international standard for medical laboratories quality and technical competency confirmation. PHL responded to pre-assessment observations from the Pakistan Nation Accreditation Council (PNAC) for its development and implementation of a medical testing quality management system with the capacity to comply with international standards. This will aid Pakistan in reliably providing accurate results for testing of maternal and

child health (MCH) conditions and diseases like COVID-19, TB, hepatitis C, and typhoid fever, enabling effective treatment of patients.

Supply. PQM+ is collaborating with several countries to build their capacity to **manufacture medical products locally**. During Q1, we supported 11 manufacturers in the production of 12 products in six countries. PQM+ continues to work with two manufacturers in Ghana on artemisinin-based combination therapies (ACTs) to treat malaria, and we are supporting Nigerian manufacturers as they work toward WHO-PQ of quality-assured antimalarial and MCH medicines (sulfadoxine+pyrimethamine, zinc sulfate, and magnesium sulfate).

In addition to our activities at the country level, PQM+ continues its core-funded work on **MCH, neglected tropical diseases (NTDs), and TB**. Our partner Muhimbili University in Tanzania is preparing an amoxicillin dispersible tablet (DT) manufacturing landscape analysis report in Africa, with the final report scheduled for dissemination in Q2. We are collaborating with manufacturers toward WHO-PQ for two NTD products, albendazole 400mg tablets and praziquantel 600mg tablets. The WHO-PQ team found the praziquantel manufacturing site compliant with the standards of Good Manufacturing Practices (GMP), and WHO has completed a full assessment of the albendazole 400mg tablets product dossier and requested additional information.

Two TB manufacturers in India are receiving our support to produce WHO-prequalified four-drug fixed-dose combinations (4FDC). One submitted a final dossier for WHO-PQ and the second is updating its 4FDC dossier for submission.

In addition to directly supporting manufacturers, PQM+ is collaborating with WHO to create a **local medical products production strategy** that will be a model for countries and regions to develop their own strategies to locally produce essential medical products. With diligent implementation, such strategies and their associated plans of action will help countries attain sustainable manufacturing of quality-assured medical products and result in the public having improved access to health products. We also supported Ethiopia and Kenya in their progress toward compliance with GMP.

Learning, Advocacy, and Awareness. During Q1, our progress included nine technical publications and presentations across the program. In Ethiopia, PQM+ submitted two abstracts for regional workshops organized by Intergovernmental Authority on Development (IGAD) and the African Union Development Agency (AUDA-NEPAD); both were accepted. PQM+ used the opportunities to disseminate information on the outcomes of USAID's investment in the regulatory and local manufacturing sector in Ethiopia.

PQM+ also conducted its third global webinar, the first in a series about supporting countries to respond to the COVID-19 pandemic. Titled "Empowering Countries to Pivot and Implement New Regulatory Tactics to Ensure Quality Medical Products," the webinar had 110 attendees. The program also finalized visuals and recordings for the online version of the medicines quality assurance module of the **Pharmaceutical Systems Strengthening ("PSS 101") course**, which the Medicines, Technologies, and Pharmaceutical Systems (MTaPS) program hosts on its eLearning platform. In Nepal, PQM+ and DDA worked on public service messages on substandard and falsified (SF) medicines to share through local radio broadcasts.

The accomplishments highlighted here are illustrative of the extensive work PQM+ performed during the first quarter of our third year. We invite you to read a more detailed accounting of our achievements in the report that follows.

Activities and Progress for Cross-Bureau Activities

PQM+ Cross-Bureau activities, funded by USAID's Office of Health Systems (OHS), primarily focus on raising awareness about the importance of medical product quality and developing new approaches to strengthening medicines regulatory functions.

Progress This Quarter

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

PQM+ continues to collaborate with USAID's Medicines, Technologies, and Pharmaceutical Services (MTaPS) program on the common minimum standards for regulatory information management system activity. Following the first consultative meeting with global and national stakeholders like WHO, national NMRAs, African Union Development Agency - New Partnership for Africa's Development, ASEAN and others in September 2021, PQM+ and MTAps held a second meeting with the same stakeholders in Q1 to develop selection criteria for identifying the common minimum standards for regulatory information management systems and to develop a "use case" (determining the stakeholders that will use the common standard and how it will be used) to ensure that document planned for development addresses all user needs.

PQM+ is collaborating with the World Health Organization (WHO) to develop a Model Strategic Plan (MSP) for Regulatory Authorities. The MSP will:

- Enable national medicines regulatory authorities (NMRAs) to operationalize their institutional development plans derived from country Global Benchmarking Tool (GBT)¹ assessments.
- Provide detailed guidance to country NMRAs on proper planning and strategic allocation of resources (managerial, technical, financial, and human).
- Define a stepwise process for successful IDP implementation.

PQM+ developed a concept note and shared it with WHO for feedback; this quarter, PQM+ incorporated WHO's feedback and shared a third version of the concept note with WHO.

PQM+ is also collaborating with WHO to develop a model strategy on local production and health products security to strengthen local manufacturing. This quarter, PQM+ met with WHO to introduce the activity and shared a concept note to secure buy-in.

PQM+ continues to deploy its MedRS tool in more program-supported countries and some non-program countries.

¹ The GBT is a globally accepted assessment tool to rank a country's national medicine regulatory authority maturity level on a scale of 1 (lowest) to 4 (highest) and to undertake reforms following an institutional development plan (IDP) that involves country-led stakeholder/donor coordination. The GBT represents the primary means by which performance of regulatory systems across countries is objectively evaluated to determine their strength. For PQM+, aligning its support to meeting the GBT requirements provides assurance that the investments are ultimately tuned to creating a regulatory pathway that ensures the safety of patients.

- To date, 11 PQM+ countries have requested access to this tool and have used, or are in the process of using, the tool for development of a risk-based post marketing surveillance (RB-PMS) protocol.
- Four non-PQM+ countries (Brazil, Egypt, Botswana, and Sierra Leone) have indicated interest in and requested access to the tool.
 - Hands-on trainings are pending, as no funding mechanism exists for PQM+ staff to support these trainings.
- Transition of the MedRS tool from the temporary developer's server to an Amazon Web Services (AWS) server supported by USP has also commenced; completion is due in Q2, after which the MedRS tool will be hosted and supported by USP's IT team.

PQM+ commenced development of a risk-based inspection (RBI) framework and tool in PY2. The RBI methodology will allow NMRAs to prioritize the selection and inspection of sites based on risk, directing limited resources to manufacturing sites that present the greatest risk to medical product quality assurance. This framework will address all regulatory inspectorate activities in Good Manufacturing Practice (GMP), Good Clinical Practice (GCP) inspections for contract research organizations (CROs), bioequivalence (BE) center inspections, and Good Distribution Practices (GDP) inspections. The beta version of the RBI tool is expected by next quarter.

Objective 3: Optimize and increase financial resources for medical product QA

Since PY 2, PQM+ has been collaborating with three of the program's academic partners (University of Washington, University of North Carolina, and Harvard University) to develop a generalizable model for estimating the health and economic costs of substandard and falsified (SF) medicines to patients (both immediate and long-term outcomes) and to, different parts of the health system (e.g., health system levels, health system building blocks). This model will help health officials estimate how the circulation of SF versions of widely used medicines will affect public health and the economy in their country. They can then make appropriate decisions for remedial interventions, including to safeguard their investment in public health programs.

This quarter, PQM+ launched the SF medicine burden model pilot in Kenya and:

- Met with initial members of the pilot core group to orient them to using the model and the roles and responsibilities of the involved entities.
- Developed orientation materials for the pilot core group and the full working group.
- Drafted the approach to assessing the pilots and the assessment tool.

The pilot is planned for next quarter after orientation and trainings. PQM+ also finalized core partner sub-awards and contracts for the new program year for continued support until the model is finalized.

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

PQM+ worked with MTaPS to translate an in-person course module on quality assurance to a virtual module. In Q1, PQM+:

- Finalized visuals and recordings for the medicines quality assurance module of the Pharmaceutical Systems Strengthening (“PSS 101”) course, which MTaPS hosts on its eLearning platform.

PQM+ conducted a webinar titled “Empowering Countries to Pivot and Implement New Regulatory Tactics to Ensure Quality Medical Products.” The webinar:

- Targeted lay and experienced audiences.
- Recorded 200 registrants and 110 attendees.
- Drew content from experiences in five PQM+ countries (Bangladesh, Burkina Faso, Ghana, Mali, and Pakistan) that implemented regulatory strategies to support a pivot during the COVID-19 pandemic and ensure continuous access to quality-assured medical products. Strategies included:
 - Emergency use authorizations to promote product entry into the countries
 - Ensuring the quality of COVID-19 medical products during distribution
 - RB-PMS to optimize limited resources while continuing to monitor the quality of medical products in the local markets.

Priority Activities for Next Quarter

In Q2, PQM+ plans to:

- Conduct an NMRA engagement meeting for the common minimum standards for the regulatory information management system activity.
- Revise and develop MSP content for IDP implementation.
- Conduct RBI tool beta version testing, incorporate changes to complete the online version, and commence offline tool development.
- Conduct the following sub-activities for the SF modeling activity:
 - Complete orientation of the full pilot core group and the working group in Kenya.
 - Support the data collection process in Kenya as needed.
 - Revise the orientation materials to reflect lessons from Kenya.
 - Launch the pilot in Pakistan.
 - Complete the assessment approach and tool.
- Plan delivery of the PSS 101 course with MTaPS.
- Conduct at least one webinar.

Activities and Progress by Country and Regional Buy-Ins

Africa Region

Benin

PQM+ works with Benin's main regulatory body, the Beninois Agency for Pharmaceutical Regulation, *l'Agence Béninoise de Régulation Pharmaceutique* (ABRP). 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) and at the request of any national institution. PQM+ is helping ANCQ strengthen its quality management system (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 test results.

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+ supported the PMS technical working group (PMS-TWG) in training 14 members (10 men and four women) on the MedRS tool. During the workshop, PQM+ supervised trainees' use of the MedRS tool in conducting risk analysis to help develop the RB-PMS protocol for antimalarial medicines. Members then drafted the RB-PMS protocol for antimalarials.

In addition, PQM+ conducted a training needs assessment to identify areas of analytical testing in which ANCQ requires support. The assessment will help PQM+ design a training curriculum, which the program will implement through September 2022, to close gaps in technical capacity identified in the PY2 baseline assessment.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Continue building the capacity of ANCQ technical staff in specific quality control techniques for testing antimalarials.
- Finalize the RB-PMS protocol for antimalarials.
- Train medicines samplers on the RB-PMS protocol and sampling strategies.

Burkina Faso

A 2018 decree created the national pharmaceutical regulatory authority, *L'Agence Nationale de Régulation Pharmaceutique* (ANRP), to strengthen the regulatory framework of the pharmaceutical sector in Burkina Faso. The Directorate of Market Surveillance and Quality Control of Health Products at ANRP is the technical body in charge of quality assurance (QA) and quality control (QC). ANRP collaborated with the Directorate for the Control of Drugs and

Non-food Products (DCM/PNA) within the *Laboratoire National de Santé Publique* (LNSP) to conduct sampling of medical products. In 2021, with PQM+ support, an official collaborative framework was established between LNSP and ANRP.

PQM+ works with ANRP through the PMS-TWG to strengthen its market surveillance function. The program is also improving LNSP's QMS to conform with ISO/IEC 17025 standards and strengthening the capacity of technical analysts to conduct quality testing.

PQM+ spent most of Q1 developing and kicking off an implementation plan for the program year.

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+ monitored confirmatory testing of 320 antimalarial samples of artesunate, artemether, and quinine injections as well as sulfadoxine/pyrimethamine tablets. Samples were taken from seven regions (Central, Central-East, Central-North, East, Haut-Bassins, North, and Plateau Central). LNSP completed confirmatory testing of 82 samples in November; the TWG (which includes LNSP) is preparing the report.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support the PMS-TWG in disseminating the RB-PMS results.
- Conduct a situational analysis for development of LNSP's strategic plan.
- Conduct a baseline assessment of LNSP.
- Train and provide supportive supervision to LNSP on equipment maintenance.

Democratic Republic of Congo (DRC)

Widespread availability and distribution of non-quality-assured artemisinin combination therapies (ACT) and non-artemisinin therapies² in DRC underscore the need for strong medicines regulatory systems, including PMS. In PY2, PQM+ began working with the Congolese Pharmaceutical Regulatory Authority (*Autorité Congolaise de Réglementation Pharmaceutique*, or ACOREP) and its National Quality Control Laboratory – Pharmaceutical Laboratory of Kinshasa (*Laboratoire National de Contrôle de Qualité – Laboratoire Pharmaceutique de Kinshasa*, or LNCQ-LAPHAKI).

² <https://malariajournal.biomedcentral.com/articles/10.1186/s12936-016-1659-x>

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 the quarter, PQM+ conducted a workshop for medicines samplers on the RB-PMS protocol for antimalarial medicines, good sampling practices, tools for sampling, and plans for sampling missions. PQM+ then supervised the sampling and collection of at least 300 samples of antimalarial medicines from Kinshasa, Maniema, and Tsopo.

To assure best practices in sample screening, PQM+ with ACOREP/DPM trained LNCQ-LAPHAKI staff on use of the MiniLab™ kit. By the end of December, LNCQ-LAPHAKI had screened all PMS samples and completed 50 percent of confirmatory testing.

PQM+ conducted four quality control training sessions for technical personnel of LNCQ-LAPHAKI. The sessions were on dissolution and UV-visible spectrophotometry (10 men, seven women trained each session); high performance liquid chromatography (10 men, eight women trained); and infrared spectrometry (12 men, nine women trained).

As part of building the capacity of LNCQ-LAPHAKI per the ISO/IEC 17025 accreditation roadmap, PQM+ supervised a management review meeting between technical personnel and LNCQ-LAPHAKI management and ensured that LNCQ-LAPHAKI applied its procedures and processes for convening the meeting. Participants at the meeting discussed the findings of the last QMS assessment conducted by PQM+, plans to implement the CAPA, and the resources required from management.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Monitor confirmatory testing of antimalaria samples.
- Support the PMS-TWG in disseminating the RB-PMS results.
- Continue building the technical capacity of LNCQ-LAPHAKI.

Ethiopia

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 mandates between EFDA and the regional regulatory bodies (RRBs), the absence of a formal reporting relationship between EFDA and those regulators, and the latter's poor capacity compromise proper regulatory oversight of medical products circulating in Ethiopia.

PQM+ works with EFDA and the RRBs to build capacity to monitor medical product quality across the supply chain and strengthen their collaborative working relationship. PQM+ also helps build local manufacturers' capacity to meet international standards, ensuring that locally produced medical products are of good quality and not harmful to end users.

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

Effective regulation of medical products, using appropriate regulatory tools and norms, promotes and protects public health by ensuring medicines quality, safety, and efficacy; promoting the adequate manufacture, storage, and distribution of medicines; and strengthening the fight against SF products. In Q1, PQM+ provided technical assistance to the Medicine Registration and Licensing Directorate in developing guidelines on:

- Post approval variation guidelines for registered vaccines.
- Reliance of regulatory decisions, based on other countries' regulatory authority reports.

This quarter, as a member of the TWG to assess EFDA's quality management system (QMS), PQM+ supported the regulatory authority to conduct a self-audit in preparation for the to-be-scheduled formal GBT assessment by WHO to determine its maturity level. In this work, PQM+:

- Provided TA in self-assessment of the various regulatory functions, with the goal of:
 - Determining the status of each regulatory function.
 - Identifying gaps.
 - Developing an IDP to rectify the gaps.
 - Implementing the IDP (with the aim of achieving WHO Maturity Level 3) prior to formal assessment by WHO.
- Used the GBT tools to support the self-benchmarking assessment of four regulatory functions:
 - Licensing establishment (LE).
 - Regulatory inspection (RI).
 - Market surveillance and control (MC).
 - National Regulatory System (RS).

Results of the self-assessment are being compiled.

To prepare the EFDA branch laboratories for accreditation, PQM+ procured an ultrasonic sonicator for each laboratory. Sonicators serve various purposes, including mixing, extraction, and homogenization of samples. PQM+ was following up the procurement of this equipment as part of progressively meeting the requirements for ISO 17025 accreditation of branch laboratories. This quarter, progress on this included:

- Equipment was shipped, cleared customs, and was delivered to the EFDA.

Despite the delayed delivery due to logistical challenges associated with COVID-19, the equipment should enhance the testing capacity of branch labs and address a main challenge the laboratories have experienced in the past (high-performance liquid chromatography analysis).

The presence of accredited laboratories at branches will substantially improve EFDA's capacity to detect substandard and falsified medical products circulating in the Ethiopian market by

conducting regular PMS with a broader geographic and product coverage. Preventing poor-quality products from reaching the public will have enormous public health outcomes and contribute to saving lives.

This quarter, EFDA's QC lab team completed testing of PMS samples collected in PY2 Q3, using the risk-based approach. Notable progress included:

- Antimalarial medicines and oxytocin were among the products tested, with 70 samples (53 antimalarials and 17 oxytocin) collected.
 - The protocol called for collection and testing of 250 product samples. 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.
- Test results indicate that all antimalarial products passed quality requirements, but one of the 17 oxytocin products (6.7 percent) failed.
- The final report writing and dissemination of results will take place in Q2.

Given the low number of samples tested and limited geographic coverage, this result does not provide an accurate picture of SF products in the country. The low failure rate must not be interpreted as an absence of SF products in Ethiopia. Given current security challenges and the destruction of health facilities in the northern part of the country, significant potential remains for infiltration of SF products to fill the gap left by the continuing lack of access to medicines in those regions. These products may then filter out to the rest of the country. Another round of PMS will begin in Q3.

This quarter, PQM+ trained new employees of EFDA's QC laboratory and delivered refresher training to existing staff at the branch laboratories. The training:

- Was fully financed by EFDA.
- Focused on laboratory QMS, measurement of loss on drying, determination of water content by KF-titration, titration, and measurement of pH. Participants included 22 laboratory staff, including three females.
- Will contribute toward maintaining accreditation of the main laboratory and enable branch laboratories to develop better testing capacity.

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

During PY2, PQM+ worked with government counterparts to explore opportunities for boosting the local production of medicines, particularly amid the ongoing COVID-19 pandemic. As part of this effort, PQM+ supported the assessment on available capacity and challenges local manufacturers face in producing Ministry of Health-identified priority medicines.

PQM+ collaborated with WHO to develop a policy brief that provides evidence-based information and recommendations to policymakers. Dissemination of the assessment findings and policy brief to relevant stakeholders and policymakers has prompted a series of government actions:

- MOH recently recruited a high-level technical expert as an advisor to the minister on local production of pharmaceuticals.

- PQM+ supported the MOH in Q1 to develop the document “Strategies to Strengthen Local Manufacturers’ Performance to EPSS’s [Ethiopian Pharmaceuticals Supply Agency’s] Award.” The document:
 - Systemically addresses the challenges of local manufacturers caused by the shortage of foreign currency and working capital; it enables them to increase their contributions to improving access to essential medicines from local sources.
 - Highlights strategic options, policy interventions, and implementation strategies to resolve the bottlenecks.
 - Includes a template for agreement between the Ethiopian Pharmaceuticals Supply and Services (EPSS) and Ethiopian Pharmaceuticals and Medical Supplies Manufacturers Association (EPMSMA), detailing each party’s roles, responsibilities, and accountabilities.
 - Should, following effective implementation of the proposed actions, streamline the business relationship and build trust between the local pharmaceutical industry and EPSS.
 - Will promote transparency, increase the accountability of local industries, and enhance the contribution of local industry in the supply of quality-assured pharmaceuticals and medical devices.
 - Was developed and reviewed by key stakeholders, including EPSS, EFDA, EPMSMA, Commercial Bank of Ethiopia, and the MOH.
- EPMSMA (representing local industries) and EPSS signed a memorandum of understanding (MOU) in December, witnessed by Her Excellency Dr. Lia Tadesse, Minister of MOH. This effort will ultimately contribute to improving the availability of quality-assured priority medicines from local sources.

During the quarter, PQM+ was nominated to join the EFDA-established Regulatory Capacity Building Technical Team for Local Pharmaceutical Industries. Notable developments include:

- A decision to develop a plan of action for the team, including implementation steps for the existing GMP guideline and Pharmaceutical Establishment Directive.
- PQM+ will develop an outline for the implementation guideline and share it with the team for review and endorsement.

In Q1, PQM+ supported the inspectorate in preparing for an audit by the Ethiopian National Accreditation Office (ENAO) for ISO 17020 accreditation. PQM+ also helped with the development of a corrective and preventive actions (CAPA) plan and its implementation to address nonconformance identified in the ENAO audit.

- As part of addressing ENAO’s audit findings, PQM+ provided technical support to develop and update forms and documents, including the CAPA registry, administrative measure registry, quality safety and efficacy complaint registry, complaint registration and tracking registry, medicine waste registry, inspection activities registry, inspected manufacturing site registry and internal audit checklist.
- Based on the audit findings, PQM+ supported revision of 19 standard operating procedures (SOPs) and provided technical assistance in preparing, recording, and compiling all documents requested by the auditor; helped provide evidence for rectification of ENAO findings; and assisted with compiling documentation for submission to ENAO for evaluation and final approval.

- Overall, ENAO reported 16 findings after the audit: three major, 10 minor, and three observations.
- EFDA has submitted the CAPA and associated documentation and is awaiting the final response from ENAO. ISO 17020 accreditation indicates an advanced level of performance for this regulatory function, which will help it prepare to achieve WHO Maturity Level 3.

Clinical trial (CT) is a core regulatory function considered 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 regulatory authority can also suspend or withdraw approval for a clinical trial, if necessary.

This quarter, as part of strengthening the quality management system of the clinical trial regulatory function, PQM+ assisted in developing six SOPs, four specific to clinical trials and two related to pharmacovigilance. The SOPs cover:

- Classification and analysis of clinical trial sites inspection findings.
- Clinical trials and advisory committees.
- Extension of clinical trials beyond the given period.
- Evaluation and review of market authorization holders' safety reports.
- Pharmacovigilance system indicator.

Proper implementation of and compliance with these SOPs assure 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.

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

The globalization of pharmaceutical production and the inadequate capacity to regulate medical products has put patients in LMICs at risk of receiving poor-quality medicines. Despite a growing awareness of the problem among some segments of the population, substantial gaps in information and ways to address medicines quality issues remain. As a result, more advocacy and information sharing are needed to achieve universal access to quality-assured medicines. As part of this effort:

- PQM+ submitted two abstracts in Q1 for regional workshops organized by Intergovernmental Authority on Development (IGAD) and the African Union Development Agency (AUDA-NEPAD) in Africa; both were accepted.
- Working with EFDA's director general and staff, PQM+ developed and submitted an abstract, "Regulatory Agility to Support the Emergency Response to COVID-19 in Ethiopia: Lessons Learnt," which was accepted for oral presentation.
- PQM+'s chief of party (COP) participated in the Fifth Scientific Conference on Medical Products Regulation (SCoMRA V) organized by AUDA-NEPAD.
- PQM+ submitted another abstract to the IGAD scientific conference, titled "Addressing the Challenges of Local Pharmaceutical Production in Ethiopia," which was also accepted. The COP presented the abstract during the conference.

- Both events were attended by experts and leaders in the pharmaceutical industry and regulatory sector, creating a perfect platform to disseminate information about medicine regulation and local production of pharmaceuticals. This will contribute to improving the regulatory environment for dealing with emergency situations and enhancing the local production of essential health commodities.
- PQM+ used these opportunities to disseminate information on the outcomes of USAID's investment in the regulatory and local manufacturing sector in Ethiopia.

Priority Activities for Next Quarter

Next quarter, PQM-Ethiopia plans to:

- Complete the data aggregation, analysis, and report writing of PMS results.
- Disseminate findings of the PMS
- Establish PMS TWG and develop/agree on the terms of reference.
- Other activities are pending approval of the PY3 work plan.

Ghana

GFDA is the national regulatory body responsible for the regulation of food, drugs, clinical trial protocols, and other products. GFDA carries out key regulatory functions through its divisions, Drug Registration and Inspections; Safety Monitoring and Clinical Trials; Medical Devices and Cosmetics; Monitoring and Evaluation (M&E); and Household Chemicals Substances. The MRA is ISO 9001-certified and, in 2020, attained Maturity Level 3. Its Center for Laboratory Services and Research is also ISO/IEC 17025 accredited. By the time of its June 2021 audit by the American National Accreditation Board, it had the largest accreditation scope in Africa.

PQM+ is helping Ghana improve the supply of quality assured medicines by providing technical assistance to select local manufacturers of artemisinin-based combination therapies (ACTs) and MCH commodities such as oxytocin.

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 Quarter 1, PQM+ monitored confirmatory testing of the antimalarial and MCH samples. Of 201 antimalarial samples (artemether injection, artesunate injection, and artemether/lumefantrine tablets) collected and screened using the MiniLab™ kit procured by PQM+, 48 were sent for confirmatory testing. All 177 MCH samples (oxytocin injection and misoprostol tablets) were also sent for confirmatory testing. The testing was completed at the end of December 2021.

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

PQM+ supervised Entrance Pharmaceuticals and Amponsah Efah Ltd. in their implementation of the roadmap toward WHO prequalification of artemether/lumefantrine tablets developed with PQM+ support in PY2. As part of this supportive supervision, the PQM+ chemistry manufacturing and control experts held working sessions on requirements for process

development, product development, cleaning validation, and revision of their batch manufacturing and batch packing records (BMR and BPR).

PQM+ published a new request for expressions of interest (EOI) in the daily newspaper for the importation and local packaging of iron and folic acid (IFA) tablets and requested manufacturers to submit an EOI for the local manufacture of amoxicillin-DT and chlorhexidine gel.

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

PQM+ participated in the GS1 virtual summit in which implementation of the GS1 codes for pharmaceuticals in Africa was discussed. As the program plans to support sensitization of local manufacturers it will align with the implementation plans of both the Ghana FDA (which will begin in 2022) and the national GS1 TWG while leveraging some of the experiences of Ethiopia and Nigeria. The GS1 readiness survey data, developed by PQM+ in PY2, is still being collected.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support FDA Ghana in disseminating the results of the PY2 RB-PMS.
- Support the PMS-TWG in developing the protocol for the second RB-PMS activity.
- Provide technical assistance to three local ACT manufacturers. Technical assistance will include training and QMS building per the roadmaps developed in PY2.
- Identify a potential local manufacturer to produce amoxicillin-DT and chlorhexidine gel.
- Continue following-up with local manufacturers to respond to the GS1 survey.

Guinea

Guinea's National Directorate of Pharmacy and Medicines (DNPM) is implementing regulatory provisions related to its mandate while strengthening its technical capacity to carry out regulatory functions. The national quality control laboratory, *Laboratoire national de contrôle qualité des médicaments* (LNCQM), conducts quality testing of medical products to facilitate decision-making by DNPM. PQM+ works with DNPM to strengthen its market surveillance function by operationalizing a PMS-TWG to implement risk-based PMS. Additionally, PQM+ has assisted LNCQM in improving its QMS to conform with ISO/IEC 17025 standards and is strengthening its technical analysts' capacity to conduct quality testing per the ISO accreditation roadmap developed in PY2.

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 Quarter 1, PQM+ traveled to Guinea to provide logistics for RB-PMS sampling missions and later supervised the sampling of antimalarial drugs from Buké, Dubréka, Dinguiraye, Labé, Singuiri, Gueckedou, and Lola. The team collected and screened 187 antimalarial and MCH samples using the MiniLab™. A pause in the use of family planning funds caused by the coup in

September 2021 led to the removal of those samples from the list of products in the PMS protocol.

PQM+ supported a workshop to build the capacity of the MEDICRIME Brigade and sensitized stakeholders on the Brigade's roles and responsibilities. This provided an opportunity to inform other stakeholders on how the MEDICRIME Brigade complements and supports the work of the DNPM and LNCQM.

PQM+ worked with LNCQM to finalize a SOP on conducting internal audits using the Stepwise Assessment Tool Towards Accreditation (SATTA). SATTA incorporates elements of quality control standards from both ISO 17025 and WHO prequalification criteria and identifies areas for improvement in laboratories' pursuit of those benchmarks). During the visit, PQM+ coached the LNCQM team on the use of the SATTA tool and trained LNCQM technical staff on CAPA plans. These trainings will allow LNCQM to address and subsequently close gaps they identified during audits.

PQM+ sent two analysts from LNCQM to Ghana for a two-week training on advanced quality control training (covering high-performance liquid chromatography, or HPLC; dissolution; and ultraviolet-visible spectrophotometry). This training will allow them to test PMS and other samples competently and in line with best practices in the laboratory.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Monitor confirmatory testing of the RB-PMS samples.
- Provide supportive supervision to the MEDICRIME Brigade to develop relevant guidelines and SOPs.
- Provide supportive supervision to LNCQM to implement its roadmap toward accreditation.

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), National Quality Control Laboratory (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 strengthen in-country stakeholders' capacity in ensuring access to quality-assured medical products in the country.

In Q1, PQM+ focused on improving governance for medical product QA systems, increasing the supply of quality-assured essential medical products of public health importance, 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

Working with the Division of National Malaria Program (DNMP) in Kenya and other stakeholders in PY1 and PY2, PQM+ supported the development of the quality assurance framework for

malaria products. This framework outlines the roles and responsibilities of, and guides coordination among, stakeholders involved in assuring the quality of the health products. The framework was adopted in Q4 of PY2.

In addition, PQM+ helped plan future TWG activities and worked with PPB to organize a pharmacovigilance (PV) and post-marketing surveillance stakeholders meeting to share recent successes and activities planned over the next two years.

PQM+ also assisted PPB and the TWG with organizing a stakeholders meeting where the TWG shared the recent successes in PMS and PV and shared the work plan for upcoming activities. The team then incorporated stakeholders' feedback into the final work plan.

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

PQM+ is supporting PPB to set up an online platform for self-directed learning. In Q1, the team continued reviewing and uploading content onto the Learning Management System (LMS) platform. The platform is available at <http://ustadi.pharmacyboardkenya.org/my/>.

The program is also working with PPB and the Pharmacovigilance and Post-Marketing Surveillance Technical Working Group (PV/PMS TWG) to strengthen quality surveillance of antimalarial and reproductive, maternal, newborn, child, and adolescent health products in the country through risk-based tools. PQM+:

- Supported development of the LMS platform and hosting at PPB servers.
- Worked with PPB subject matter experts to develop content for the system (currently being reviewed and uploaded).
- Supported collection of samples (based on the developed RB-PMS protocol); the last batch of samples are undergoing compendial testing at NQCL.

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

PQM+ is working with the National Quality Control Laboratory (NQCL) to analyze costs and fees of NQCL's medicines quality testing services to identify ways to make the lab financially sustainable. The activity includes comparing current NQCL fees with the costs its peers within and outside the country charge.

- PQM+ is reviewing the final report before sharing it with key stakeholders.
- The report identifies opportunities to strengthen the financial sustainability of NQCL.

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

PQM+ collaborated with PPB to strengthen the board's capacity for regulatory oversight of good manufacturing practices (GMP) and promoting GMP compliance by local manufacturers of antimalarial medicines, MCH medicines, and reproductive health and family planning medicines, among other medical products. PQM+:

- Identified challenges and opportunities to support the local production of quality-assured antimalarial, reproductive and MCH, and other medicines in Kenya

- Conducted feedback and training meetings with PPB and the pharmaceutical manufacturers to share findings from the study and build capacity in some areas identified as deficient, and is reviewing the final report.

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

PQM+ is supporting PPB to analyze data from previous PMS data and review the PMS reports with the target of drafting and submitting a manuscript for publication in a scientific journal.

In addition, PQM+ prepared and submitted three abstracts to the Pharmaceutical Society of Kenya (PSK) and to the Fifth Biennial Scientific Conference on Medical Products Regulation in Africa (SCoMRA V). PQM+:

- Worked with PPB and the NQCL to develop an abstract on RB-PMS that was presented during the PSK annual meeting.
- Assisted NQCL to develop an abstract, “Using a Systems Approach to Strengthen National Quality Control Laboratories in Africa to Build Back Better after the COVID-19 Pandemic,” that was accepted by the SCoMRA V scientific conference.
- Helped PPB develop an abstract, “Leveraging Open-Source Learning Platforms for Self-Directed Competency Development of Regulatory Staff, Post-COVID-19: Kenya’s Experience,” that was also accepted by the SCoMRA V conference.

Priority Activities for Next Quarter

Next quarter, PQM+ in Kenya plans to:

- Support national and county-level implementation of quality assurance strategies of the MOH DHPT and DNMP.
- Disseminate the quality assurance framework for malaria commodities to remaining counties.
- Disseminate results of RB-PMS of antimalarial and reproductive, maternal, neonatal, child, and adolescent health products to the key stakeholders involved to quality assurance of health commodities.
- Disseminate the NQCL costing study to relevant stakeholders.
- Finalize the report on support to PPB and local manufacturers of quality-assured antimalarial, reproductive and MCH, and other medicines in Kenya.
- Assist PPB to finish establishing an online platform for self-directed learning.
- Complete the analysis and synthesis of local data from previous PMS activities to inform policy direction for QA of malaria and reproductive and MCH products.
- Support the PV/PMS TWG quarterly meeting.

Liberia

In Liberia, PQM+ is strengthening the country’s regulatory system, specifically focusing on supporting the Liberia Medicines and Health Products Regulatory Authority (LMHRA) and its quality control laboratory.

PQM+ has donated nearly USD \$113,000 in laboratory equipment and consumables to the LMHRA. The donation is part of the plan by PQM+ to help the LMHRA begin testing of medicines entering the country. PQM+ and the LMHRA identified an additional 10 priority regulations needed to support implementation of the 2010 act that established the LMHRA. The regulations will support medical products registration and monitoring.

Progress by PQM+ Objective

Objective 1: Improve governance for medical product quality assurance systems

PQM+ coordinated with the LMHRA to identify 10 new priority regulations in accordance with the LMHRA Act of 2010, the Five-Year Strategic Plan, and the LMHRA 2021 WHO Global Benchmarking Self-Assessment Institutional Development Plan. The new regulations address:

- Product variations;
- LMHRA Reliance Policy on market authorization;
- Registration of medical devices;
- Trace and track;
- Quarantine;
- LMHRA Reliance Policy on inspection;
- Foreign and local inspections;
- Emergency use authorization;
- Subcontracting of testing services; and
- LMHRA consideration of decisions, information, and data from other NCLs.

The new regulations will support medicines registration and post-marketing surveillance. These regulations follow the seven that PQM+ helped the LMHRA develop in PY2.

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

This quarter, PQM+ donated USD \$112,914.44 worth of laboratory equipment and consumables to the LMHRA. The donation, which will support the LMHRA to begin compendia testing, including the following items:

- Dissolution machine;
- Fourier-transform infrared spectrometer (FTIR);
- MiniLabs™;
- Glassware;
- HPLC columns; and
- Reagents.

PQM+ has completed the installation qualification of both the FTIR and dissolution machine. Speaking at a handover ceremony, the USAID President's Malaria Initiative (PMI) advisor

lauded the technical support the LMHRA has received from PQM+. In December 2021, PQM+ trained seven lab staff on the use of FTIR and dissolution machine.



1) The PMI advisor tours a QC lab sample storage and chats with the QC manager. 2) PMI advisor and the LMHRA managing director tour LMHRA's new lab construction site. 3) PQM+ hands over a donated items document to LMHRA's managing director. 4) Technicians install the newly procured dissolution machine. 5) PMI advisor and LMHRA managing director take a photo with lab staff.

In November, PQM+ supported the LMHRA to complete a questionnaire for the 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. The Centre for Innovation in Regulatory Science (CIRS) will use the completed questionnaire to develop a country report for Liberia, which will include findings and recommendations to help strengthen the marketing authorization process at the LMHRA.

PQM+ completed the confirmatory testing of PMS samples from PY2 this quarter. The results will inform the LMHRA in carrying out regulatory actions. In October 2021, PQM+ trained 25 people from the LMHRA, NMCP, Pharmacy Board, and Ministry of Health on the MedRS web-based tool. During the training, PQM+ supported participants to develop a new PMS protocol that will guide the upcoming sample collection and testing.

In October, PQM+ worked with the LMHRA to develop a PMS curriculum for the NMCP, which is part of NMCP's malaria surveillance guidelines.

PQM+ also coordinated with the LMHRA to complete the drafting of a communication strategy for the LMHRA. The LMHRA has begun applying the strategy by setting up a LinkedIn page and sending out SMS text messages.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Coordinate with CIRS to complete the OpERA country report.

- Train technical advisory committee members.
- Draft priority regulations.
- Train PMS samplers.
- Start PMS sampling.
- Start and complete MiniLab™ screening.
- Disseminate PY2 PMS results.

Madagascar

PQM+ collaborates with Madagascar's Medicines Regulatory Authority ("the Agency," *Agence du Médicament de Madagascar*). As the sole medicines regulatory authority in the country, it performs all regulatory functions through four technical departments: Pharmaceutical Inspection, Registration, Pharmacovigilance, and Quality Control. The National Pharmaceutical Quality Control Laboratory (LNCQM, *Laboratoire National de Contrôle de Qualité des Médicaments*) is part of the Agency's quality control department. PQM+ is helping the Agency strengthen the LNCQM's capacity to prepare for ISO/IEC 17025 accreditation and WHO prequalification.

In PY3, in addition to laboratory capacity strengthening, PQM+ will focus on implementing the PMS system on the quality of medicines in the country.

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+ is assisting the MRA to prepare for implementation of PMS activities in Madagascar. In Q1 PY3, the program:

- Gave a virtual introductory training on risk-based post-marketing surveillance (RB-PMS) and an overview of the MedRS tool to the Agency staff (eight participants: one male, seven female).
- Helped create the multisectoral Post-Marketing Surveillance Technical Working Group (PMS-TWG), with proposed members including representatives of the Agency; the national MNCH, family planning/reproductive health (FP/RH), malaria, tuberculosis, and HIV/AIDS programs; the national orders of pharmacists and medical doctors; manufacturers, distributors, and the consumers association; and the purchasing center for essential medicines and medical material of Madagascar (SALAMA, *la Centrale d'Achats de Médicaments Essentiels et de Matériel Médical de Madagascar*).
- Assisted the MRA in drafting PMS documents, including the PMS-TWG terms of reference, the national guidance for risk-based PMS, the ministerial decree to establish the PMS-TWG, and the invitation letter for nomination of the TWG members.
- Began a desktop review of laboratory-related documentation, including SOPs and the quality manual. This will help as the laboratory prepares for a capacity assessment using the SATTa tool.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Assist the Agency with conducting at least two PMS workshops: an inaugural workshop and a training on the MedRS tool for the TWG members;
- Conduct the SATTA assessment and inform the laboratory development plan.

Mali

In Mali, the Directorate of Pharmacy and Medicines (DPM) and the National Health Laboratory (*Laboratoire National de la Santé*, LNS) oversee medicines regulation. The DPM is a Maturity Level I agency. The LNS tests the quality of medical products, food, beverages, or any substance imported or produced in the country that is intended for therapeutic or dietary purposes, but it lacks either ISO/IEC 17025 accreditation or WHO prequalification.

PQM+ works with the DPM to strengthen its market surveillance function through establishing and operationalizing a PMS-TWG to implement risk-based PMS and improve the capacity for medicine registration. In addition, PQM+ has been providing tailored technical assistance to the Medicines Quality Control Laboratory (LCQM) within LNS to attain ISO/IEC 17025 accreditation. This would assure the reliability of testing, increase the public's confidence in ANCQ test results, and help DPM take sound regulatory actions.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

To facilitate the development of a five-year strategic plan for Mali, PQM+ completed a situational analysis by reviewing key country documents and joining LNS staff in interviewing medicines quality assurance stakeholders.

At the end of the quarter, PQM+ provided supportive supervision to the human resources department and management to conduct a performance evaluation process, applying the SOPs PQM+ supported LNS to develop in PY2.

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

PQM+ supervised the sampling of antimalarial and MCH medicines for the second round of PMS, applying the risk-based PMS protocol developed in PY2 Q3 and applying the fixed-award agreement (FAA) mechanism established between PQM+ and LNS Mali. The PMS included 314 antimalarial samples collected from five regions: Kayes, Koulikoro, Sikasso, Segou, and Bamako.

Following a mock audit that PQM+ conducted in September 2021, the program provided supportive supervision to LCQM to resolve identified gaps. In addition, PQM+ coached the LCQM analysts on the analytical techniques in the proposed accreditation scope to help prepare them for the method witnessing component of the planned accreditation audit. In addition, PQM+, through a regional equipment maintenance specialist, qualified the four key pieces of equipment required for testing in the lab's proposed accreditation scope: HPLC, dissolution, UV-visible spectrophotometer, and the Fourier Transform IR spectrometer.

CIRS completed the evaluation of data provided by DPM and finalized the country report for Mali. The report indicated that as of 2020, it takes DPM approximately 18 months from the receipt of the product dossier to issue a marketing authorization. The report attributes this to reasons that include:

- Inadequate training of the dossier evaluation committee;
- Lack of financial and human resource; and
- Lack of autonomy of the DPM.

Priority Activities for Next Quarter

Next quarter, PQM+ in Mali plans to:

- Conduct a stakeholder workshop to develop the strategic plan.
- Monitor the testing of RB-PMS samples.
- Support DPM and LNS in disseminating the results of their second RB-PMS.

Mozambique

Mozambique recently established an autonomous medicines regulatory authority, ANARME (*Autoridade Nacional Reguladora de Medicamentos, Instituto Publico*), which encompasses the Department of Quality Check or DCQ (the *Departamento de Comprovação da Qualidade*). PQM+ has been providing technical assistance in the transition to an autonomous NMRA and assistance moving ANARME toward attaining WHO GBT Maturity Level 3 and achieving ISO 9001:2015 certification. Additionally, PQM+ has been assisting the DCQ to identify and bridge gaps toward attaining ISO 17025:2007 accreditation for the lab, including developing the necessary QMS documents, manuals, and processes.

Progress by PQM+ Objective

Objective 1: Improve governance for medical product QA systems

PQM+ assisted ANARME toward achieving ISO 9001:2015 QMS certification by:

- Facilitating the publishing of the ANARME statute in Mozambique's official government bulletin, a necessary step to operationalize ANARME. This is ongoing.
- Working with ANARME to identify and hire an organization to undertake the ISO 9001:2015 audit and certification.

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

In the last quarter of PY2, PQM+ supported the DCQ to conduct a mock audit to identify gaps to be addressed for the lab to attain good laboratory practices and ISO 17025:2017 accreditation. In Q1, PQM+ assisted the DCQ to:

- Conduct a workshop from November 29 to December 3 for DCQ and other ANARME staff on ISO/IEC 17025:2017 standards, QMS, and documentation practices.

- Build the capacity of 12 female and eight male attendees on QMS and QA/QC topics, using interactive in-person and group work approaches.
- Facilitate the development and review of key QMS documents: a) Quality Manual, b) DCQ Quality Policy, c) Impartiality, Confidentiality, and Conflict of Interest Policy, d) Good Documentation Practices (GDocP) and Data Integrity SOP, e) corrective and preventive action SOP, f) quality risk management SOP, and g) risk management worksheet.

Other technical assistance provided by PQM+ to the DCQ to implement actions in the updated accreditation roadmap and their operations included:

- Providing the necessary reagents and technical support to conduct proficiency testing (PT) of HPLC, pH, loss on drying, and UV spectroscopy, as well as for report compilation and submission.
- Conducting a root cause analysis of failed PT.
- Providing a hands-on demonstration on laboratory waste management.
- Performing mechanical servicing on and restoring functionality of two Walters HPLCs.
- Reviewing and approving equipment certificates for the calibration or performance verification of major lab equipment supported by PQM+ in PY2 Q4.
- Returning the calibrated Dissolution Performance Verification Testing (PVT) kit to DCQ.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Continue technical support to the DCQ to correct gaps identified in the previous mock audit and finalize preparation for accreditation.
- Work with the DCQ to reschedule incomplete activities and training disrupted by the COVID-19 virus omicron variant threat, and any additional training as may be requested by ANARME or DCQ.

Nigeria

PQM+ is focused on helping ensure the quality of medicines and other medical products in Nigeria, with an emphasis on malaria and MCH 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.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ started discussions with relevant stakeholders about developing a National Strategic Plan for the Pharmaceutical Sector:

- PQM+ shared the draft concept note with the director of the Food and Drug Services Department at the Federal Ministry of Health and is scheduling a date to present to the Minister of Health.

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

In Q1, PQM+ continued to collaborate with the Pharmacists Council of Nigeria (PCN) to implement activities to strengthen state-level regulatory and quality assurance systems as it pertains to private for-profit retailers (pharmacies and patent medicines shops) of medical products in communities. In this work, PQM+:

- Delivered thousands of copies of job aids and pharmaceutical quality assurance posters communicating key messages to practitioners and clients of retail medicines outlets. The materials detail steps to assure the quality of medicines and consumables. PCN offices in Bauchi, Ebonyi, and Sokoto states received the materials for further distribution to retail medicines outlets.
 - PQM+ has also initiated plans to produce more of these job aids for distribution in three new states (Abuja, Benue, and Kebbi) and more outlets in the previous states.
- Presented its planned PY3 activities to PCN, which gave approval.
- Supported PCN to institutionalize a QMS; in December, PCN underwent an audit by the certification body for ISO 9001:2015 certification.
 - To further strengthen QMS at PCN, PQM+ commenced engagement with various departments to understand their data management requirements and challenges. The goal is to help them set up a structured information management and monitoring and evaluation system.
- Developed protocol and commenced preparation for regulatory and QA system assessment for Abuja, Benue, and Kebbi states.
- Represented by the deputy chief of party and the state consultant, participated in USAID Nigeria's Health, Population, and Nutrition Office's field visit to Bauchi state.
- Supported the capacity building of equipment engineers at all National Agency for Food and Drug Administration and Control (NAFDAC) laboratories in preventive maintenance and first-line repairs of laboratory equipment. This will reduce equipment down time and help NAFDAC close a gap identified by WHO during its prequalification audit and GBT Maturity Level 3 assessment.
- Supported NAFDAC to develop the first risk-based protocol for malarial medicines PMS in 11 PMI states and the Federal Capital Territory (FCT-Abuja).
- Supported NAFDAC in a virtual training in December for 30 sample collectors to prepare for the malarial medicines risk-based PMS (RB-PMS).
- Supported NAFDAC to mobilize 28 sample collectors to the field for the first RB-PMS of Malarial medicines in 11 PMI states and the FCT-Abuja (December 16-22, 2021).

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

In Q1, PQM+:

- Carried out a virtual capacity building workshop for professionals from the pharma manufacturing industry on validation, a critical Good Manufacturing Practice requirement to produce medicines that consistently meet predetermined quality, safety, and efficacy standards.
- Received notification that the WHO PQ team accepted results of the test report on the risk of migration of ink and adhesive into magnesium sulfate 50%w/v injection, following an evaluation report submitted by Juhel Nigeria Ltd.
- Learned that the WHO PQ team accepted the product dossiers in the common technical document for sulfadoxine 500mg + pyrimethamine 25mg and zinc sulfate 20mg dispersible tablet, earlier submitted by Swipha Nigeria Ltd., for full evaluation.

Priority Activities for Next Quarter

In Quarter 2, PQM+ Nigeria plans to:

- Continue efforts to develop the National Strategic Plan for the Nigeria Pharmaceutical Sector, including:
 1. Develop terms of reference (ToR) for TWGs.
 2. Select and inaugurate the TWG from the public and private sectors and identify principal officers (chairman, secretary, etc.).
 3. Organize a workshop to present findings of the NAFDAC-led GMP roadmap project supported by PQM.
- Conduct an assessment of regulatory and quality assurance systems for retail pharmaceutical outlets in Abuja, Benue, and Kebbi states.
- Address corrective actions from the official assessment of PCN and obtain ISO 9001:2015 certification for PCN.
 - Commence final preparation toward Maturity Level 3 assessment by WHO GBT for licensure of PCN.
- Collate and analyze laboratory test data and draft a report on the ongoing RB-PMS of antimalarial medicines in preparation for dissemination.
- Conduct a training of trainers for NAFDAC on using the online MedRS tool for risk-based PMS and begin developing protocols for the next round of RB-PMS.

Rwanda

As the medical products regulatory field changes, the WHO GBT requires NMRAs to have institutional plans for workforce capacity development in place. One indicator of organizational development and the institutionalization of best practices is an established system for tracking trainings offered to and used by regulatory authorities. The 2018 WHO GBT assessment of Rwanda FDA recommended developing an institutional competency framework to guide workforce capacity development. Rwanda FDA sought support from PQM+ to undertake a training needs assessment in alignment with the WHO global regulatory competency framework.

Objective 1: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

Training needs assessment (TNA) and capacity development plan: In Q1, PQM+ conducted a training needs assessment to support the Rwanda FDA in developing systematic workforce development processes and practices. The technical assistance resulted in five deliverables: training needs assessment report, training plan, competency framework, training tracking tool, and an SOP on how to develop, implement and assess the training plan. These methodologies, tools, and SOPs help institutionalize procedures and practices and build the Rwanda FDA's ability to manage its workforce.

The assessment team developed an electronic competency matrix tool that they used to identify competency gaps of 172 staff. The TNA focused on current Rwanda FDA functions and staff competencies. Functions covered by the assessment include:

- Office of the Director General;
- Office of the Deputy Director General;
- Department of Drug and Food Assessment and Registration;
- Department of Food and Drugs Inspection and Safety Monitoring;
- Quality Control Laboratory Division; and
- Office of the Chief Finance Officer.

When completed, the suite of products will boost Rwanda FDA's workforce capacity to systematically and sustainably develop workforce performance across all medical product regulatory functions assessed by the WHO GBT, which will contribute significantly to enhancing its GBT maturity level.

Training needs assessment (TNA) and capacity development plan: In Q1, PQM+ conducted a training needs assessment to develop an institutional capacity development plan and competency framework for Rwanda FDA. This included the following:

- Development of an electronic competency matrix tool, which was used to identify performance gaps for 172 staff and assess existing competence against the required organizational development and the institutionalization of best practices.
- A focus on all Rwanda FDA functions and staff.³

³ Involved entities include the Office of the Director General; Office of the Deputy Director General; Department of Drug and Food Assessment and Registration (Human Medicine and Devices Assessment and Registration Division, Cosmetics and Household Chemicals Assessment and Registration Division, Veterinary Medicine Devices and Assessment and Registration Division, Food Assessment and Registration Division); Department of Food and Drugs Inspection and Safety Monitoring (Food and Drugs Import and Export Control Division, Food and Drugs Inspection and Compliance Division, Pharmacovigilance and Food Safety Monitoring Division); Quality Control Laboratory Division (Food Testing Unit, Medicines and Cosmetics Testing Unit, Medical Devices and Instrumentation Testing Unit, Pesticides and Poisonous Substances and Chemical Unit); Office of the Chief Finance Officer (Planning Unit, Human Resource and Administration Unit, Finance Unit).

When completed, the institutional capacity development plan will guide Rwanda FDA's workforce capacity building in attaining institutional capacity development maturity level 3, one of its prioritized strategies in strengthening the country's regulatory systems.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Strengthen PMS and RB-PMS of medicines quality in Rwanda.
- Strengthen the capacity of the Rwanda FDA's Drug Quality Control Laboratory.
- Strengthen the GMP regulatory inspection and quality assurance systems of local essential medical products manufacturers.
- Review and strengthen the quality assurance policies and guidelines of Rwanda Medical Supply Limited (RMS LTD).
- Collaborate with University of Rwanda to introduce course modules on quality assurance of medical products.

Senegal

The Government of Senegal recently developed a five-year (2019–2023) Integrated Strategic Plan for the Directorate for Pharmacy and Medicines (DPM) and the National Medicines Control Laboratory (LNCM). The plan recognizes progress made over the past decade, in part due to the support provided through USAID's Promoting the Quality of Medicines (PQM) program, but much work remains to be done. PQM+ works primarily with the DPM to strengthen its market surveillance function through the establishment and operationalization of a PMS-TWG to implement risk-based PMS and to improve their capacity for medicine registration. In addition, PQM+ provides support to LNCM to improve its capacity to test medicines.

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+ conducted a refresher training on Good Laboratory Practices (GLP) and Good Documentation Practices (GDP) for 10 people (8 female, two male) to improve basic practices during analytical testing in the laboratory.

The program also conducted a training on analytical method validation (AMV), a key advance requirement of the ISO/IEC 17025 standard. Nineteen people (10 female, nine male) received training to conduct AMV and now have the capacity to meet this requirement, which was previously a non-conformity in LNCM's quality management system.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Train the PMS unit on the online version of the MedRS tool.
- Conduct training of trainers on the ISO 17025 standard and internal auditing.
- Baseline assessment of Senegal DPM as per the ISO 9001:2015 standard.

Asia Region

Asia Bureau

PQM+'s technical assistance funded by USAID's Asia Bureau aims to promote regional regulatory convergence and reliance. PQM+ will work through regional health networks that include the Association of Southeast Asian Nations (ASEAN) Pharmaceutical Product Working Group (PPWG) and the South-East Asia Regulatory Network (SEARN) to strengthen regulatory and quality assurance systems. This work leverages the current PQM+ work in Southeast and Central Asia. The PY3 workplan was approved in December 2021.

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 November, PQM+ and MTaPS jointly presented at the 32nd ASEAN PPWG meeting. The programs presented a proposal for PY3 planned activities concerning the regional network and their modality for implementation. The presented activities aim to address regional technical needs identified by PPWG in the areas of marketing authorization, post-marketing surveillance, quality management, lot release, regulatory information management system, and pharmacovigilance. Following the presentation, PPWG requested that MTaPS and PQM+ identify the geographic scope for each activity (country-specific vs. regional). PQM+ and MTaPS shared the requested information and are waiting to receive final approval from the working group to start implementation.

Priority Activities for Next Quarter

Next quarter, PQM+ Asia Bureau plans to:

- Conduct a virtual technical side session at the Prince Mahidol Awards Conference (PMAC) 2022.
- Kick off implementation of approved work plan activities pending formal consent from the ASEAN regional network.

Bangladesh

In Bangladesh, PQM+ works with the Directorate General of Drug Administration (DGDA), which oversees medical product quality in Bangladesh and 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. One of DGDA's key functions is PMS of medical products, including vaccines and medical devices.

PQM+ is helping the DGDA toward achieving WHO Maturity Level 3 (ML3) in terms of vaccine regulation; 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 and good manufacturing practice.

In Q1, PQM+ focused on implementing activities under all four program objectives in the PY3 work plan and on completing activities from the last quarter of PY2.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

Activity 1.1: Support development of DGDA regulatory framework: PQM+ started working to identify all DGDA activities and the legal basis for those activities, including acts, rules, ordinances, policies, guidelines, manuals, SOPs, working procedures, and checklists. To develop DGDA's regulatory framework document, PQM+ is reviewing the IDP report, DGDA documents, and other international regulatory framework documents.

PQM+ reviewed the following documents related to the DGDA IDP:

- Framework for good governance in the public pharmaceutical sector.
- Report on a World Health Organization technical working group meeting on good governance in the public pharmaceutical sector.
- Framework for Good Governance in the Public Pharmaceutical Sector, Ministry of Health, Malaysia.
- Administrative structure and functions of the Drug Regulatory Authority in India.

Activity 1.3: Provide technical assistance to Plasma Plus Application and Research Laboratory to achieve international standards for medical product testing (WHO-PQ, ISO/IEC 17025:2017): In December, PQM+ met with Plasma Plus Research and Testing Laboratory of International University of Bangladesh to plan a kickoff meeting with DGDA, NCL, and USAID next quarter toward establishing a third-party laboratory in country. The meeting will help identify what support the lab needs to align with international standards.

Activity 1.4: Support DGDA to prepare ethical marketing and promotion guidelines for pharmaceutical products: Control of pharmaceutical marketing and promotion is a key function of DGDA to promote the rational use of medicines and control substandard and falsified medical products in the market. According to WHO GBT sub-indicator MC04.03, DGDA needs established procedures and guidelines to actively monitor the marketing and promotion of medical products, including documentation of data collected, screening, review, and regulatory decision-making. DGDA representatives sit on the Ministry of Health and Family Welfare (MoHFW) "Code of Pharmaceutical Marketing Practices Committee," which conducted the following key activities during the first quarter of PY3:

- Conducted a primary meeting with the member secretary and chair of that committee regarding updating the code of pharmaceutical marketing and development of a new guideline on ethical pharmaceutical promotion.
- Reviewed several international guidelines and the existing code of pharmaceutical marketing in Bangladesh.
- Collected all relevant available documents for the next step toward developing a guideline on ethical pharmaceutical promotion.

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

SUB-OBJECTIVE 2.1. Support DGDA to make improvements across nine regulatory functions toward sustainable systems development for DGDA

Activity 2.1.1: Provide technical assistance to DGDA to address observations made during WHO GBT formal assessment: DGDA received observations from a WHO formal assessment conducted in July 2021. Based on those observations, PQM+ developed a CAPA plan developed for nine DGDA functions. Since August 2021, PQM+ has been working with DGDA to address the CAPA plan, with numerous meetings taking place with the technical team of each function for updating and finalization of the CAPA plan.

In Q1, PQM+ provided support to address the CAPA plan through the review and development of various quality documents, including the following:

- Developed a CAPA plan for nine functions.
- Reviewed and updated the quality manual for effective QMS.
- Developed an action plan on QMS functions.
- Supported development of the following SOPs:
 - Procedure on risk analysis and risk management plan;
 - Procedure on preparation of annual performance report;
 - Procedure on review and update of existing legal provisions;
 - Procedure on change control; and
 - Procedure on key result areas and key performance indicators.
- Reviewed and updated the following SOPs:
 - Procedure on the development of functional organogram and organizational chart;
 - Procedure on the preparation of job descriptions;
 - Procedure on continuous temperature monitoring and recordkeeping;
 - Procedure on employee training and training effectiveness;
 - Procedure on management review meetings;
 - Procedure on Good Documentation Practices;
 - Procedure on planning, preparation, and monitoring of GxP inspections;
 - Procedure on communication and decision-making covering established mechanisms and systems related to channels of communication;
 - Procedure on mechanisms and criteria toward selection of NRA for reliance and recognition
 - Procedure on confidentiality management and handling potential conflict of interest
 - Procedure for analytical method transfer and method validation/verification in vaccine wing

- Lot release procedure for locally manufactured and imported vaccines.
- Procedure for communication with all stakeholders of NCL
- Procedure to withheld, suspend, withdrawn or cancel a registration / marketing authorization in the event of adverse finding related to quality, safety and efficacy of the medical products.
- Procedure for subcontract of NCL

In November, PQM+ facilitated the Coalition of Interested Partners (CIP) task force meeting in collaboration with DGDA and WHO. Seventy people attended, including representatives from USAID; World Bank; UNICEF; Food and Agriculture Organization; Foreign, Commonwealth, and Development Office (FCDO); MTaPS/Management Sciences for Health, and others. The assessors from WHO headquarters and WHO South-East Asia Region (SEARO) also attended the meeting. Participants determined next steps and a support plan to reach the milestone of WHO ML 3.

Activity 2.1.3: Support DGDA to implement appropriate mechanisms for using WHO Collaborative Procedure for Accelerated Registration (CPAR): In Q1, PQM+ worked with DGDA on dossier evaluation, regulatory inspection, and communication toward establishing CPAR between DGDA and WHO, meeting twice in November with DGDA personnel.

Achievements include:

- Agreement for Collaborative Procedure for Accelerated Registration (CPAR) signed by DGDA and sent to WHO for review and signature.
- A training and a workshop conducted by WHO in December for five DGDA officials and one PQM+ staff member aimed to raise awareness among national regulatory authorities (NRAs) that are new to prequalification assessment.
 - Topics included requirements, processes and procedures, and the CRP and other reliance-based approaches for marketing authorization and product life cycle management.
 - The workshop focused on the WHO PQ assessment, the inspection process for medical products, and procedures for sharing assessment and inspection reports from PQ and WHO listed authorities to facilitate national decision-making.

Activity 2.1.4: Support DGDA toward achieving PIC/S membership: PQM+ supported DGDA to attend the 2021 PIC/S virtual seminar on “**GMP Assessment Approaches in the Post-COVID-19 Era.**” DGDA’s focal person for PIC/S membership attended the seminar, organized by the Ministry of Food and Drug Safety of the Republic of Korea in November.

Activity 2.1.8: Provide support to DGDA and NCL to implement RB-PMS of anti-TB medicines: Sampling and testing protocols for first-line TB medicines will help detect and prevent the availability of SF TB medicines on the market. PQM+ supported NCL to prepare the following:

- Assisted with preparing draft sampling and testing protocols for first-line TB medicines.
- Helped prepare a requirement list to conduct MiniLab™ tests and laboratory confirmatory tests.
- Helped NCL prepare a reference standard list with proper justification of end-use, along with the amount required during testing.

Activity 2.1.9: Rapid assessment of SF anti-TB medicines in the private sector: To conduct the rapid assessment of SF anti-TB medicines, PQM+ helped with preparing a scope of work and will provide technical support with this activity.

SUB-OBJECTIVE 2.2. Medical product QCL capacity strengthening to support sustainable PMS programs

Activity 2.2.1: Enhance capacity of NCL for supporting RB-PMS system of priority medicines (i.e., TB, MCH, family planning, and animal health products): Sample testing from PMS is a top priority of NCL. To build capacity for testing of MCH, family planning, and animal health products in NCL, proficiency testing is a key tool to make the analysts competent enough to conduct analyses in the lab. This quarter, PQM+ supported an NCL analyst in performing proficiency testing of a sample using FTIR.

Activity 2.2.2: Continue provide technical assistance to NCL to increase the vaccine laboratory's capacity of testing: Toward achieving WHO ML 3, PQM+ supported closing CAPA gaps for lot release and laboratory access and testing functions. In Q1, PQM+ provided technical assistance to accomplish the following activities:

- Writing the method validation report writing on the meningococcal vaccine potency test.
- Reviewed and updated the following SOPs:
 - Management of vaccine samples;
 - Procedure for communication with all stakeholders of NCL;
 - Procedure for laboratory safety in NCL; and
 - Lot release procedure for locally manufactured and imported vaccines and checklist for each vaccine.
- Subscription to various journals on vaccine for access of laboratory staff.
- Reviewed the analytical method validation protocol of the hepatitis B vaccine.
- Supported implementation of the measurement uncertainty for weighing balance in the vaccine unit chemical lab.

This quarter, PQM+ conducted the following trainings:

- Theoretical training on COVID-19 vaccine testing toolkit developed by USP.
- Theoretical training on cell culture procedure and use.
- Four analysts (three male, one female) learned to conduct analytical method validation, a key ISO/IEC 17025 standard requirement.

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

Activity 4.1: Continue to provide technical support to ACI Healthcare Ltd toward prequalification of first-line TB medicines: In October, PQM+ conducted GMP audit at ACI HealthCare Limited (AHL) to assess the GMP compliance of the manufacturing site on activities related to four-drug fixed-dose combination (4FDC) production. PQM+ HQ GMP expert Teferi Bedane and local GMP expert Shaiful Khan attended the inspection, conducted using the remote inspection tool Avatour. The inspection successfully reviewed all key documents in

relation to the first-line anti-TB project and concluded with a good impression and no critical observations. ACI's plant management committed to addressing the gaps found during the inspection. PQM+ experts assured that the program will provide continuous technical assistance to ACI to produce bio batches of first-line anti-TB medicines.

In November, ACI and PQM+ signed a subaward agreement and held a kick-off meeting. The meeting covered the roles and responsibilities of the person assigned to follow on the milestone completion per the subaward agreement for TB project.

Activity 4.2: Capacitate local public manufacturer (SOE-EDCL) to implement GMP for the production of first-line anti-TB medicines: PQM+ is closely working with EDCL to conduct a training needs assessment (TNA) to identify required trainings and subsequent technical assistance. PQM+ partner IntraHealth has begun providing support to conduct the assessment.

Activity 4.4. Provide technical assistance to DGDA in preparation for the ending of TRIPS flexibilities: This quarter, PQM+ achieved the following:

- Developed a concept paper on upcoming challenges associated with Bangladesh's transition from a least-developed country (LDC) to a developing country.
- PQM+ Bangladesh's chief of party attended a workshop and discussion on the existing position and upcoming challenges of the transition.

Activity 4.5: Collaborate with the Bangladesh Association of Pharmaceutical Industries (BAPI) to raise awareness of good practices for manufactures of medical products:

PQM+ organized a preliminary meeting with BAPI for providing technical support to enhance capacity of API manufacturing in Bangladesh and to explore ways for collaboration to strengthen manufacturers' overall capacity to ensure the promotion of quality products and promote compliance with global standards. BAPI is highly interested in creating a collaborative training platform for personnel from pharmaceutical industries to enhance competency specially for API manufacturing. The following activities took place:

- Conducted a meeting with BAPI in October regarding a collaborative training program for pharmaceutical industry officials.
- Selected training topics and drafted a plan for training/ workshop on skill development for the active pharmaceutical ingredient (API) industry of Bangladesh.

Priority Activities for Next Quarter

- Draft regulatory framework document for DGDA.
- Provide technical support for compliance with CAPA plan, update, and monitoring.
- Draft a guideline and SOP for implementation of CRP.
- Draft an SOP for monitoring implementation of national drug policy 2016.
- Draft ethical pharmaceutical promotion guideline.
- Complete PIC/S questionnaire and audit checklist along with application for pre-accession.
- Organize a training on the MedRS tool for DGDA staff and assist the PMS unit on adoption of this tool.
- Support conducting a GrevP gap analysis.

- Provide guidance for the selection of a contract research organization (CRO).
- Conduct method validation and write report on potency tests of the following vaccines: tetanus, hepatitis A, typhoid, thiomersal, rabies, and influenza.
- Conduct internal audit in physiochemical and microbiology laboratory of NCL, vaccine wing.
- Prepare of standard testing procedure for the human papilloma virus vaccine.
- Establish the reagent stability study in vaccine chemical lab
- Conduct strengths, weaknesses, opportunities, and threats (SWOT) analysis to support DGDA to develop a five-year strategic plan for the NCL.
- Quarterly lab visit report and progress report of CDTL.

Burma

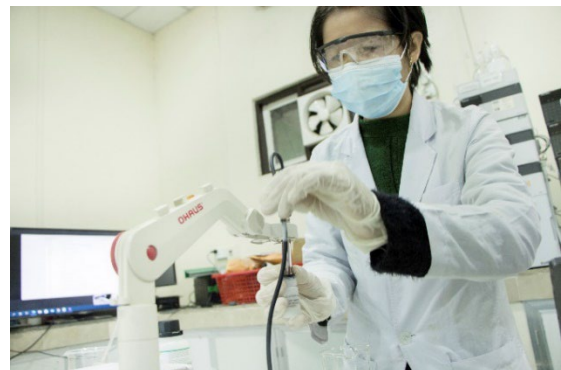
PQM+ in Burma is working to build the capacity of Burma's Department of Food and Drug Administration (DFDA) toward a resilient medical product quality monitoring system. At the same time, PQM+ is working with private manufacturers to achieve WHO PQ for locally manufactured antimalarials. PQM+ aims to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

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

DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory successfully completed the ISO 17025:2017 annual surveillance assessment by the American National Standards Society National Accreditation Board (ANAB).

- PQM+ built the capacity of the new QA team at DFDA Nay Pyi Taw laboratory to maintain and improve their QMS. For most team members, it was their first ISO 17025:2017 assessment.
- The new QA team underwent the virtual assessment in November. The assessor identified just one non-conformity, which the team addressed satisfactorily in the allocated time.
- The current ISO 17025:2017 accreditation of DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory includes 10 scopes of testing. The accreditation is valid until December 2022.



A participant from the DFDA laboratory performs preventive maintenance on a pH meter as part of the hands-on training.

PQM+ delivered week 1 of virtual metrology training at DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory.

- To adapt to the virtual format, PQM+ planned to deliver the metrology training over three nonconsecutive weeks, with PQM+ organizing week 1 in November/December 2021. Fourteen participants from the laboratory attended.
- In collaboration with USP Ghana, PQM+ developed instructional videos for the hands-on part of the preventive maintenance (PM) and post-PM verification.
- Participants said the detailed instructional videos helped them understand the procedures better and provided the opportunity to learn on demand.

PQM+ organized a technical webinar on the “analytical laboratory relocation process.”

- PQM+ organized the technical webinar in collaboration with senior staff from the USP Reference Standards Laboratory, who shared their recent experience in relocating an ISO 17025:2017 accredited laboratory.
- Eighteen participants from DFDA Nay Pyi Taw, Yangon, and Mandalay laboratories attended the webinar.
- The opportunity to learn about the first-hand experience of laboratory relocation from a U.S.-based laboratory will help Nay Pyi Taw Pharmaceutical Chemistry Laboratory better plan and execute its relocation process, reducing downtime to minimize disruptions in the national medicines regulatory system.

Priority Activities for Next Quarter

Next quarter, PQM+ Burma plans to:

- Deliver weeks 2 and 3 of metrology training to DFDA Nay Pyi Taw Laboratory.
- Provide technical assistance in relocating DFDA Nay Pyi Taw Laboratory.
- Deliver a virtual training on measurement uncertainty to DFDA laboratories.
- Provide technical assistance to eligible private laboratories to prepare for ISO 17025:2017 accreditation.
- Provide technical assistance to eligible private manufacturers to achieve WHO PQ for locally produced antimalarials.

Nepal

PQM+ provides technical assistance to Nepal’s Department of Drug Administration (DDA) to strengthen medical product quality assurance (QA) and quality control (QC) systems and is enhancing the testing capacity of National Medicines Laboratory (NML) to complement the regulatory activities of DDA. PQM+ is also working with local public and private manufacturers to increase the domestic supply of quality-assured medicines.

Reaching its third year of implementation, many activities continued as an extension of the previous year, while new activities include public manufacturer strengthening and introducing quality procurement guidelines for the national health insurance system.

Objective 1: Governance for Medical Product Quality Assurance Systems Improved

PQM+ assisted DDA in Nepal to improve medicine related legislation, policies, and regulations and promote collaboration among different stakeholders. PQM+ also closely worked with

MTaPS by participating in a consultative meeting organized by DDA to look into the gaps of the existing drug law and proposed revisions. Other major progress under this objective were:

Revision of the national GMP code: In PY2, PQM+ supported the DDA to update the existing national GMP code in line with the WHO GMP guidelines. In the reporting quarter:

- DDA formed an internal committee to review the revised code to ensure consistency with the Drug Law and other legislation.
- The committee completed the review process and prepared for formal approval in the coming quarter.
- Following approval, PQM+ will support dissemination of the changes among manufacturers.

Revision of the national code on sales and distribution of drugs: PQM+ and partner MTAaPS collaborated to analyze the gaps in the national code on sales and distribution of drugs in line with WHO's Good Sales and Distribution Practices (GSDP). Based on the gap analysis report and in consultation with DDA, both programs are now revising the code to submit it to DDA.

High-level consultative forum: Under DDA's guidance, PQM+ supported formation of a high-level multi-sectoral group to discuss medicine regulation policy issues. The group met in Q1 with the minister of health and other high-ranking officials from government and the private sector in attendance. PQM+ is supporting DDA to draft a policy paper for pharmaceutical sector reform. DDA presented the outline of the policy paper at the national joint annual review meeting between the government and development partners.



Nepal's health minister speaks at the high-level meeting.

Objective 2: Country and Regional Regulatory System to Assure the Quality of Medical Products in the Public and Private Sectors Improved

Strengthen risk-based (RB) inspection of DDA: PQM+ facilitated drafting of risk-based inspection framework which was reviewed during the inspection TWG meeting and agreed to approve with minor amendments. Next quarter, PQM+ will provide technical support to draft four SOPs related to inspection. Similarly, PQM+ facilitated a demonstration of Avatour, technology for remote inspection, to DDA and NML staff.

Strengthen RB-PMS of DDA: PQM+ worked with DDA's Management Division and RB-PMS TWG to institutionalize risk-based approach in DDA's functions:

- Through the TWG meeting, PQM+ supported finalizing the schedule for the RB-PMS pilot in one province in Nepal. The TWG is also reviewing the Nepal-specific RB-PMS guidelines and framework.
- PQM+ advocated to incorporate nine FP/RH and MNCH medicines in the list of 43 for PMS and supported identification of resource requirements to test those medicines, such as reagents, column, chemicals, etc.

- PQM+ facilitated populating the database in the MedRS tool. Similarly, PQM+ oriented the PMS unit and two DDA staff members on a mock risk-scoring exercise in the MedRS to demonstrate risk-based sampling for RB-PMS.
- Next quarter, PQM+ will facilitate an RB-PMS protocol development workshop to the PMS unit and TWG members and begin field sample collection.

Support NML toward ISO 17025 accreditation: At the start of the quarter, PQM+ and DDA signed the IDP to put the NML on the path to accreditation. Based on the IDP, PQM+ and NML collaborated to enhance testing capabilities, improve facilities, and upgrade staff competency.

- PQM+ supported finalizing the list of priority trainings for NML and conducted two of them for 21 technical personnel: Introduction to ISO 17025:2017 and Internal Audit Program.
- PQM+ collaborated with the GHSC-PSM project to arrange a demonstration of the electronic logistic management information system (eLMIS) for NML. The Ministry of Health and Population (MoHP) is scaling the tool up to all public sector health facilities.
- PQM+ assisted NML to design phase-wise implementation of QMS documents such as SOPs.
- Next quarter, PQM+ will support the lab with hands-on training by a USP expert and help the lab acquire equipment to strengthen their testing capacity.

Regulatory workforce development: PQM+ is engaging consortium partner IntraHealth to conduct a training needs assessment of NML. PQM+ supported organizing interviews for information collection and assisted with gathering secondary information. Next quarter, PQM+ will share the draft assessment and training plan with NML. PQM+ is also planning to start a training needs assessment of DDA.

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

To improve the local supply of quality-assured essential medicines, PQM+ is working with private and public pharmaceutical manufacturers.

Private manufacturers: Previously, PQM+ collaborated with DDA to select six pharmaceutical manufacturers to provide technical assistance in four selected medicines for WHO prequalification (PQ) by floating an expression of interest. In the reporting period:

- PQM+ conducted rapid assessment of six manufacturers to verify their documents, followed by the external expert conducting a detailed baseline assessment.
- PQM+ oriented manufacturers and DDA on the WHO PQ process and organized a debriefing session to DDA, USAID, and manufacturers to share the assessment findings.
- DDA actively participated in the process, an opportunity to build their capacity in industry inspection.
- Next quarter, PQM+ will draft CAPA plans for each manufacturer.



PQM+'s expert conducts a detailed baseline assessment.

Public manufacturer: PQM+ and the only public pharmaceutical company, Nepal Ausadhi Limited (NAL), signed a CAPA plan for the latter's compliance towards national GMP. Specifically, PQM+ technically assisted NAL to re-design their microbiology section layout meeting the national regulatory standards and optimize their water treatment system. In the next quarter, PQM+ will assist NAL in improving the section in accordance with the approved layout and help NAL to improve the water treatment system to meet the national GMP compliance standards.

Nepal pharmaceutical manufacturing strategy: PQM+ is collaborating with DDA and other national stakeholders to develop Nepal pharmaceutical manufacturing strategy. PQM+ engaged consortium partner IQVIA to conduct a landscape analysis of the Nepali medicines market. PQM+ is drafting the analysis report after completing a desk review and primary data collection. Next quarter, PQM+ plans to share the draft report with stakeholders.

Quality procurement guidelines: To assure quality in the procurement process for medicines, PQM+ has engaged the National Health Insurance Board and a local government unit to assess the medical product procurement process and develop a guideline for quality assurance during procurement in both entities. In the reporting period,

- PQM+ started the assessment of the quality of procurement process at health facilities affiliated with the National Health Insurance Board.
- A local government unit, upon PQM+ request, has agreed for technical collaboration to develop a standard procurement guideline of medical products in their jurisdiction.
- Next quarter, PQM+ will complete the assessments of health facilities enlisted with the National Health Insurance Board and the local government and share the reports.

Objective 5: Global Medical Product Quality Assurance Learning and Operational Agenda Advanced

Activities to promote awareness of SF medical products in the community will gather pace in next quarter. This quarter, PQM+ and DDA discussed public service messages on SF medicines to be relayed through local radio stations. PQM+ also met with Association of Pharmaceutical Producers of Nepal (APPON) to garner their support for awareness. Similarly, PQM+ is developing session plans to train community pharmacists on SF medicines. To gauge the changes in knowledge and behaviors of community pharmacists on SF medicines, PQM+ is designing a pre-post study.

Pakistan

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

The PQM+ Pakistan 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.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

Activity 1.1: Continue technical assistance for the implementation of organizational restructuring and strengthen performance improvement functions of DRAP: PQM+ supported DRAP to revise its five-year strategic objectives and supported DRAP's participation in a roundtable event for drafting annual performance objectives and a set of indicators that DRAP can use in its regulatory processes evaluation. This exercise proposed organizational restructuring for better reporting compliance and harmonization of practices among the divisions of DRAP. In Q1, PQM+ continued its support to DRAP to implement new performance objectives and the periodic review of indicators. PQM+ developed draft outlines of key performance indicators (KPIs)⁴ to provide a view of performance management, compliance management, and KPIs for measuring the efficiency and effectiveness of various regulatory functions at DRAP.

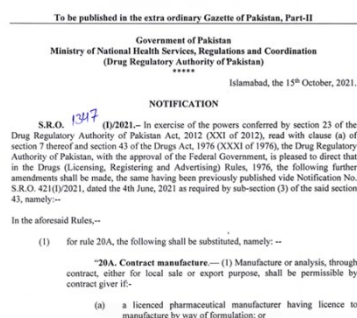
Activity 1.2: Continue support for the implementation of the regulatory framework to handle regulatory actions based on the national AWaRe list: PQM+ Pakistan conducted a desk review of best practices and WHO guidance on registering antimicrobials, and shared findings in a consultative meeting with the Drug Registration Board. Taking into account the classifications of antimicrobials (**A**ccess, **W**atch, and **R**eserve, known as the AWaRe classification), PQM+ developed a guidance document (intervention plan) that incorporates a framework for guiding regulatory actions for: (1) establishment licensing; (2) registration/market authorization; and (3) post-marketing surveillance of antimicrobials from the AWaRe list.

Activity 1.3: Support DRAP in developing/revising its policy on contract manufacturing: PQM+ Pakistan conducted a desk review of best practices in contract manufacturing, using lessons learned from reference countries. The review helped DRAP to establish a working group on contract manufacturing with representation from all relevant stakeholders (government, multinational pharmaceutical manufacturers, and domestic manufacturers) to consider findings from the desk review. PQM+ Pakistan and DRAP incorporated comments and feedback from the working group deliberations into a draft contract manufacturing policy (regulations/guidelines), and then reconvened the working group to consider these regulations/guidelines.

With PQM+ support, draft amendments were proposed to be made by DRAP in the Drug (Licensing, Registering and Advertising) Rules, 1976, with further approval of the federal government.⁵ The key amendments included regulations for the contract manufacturer, production, analysis, quality control, quality assurance, QMS, supply chain, pharmacovigilance, recalls, and compliance to Drug Act 1976 and DRAP act 2012. The key achievement during the reporting quarter is the Cabinet's approval in October of DRAP's proposed amendments to the Drug (Licensing, Registering and Advertising) Rules, 1976.

⁴ Draft outlines of KPIs

⁵ Notification for draft amendments (October 2021). Weblink: [Notification for Draft Amendments on Contract Manufacturing](#)



Activity 1.4: Support DRAP for the development of institutional developmental plans (IDPs): In 2018, at DRAP's request, the USAID-funded Promoting the Quality of Medicines (PQM) project extended its technical support to DRAP for the development of institutional developmental plans (IDPs) based on self-assessment gaps. One major finding was the lack of an organizational QMS. PQM provided technical assistance to DRAP to achieve ISO 9001:2015 certification. This certification is helping DRAP develop and implement a QMS, which is a set of coordinated activities to direct and control an organization to continually improve the effectiveness and efficiency of its performance. The QMS for DRAP has led to job descriptions for each position being defined, documented, and controlled for the first time per ISO standards. Moreover, QMS assisted with the development of key performance indicators, redefining process workflows with timelines, risk management, and mitigation of critical processes, as well as transparency and accountability in all processes.

After the implementation of QMS and other major IDPs, which include implementation of the Common Technical Document (CTD) for market authorization application; adaptation/revision of policies/guidelines; GMP inspection (checklist) including PIC/s requirements; 2D Barcode implemented to check SF products in the supply chain; development of the prototype for the Integrated Regulatory Information Management System; and RB-PMS, these interventions improved the Maturity Level score of all nine regulatory functions.

In Q1PY3, PQM+ assisted DRAP to complete IDPs related with following areas;

- Best practices in clinical trials and adaptation of international guidelines.
- Good Clinical Practices (GCP).
- Assessment and evaluation of pre-clinical and clinical trial data.

Furthermore, during the reporting quarter, USAID/PQM+ organized a series of trainings for National Control Laboratories for Biologicals (NCLB) staff at the National Institute of Health (NIH), Islamabad. The trainings aimed to assist DRAP in completing a few IDPs related to the lot release function. The PQM+ microbiologist delivered a training on Good Microbiological Practices. A series of sessions included trainings on the bacterial endotoxin test, sterility testing, equipment qualification, biosafety levels, classification of biosafety cabinet, sterilization, disinfection, and aseptic techniques. Hands-on trainings included the bacterial endotoxin test, donning and doffing, and the sterility test. Dr. Faisal Sultan, special assistant to the Prime Minister on health, visited the NCLB Microbiology lab at NIH, Islamabad and appreciated the hands-on training at NCLB.

This series of trainings worked to improve the lab staff's technical testing expertise. Main achievements are:

- Understanding the requirements of the test and its validation.
- Helping review technical documents in light of regulatory requirements.
- Validating testing methods and qualification of equipment.
- Fulfilling the requirements to obtain ISO 17025 and WHO prequalification.

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

Activity 2.1: Improve the laboratory quality system by preparing additional laboratories for international certification: PQM+ completed the gap assessment of the Public Health

Laboratory (PHL) at the Institute of Public Health (IPH) in Lahore toward the achievement of ISO 15189 accreditation (an international standard for medical laboratory requirements regarding quality and competence). As a result of the PQM+ assistance, Pakistan National Accreditation Council (PNAC) completed a pre-audit for ISO 15189 in September. This accreditation would enable PHL to improve its lab testing reliability going forward. The key achievements are:

- Provided technical assistance on the preparation of a CAPA plan based on the PNAC pre-assessment observations. The PQM+ team supported proper implementation of the CAPA in pursuit of ISO 15189:2012 Laboratory Quality Management System accreditation for the IPH Medical Lab.
- The CAPA report has been submitted to PNAC for review and the lab is awaiting the final audit.

ISO 17025:2017 (calibration) of Drug Testing Laboratory (DTL) Lahore: National quality control laboratories in Pakistan use calibration services from sources outside the country. Because this is expensive and can lead to delays and interruptions in services (such as during the coronavirus pandemic), Pakistan seeks to build in-country capacity to provide these services. PQM+ Pakistan is helping DTL Lahore achieve ISO 17025 accreditation for calibration. Currently, the lab provides analytical services only and is responsible for the analysis of drug samples. The main scope of tests includes physical tests, chemical analysis, identification tests, assay, and impurities tests. However, competence related to calibration needs to be established to meet the accreditation requirements. PQM+ completed a gap assessment of DTL Lahore and delivered trainings on general requirements of ISO17025:2017 in October at DTL Lahore.

In addition, PQM+ and the WHO prequalification team established a partnership for peer audits and conducted a three-day peer audit for DTL Lahore. PQM+ led the peer audit and assisted in the preparation of the CAPA plan, which DTL Lahore submitted to WHO.

PQM+ Support to DTL Multan (ISO 17043 Accreditation): PQM+ provided support to address queries on the laboratory information file (LIF) against ISO 17043 standards on proficiency testing⁶ from PNAC. Following continuous support from PQM+, PNAC has recommended DTL Multan for ISO 17043 certification. Attainment of ISO 17043 by Multan DTL will ensure the availability of proficiency testing services to other quality control labs in and outside Pakistan.

Quality control laboratories now depend on international resources for proficiency testing services, which are both expensive and time-consuming. With support from PQM+, DTL Multan will be positioned to offer these services to other quality control laboratories nationally and internationally.

PQM+ and the WHO prequalification team established a partnership for peer audits to strengthen the quality control lab system in Pakistan. PQM+ visited DTL Multan to prepare for peer audits, and DTL Multan submitted its CAPA plan to WHO.

PQM+ support to DTL Bahawalpur: PQM+ also assisted DTL Bahawalpur to review and submit the LIF for WHO prequalification, which WHO has accepted and approved. PQM+ and WHO visited DTL Bahawalpur in December for a peer audit. The report for the peer audit is being prepared.

⁶ Proficiency testing (PT) is interlaboratory comparisons that are organized regularly to assess the performance of analytical laboratories and the competence of the analytical personnel.

PQM+ support to DTL Rawalpindi. PQM+ assisted Rawalpindi DTL to submit its LIF, which has been approved. In April, 2021, PQM+ provided technical assistance to Rawalpindi DTL during the WHO prequalification audit. As a follow up activity, PQM+ assisted the DTL for CAPA preparation and submission to WHO.

Central Drug Laboratory (CDL) Karachi Peer Audit – WHO Prequalification: PQM+ supported CDL for moving toward international accreditation to become a WHO Listed Authority. In initial phases, CDL has been assessed for quality management system certification and is continuously engaged with WHO for its prequalification as one of the quality control laboratories in Pakistan. In this regard, PQM+ collaborated with the WHO-PQ team to conduct a peer audit, followed by submission of the CAPA plan to WHO. With PQM+ support, CDL Karachi will be positioned to offer these services to other quality control laboratories nationally and internationally.

Table 1. Status of Labs Accreditation

Laboratory	Accreditation sought	Initial Gap Assessment	CAPA	QMS	PT/LT	Official Inspection/ Pre-assessment
IPH Lab	ISO 15189	Completed	Completed	Completed	Completed	Completed
Appellate lab	ISO 17025	Completed	Ongoing	Developed, under implementation and PT pending	Ongoing	
Ferozsons	PIC/s	Completed	Ongoing	will be followed up by CAPA.		
Laboratory	Accreditation Sought	QMS	Initial Gap Assessment	CAPA	LIF	Official Inspection/ Pre-assessment
DTL, Rawalpindi	WHO-PQ	Completed	Completed	CAPA plan is currently under review		
DTL Multan	WHO-PQ	Completed	Completed	Completed	Submitted and approved	Completed
DTL, Lahore	WHO-PQ	Completed	Completed	Completed and submitted	Submitted and approved	Completed
CDL, Karachi	WHO-PQ	Completed	Completed	Completed and submitted	Submitted and approved	Completed
DTL, Bahawalpur	WHO-PQ	Completed	Completed	CAPA plan is currently under review	Submitted and approved	Completed on (December 6-9)

Objective 3: Supply of quality assured essential medical products of health importance increased

Activity 3.1: Optimize allocation and use of regulatory investments through risk-based approaches: PQM+ Pakistan completed a desk review of international best practices for assigning a risk score (risk priority number) for product quality during the pre-market phase. Based on the desk review, PQM+ met with DRAP on drafting guidance for the adoption of risk-

based approaches to regulatory activities. The guidance document⁷ will help users monitor the safety, efficacy, and quality of generic products manufactured by pharma industries in Pakistan prior to granting them market authorization. In addition, the document discusses the generation, acquisition, analysis, and presentation of premarketing safety data

Activity 3.1: Development of a National Pharmaceutical Strategy: A focus of PQM+ in this activity was to help foster a business-enabling environment that encourages private sector investment in pharmaceutical manufacturing. Pakistan exports approximately \$230 million in pharmaceutical products, a small percentage of the more than \$1 trillion global market for pharmaceuticals. With careful planning, strategic policymaking, and investments, as well as a strong commitment from the government and the pharmaceutical industry, Pakistan’s share of the global pharmaceutical market can increase exponentially. This will both bolster Pakistan’s economy and generate substantial foreign exchange, as well as ensure the provision of safe, effective, and quality-assured drugs in Pakistan.

During the reporting quarter, the team accomplished a series of key tasks as part of this activity.

Preliminary Findings: The first round of consultations conducted in the last quarter were conducted using topic guides formed based on a desk review exercise. Table 2 summarizes the key challenges identified in the desk review exercise.

Table 2. Key Challenges Identified During Desk Review

Industry-Related Challenges in Secondary Research	Export-Specific Challenges in Secondary Research
<ul style="list-style-type: none"> i. Dependence on imports for key raw materials (95%) – resulting in high exposure to exchange rate fluctuations and supply chain challenges. ii. Absence of guidance documents for Policies for ease of regulatory compliance. iii. Pricing controls create perverse incentives leading to restricted availability of essential drugs due to artificial shortages, compromised quality of drugs, and increased out- of-pocket expenditures for patients because newer & higher priced drugs enter the market. iv. Physician-Pharma transactional relationships which lead to over-prescription, causing increased drug resistance and increased out-of-pocket expenditures for patients. v. High infrastructure and operating cost (high interest rates, energy shortage and the historically uncertain security situation). vi. Questionable quality of medicine (however no systematic data is available). vii. Inconsistent government policies. viii. Lack of research and development facilities. 	<ul style="list-style-type: none"> i. Tariffs on imports of key raw materials, plant and machinery which are used for manufacturing products for export. ii. High infrastructure and operating cost (high interest rates, energy shortage and the historically uncertain security situation). iii. Inconsistent government policies. iv. Pricing controls in the domestic market lead to pricing caps in export markets where domestic pricing parity is required. v. Lack of research and development facilities. vi. High cost of bioavailability/bio-equivalence studies which are required for export permissions. vii. Lack of appropriately skilled contractors for such research available locally. viii. Lack of USFDA and other Stringent Regulator Authority approved manufacturing facilities. ix. Lack of Regulator’s compliance to international standards such as PIC/S and WHO.

⁷ [Guidance Document for Pre-Marketing Risk Assessment Tools](#)

A first-line analysis of the consultations completed with industry in the last quarter revealed the following key areas highlighted by the private sector for intervention.

- Optimizing regulatory compliance journeys.
- Incentivizing investment by industry in high-quality manufacturing facilities in compliance with stringent regulatory authorities (SRAs) and international standards such as PIC/S and WHO.
- Upgrading regulatory capacity and practices for compliance with international standards such as PIC/S and WHO.
- Limiting price control of pharmaceutical products.
- Reforming contract manufacturing policy to remove hurdles for industry.
- Uniform quality assurance and enforcement of GMP by the regulator for small and large firms.
- Explore performance-linked incentive schemes to encourage industry to realize high export potential.

Within the area of optimizing regulatory compliance journeys, the team mapped three key regulatory journeys: new product registration, GMP certificate, and drug manufacturing license renewal, as well as the supply of products to export markets.

Ongoing Engagement and Advocacy with Government: As part of the ongoing engagement with multiple government departments and ministries, PQM+ identified a new strategic partner for this work. Until now, the primary sponsor was the Policy Wing within the Board of Investment in the Prime Minister's Office. However, due to changes in key officeholders and mandates in that wing, PQM+ identified a potential collaborator in the Pakistan Regulatory Modernization Initiative (PRMI), a newly launched initiative by the Additional Secretary of the Business Environment Reforms (BER) Wing of the Board of Investment. PQM+ coordinated an introductory meeting with the leadership of PRMI in October to share the objectives, progress, and ambition of the strategy development exercise. The team also shared preliminary findings resulting from the first round of consultations conducted, along with key regulatory hurdles that discourage investment in the sector.

The PRMI leadership appreciated the strategy initiative and shared their objective of modernising the regulatory regime across all major sectors in Pakistan, and helping the private sector grow through expansion in domestic and export markets. The PQM+ team shared the program's substantial period of engagement (since 2015) with key stakeholders in the pharmaceutical sector, track record of success, and the significant experience and expertise of the key personnel to support the PRMI's ambition of modernizing the pharmaceutical sector. Consequently, the PRMI team expressed interest in collaborating with PQM+ and requested the team to share a reform proposal as a test case on their prescribed template.

The PQM+ team held internal deliberations and identified the Progressive Licensing and Risk-based Inspection as a priority reform proposal. PQM+ drafted a proposal on the PRMI prescribed template and shared it in November, after which PRMI expressed interest in engaging PQM+ as subject matter experts for their reform ambitions for the pharmaceutical sector. PQM+ and PRMI agreed to collaborate with PQM+ extending technical assistance based on the team's deep technical expertise, knowledge of global best practices, and a nuanced understanding of the local context of the pharmaceutical sector/regulatory regime to

support PRMI. PRMI agreed to become the lead partner for the strategy work in the government and take this process forward.

In December, the Additional Secretary/Executive Director General of the Board of Investment BER wing led a consultative session with participation from the pharmaceutical industry association and the Pakistan Business Council, senior corporate leaders from the industry, representatives from development partners (including the World Bank and International Finance Corporation IFC). The participants agreed to work together to identify a series of recommendations (including regulatory reforms and incentives for industry) ranging from short-term, “low-hanging fruit,” to medium- and long-term recommendations. The overall goal would be to increase investment in and competitiveness of the Pakistani pharmaceutical sector; support the industry and regulator to comply with global quality standards such as PIC/S, WHO and those of SRAs; and increase share in the global pharmaceutical market through exports.

Participants also agreed to hold a larger roundtable, inviting all stakeholders in the Q2 to present key recommendations for feedback and endorsement. PQM+ has started working with PRMI to plan this.

Second Pakistan Africa Trade Development Conference (PATDC) and Single Country Exhibition: During the stakeholder consultations with the Ministry of Commerce, the Joint Secretary for Commerce shared a request for support in organizing a trade exhibition, conference, and business-to-business (B2B) meetings for the pharmaceutical sector delegation going to PATDC in November in Lagos, Nigeria.

The PQM+ team conducted meetings with the relevant trade and investment attaché and Pakistan’s High Commissioner to Nigeria to better understand their needs and subsequently connected them with PQM+ senior management in Nigeria for the required support.

Through a cross-country collaboration between its Pakistani and Nigerian teams, PQM+ extended the required support to the Pakistani government and pharmaceutical industry. This will help improve the supply of quality-assured pharmaceutical products to Nigeria and work to mature the Nigerian pharma industry through partnerships with Pakistani industry. Other outcomes include improved public health outcomes in Nigeria, higher exports for the Pakistani pharma industry, and economic growth for Pakistan. At the conference, the news outlet Pro Pakistani reported, “five memoranda of understanding (MOUs) were signed by Pakistani pharmaceutical companies, with trade deals worth \$6 million with Nigerian companies and a Senegalese company.”⁸

Priority Activities for Next Quarter:

Next quarter, PQM+ plans to:

- Develop a National Medicines Policy (NMP) implementation plan and guidelines for the quality assurance of medical products (including antimicrobials).
- Provide technical assistance to two bioequivalence study centers, one in the public sector and one from the private sector.
- Identify appropriate pharmaceutical sector partners and design a training curriculum in collaboration with DRAP.
- For IPH Lahore’s ISO 15189 accreditation path, follow up with PNAC for the final assessment.

⁸ <https://propakistani.pk/2021/11/25/razak-dawood-calls-for-closer-economic-ties-with-africa-as-patdc-concludes/>

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 PY3, 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 Q1, PQM+ continued technical assistance to the Almaty and Karaganda MQCLs to help them achieve and maintain WHO prequalification (PQ).

- PQM+ continued technical assistance to Almaty MQCL in implementation of a CAPA plan prepared by the lab after PQM+ peer audit. For example, PQM+ provided a virtual two-day refresher training on WHO Good laboratory practices (GLP) focused on addressing the gaps identified by PQM+ during the peer audit. The training was attended by 53 staff of the Almaty and 11 staff of the Taraz MQCL.
- PQM+ met with WHO prequalification (PQ) team to discuss the Almaty peer audit report. WHO PQ team reviewed the report and requested additional information from the MQCL. Almaty MQCL is revising the reviewed procedures to include additional information requested by WHO; MQCL will send the CAPA plan, relevant supporting documents, and additional procedures to WHO for review. WHO scheduled their inspection of Almaty laboratory for July 2022.
- PQM+ arranged a two-day on-site, hands-on training on computerized system validation (CSV). The training was conducted in Almaty MQCL by PQM+; the training was attended by 25 participants from Karaganda and Almaty MQCL and the pharmaceutical inspectorate.
- The PQM+ funded equipment for Karaganda laboratory (pH-meter, conductometer and Karl Fischer titrator) essential for maintaining WHO PQ was delivered to Kazakhstan and is undergoing custom clearance.

PQM+ is supporting Kazakhstan in strengthening the pharmaceutical inspectorate and preparing for ascension to PIC/S. PIC/S membership will facilitate reliance and open access to the Good Manufacturing Practices (GMP) inspection mechanism with other PIC/S member

countries; resources for capacity development; and access to quality-assured medicines in the country.

- PQM+ met with the deputy chairman of the Committee for Medical and Pharmaceutical Control (the Committee) and management of GMP Inspectorate. The deputy chairman confirmed commitment to support preparation for PIC/S accession and to address the WHO recommendations from the Global Benchmarking Tool (GBT) audit in September 2021.
- PQM+ reviewed the WHO GBT results from the September audit. Since the GBT and PIC/S requirements are similar, PQM+ recommends that addressing GBT gaps and PIC/S accession should be done in parallel.
- PQM+ continued technical assistance toward advancing on the roadmap to PIC/S ascension. In PY3, Q1 the inspectorate updated the roadmap with details and set up concrete steps to implement the road map. The road map will help monitor the progress in preparation for WHO accession. PQM+ also assisted the Inspectorate in drafting their quality management system (QMS) documents which is now being finalized.
- In PY3, Q1 PQM+ also provided a three-day virtual training on Inspection of Vaccine manufacturer for the Inspectorate. The training covered discussion of GMP requirements for vaccines manufacturer, inspection of vaccines manufacturer, typical findings, and deficiencies during the inspections. The training was attended by 26 participants from the Inspectorate and the Department of Pharmaceutical expertise of medicines, NCEM.

The WHO GBT assessment also identified gaps in market surveillance and control in Kazakhstan. In PY3, PQM+ continues to build on the collaborative work conducted in PY2.

- PQM+ started preparations for an onsite training of the NCEM staff on the MedRS tool in January 2022. PQM+ is working with the NCEM to identify participants for this training.
- PQM+ also finalized translation of MedRS into Russian.
- PQM+ provided recommendations on the RB-PMS business process map developed by the NCEM.

PQM+ continued work with the 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 PY3 Q1 the SEC received the institutional accreditation by Eurasian Center for Accreditation and Quality Assurance in Higher Education and Healthcare. SEC can now provide educational services.
- PQM+ delivered a five-day virtual training sessions on Designing Effective Teaching for the SEC's trainers. PQM+ discussed instructional design approach; elements of training design; how to develop a session plan; and how to prepare and implement the training; and methods of evaluation. Two of the five training sessions were based on the training on the Rules of Pharmaceutical Inspection developed by SEC. PQM+ explained how to design training, and how to apply different teaching techniques depending on the training content and target audience. The participants received assignments to develop session plan based on the training principles. The training was attended by 30 participants.

PQM+ continues assistance to NCEM in improving the medical devices (MD) inspectorate. PQM+ identified four areas of technical assistance: development of MD inspectors' group, development of QMS, training of inspectors, and evaluation of dossier applications.

- In Q1 PQM+ discussed the approaches to development of QMS of the MD inspectorate. The MD Inspectorate prepared a draft plan containing key documents related to QMS. They also provided several draft SOPs, and PQM+ is reviewing these documents.

The NCEM started working on development of the five-year (2021–2025) strategy. The strategy should address key areas of the pharmaceutical industry development in the context of EAEU harmonization and WHO GBT assessment.

- NCEM provided an updated draft strategy for PQM+ review. PQM+ discussed with the NCEM their specific expectations and requirements regarding the strategy development. PQM+ is reviewing the Strategic plan developed by NCEM and provided the first set of recommendations.

PQM+ continued engagement with NCEM to provide technical assistance to address the gaps in the registration system and to work toward achieving WHO GBT Maturity Level 3. WHO GBT audit identified four registration sub-indicators which require additional improvement. PQM+ had internal discussions on how to better assist the NCEM in these areas.

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

Kazakhstan has two associations of local pharmaceutical manufacturers. PQM+ initiated engagement with the Kazakhstan Pharmaceutical Manufacturers' Associations to understand their needs.

- PQM+ started work on the design of the training needs assessment of the local manufacturers. PQM+ developed a list of topics for the questionnaire and a draft format for the questionnaire.
- PQM+ discussed with SEC on how to engage with the Manufacturers' Associations. As soon as the needs assessment questionnaire is ready, PQM+ in coordination with the SEC will start discussion with the Manufacturers' Associations and explain the goal of the assessment – to understand the manufacturers' needs for further improvement of their GMP compliance.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Assist the Almaty MQCL in preparation for WHO PQ inspection.
- Continue technical assistance to the PIC/S working group in the areas outlined in the PIC/S accession roadmap.
- Continue technical assistance to the NCEM on developing approaches and procedures for RB-PMS.
- Continue technical assistance to the SEC to build capacity on workforce development.
- Provide technical assistance to the MD inspection group to become operational and compliant with international standards.

- Provide technical assistance to NCEM in preparation of a five-year strategy.
- Address findings related to GLP from the GBT follow up assessment in collaboration with NCEM and the Committee for Medical and Pharmaceutical Control.
- Assist the Committee in establishing ISO 9001 QMS.
- Assess the training needs of the local manufacturers.

Tajikistan

PQM+ is strengthening the medicines regulatory system in Tajikistan by providing technical assistance to the State Surveillance Service over Healthcare and Social Protection of the Population (SSSHS). The main objectives are to improve the medicines registration system and to support medicines quality control laboratory (MQCL) so that they can test the quality of medicines reliably and accurately according to the international standards.

In PY3, PQM+ will help:

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

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

Tajikistan requires implementers to officially meet with the government counterpart prior to starting the activities. Archil Salakaia, Health Elements Director, traveled to Tajikistan in November. He met with SSSHs to introduce PQM+ and officially launch the program activities.

Following the program launch, PQM+ organized an introductory meeting with the medicine registration department. SSSHs established a technical working group (TWG) on registration systems strengthening to work with PQM+. PQM+ adapted a questionnaire for the assessment of the medicine registration system. PQM+ introduced the questionnaire to the TWG with guidance on completing the questionnaire.

PQM+ also organized an introductory meeting with the national MQCL team. The national MQCL established a TWG on quality management system (QMS) to work with PQM+. PQM+ shared an overview of and best practices from its work in Central Asia.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Receive and review completed assessment from the medicine's registration department
- Identify gaps and areas of support needed from PQM+ to improve medicine registration
- Conduct assessment of the national MQCL

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. PQM+ assists the Agency on Development of the Pharmaceutical Industry (“the Agency”) around medicines regulatory systems strengthening, including improving the medicines review and registration system, supporting MQCLs to test the quality of medicines reliably and accurately, preparing the GMP inspectorate for PIC/S accession, and introducing RB-PMS to detect substandard and falsified medicine. The program also focuses on increasing the supply of locally manufactured, quality-assured TB medicines by providing technical assistance to pharmaceutical manufacturers.

In PY3, PQM+ will:

- Improve governance for medical product quality assurance system
- 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 1: Governance for medical product quality assurance system improved

PQM+ is providing technical assistance to the Ministry of Health (MoH) in development of the “pharmaceuticals and medical devices” strategic block of the MoH’s Health Strategy 2030. PQM+ connected with the national counterparts from the chamber of innovative healthcare management, a subdivision of the MoH tasked with leading the development of the health strategy 2030. With the chamber, PQM+ is outlining plans for establishing a working group on pharmaceuticals and medical devices strategic block. PQM+ will co-lead the working group and develop strategy on the pharmaceuticals and medical devices.

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

In Q1, PQM+ organized the visit of the USAID Uzbekistan Mission to the Tashkent Pharma Park, a pharmaceutical cluster construction site. During this visit, Director of the Agency Sardor Kariev; Deputy Director Alisher Temirov; Tashkent Pharma Park Director Sanjar Babadjanov; and Pharma University lead Abdumalik Djumanov presented the Tashkent Pharma Park project to USAID. The pharma park houses the regulatory, manufacturing, and research and development functions related to the medical products in one modern unit, representing the highest level of commitment of the government to advance the pharmaceutical industry in Uzbekistan.

In Q1, PQM+ hit an important milestone in advocating and providing technical assistance for using the collaborative registration procedure (CRP) for accelerated registration of WHO-prequalified medicines in Uzbekistan. Two TB medicines, cycloserine and protionamide, were registered through the WHO CRP. This important milestone means that WHO CRP is starting to work in Uzbekistan, which will help accelerate the registration of WHO-prequalified, quality-assured medicines and in removing registration-related obstacles in procuring or importing these products. The Agency is currently reviewing the dossiers for other WHO-prequalified TB medicines. PQM+ is also working with the stakeholders to ensure that other manufacturers of

WHO-prequalified products also submit corresponding dossiers to the Agency to register their products in Uzbekistan through WHO CRP.

PQM+ also continued to provide technical assistance to strengthen the medicines registration system. 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.

This quarter, the Agency established a new working group at the newly established Good Practices (GxP) Center, responsible for GMP inspection. PQM+ engaged with the working group on the development of updated version of the GMP guideline, training programs for inspectors, job descriptions for inspectors, and SOP on inspection process. In addition, PQM+ conducted a training with 11 participants of the working group on the GMP Guideline.

With PQM+ technical assistance, Tashkent and Andijan laboratories received accreditation on the local ISO 17025. PQM+ organized an equipment hand-over event of the HPLC at the Andijan MQCL with participation of the USAID Mission and Agency's senior management. Adding the HPLC capability will help strengthen the MQCL infrastructure to test the quality of medicines.

In PY2 Q4, the government introduced a clause on the development of a roadmap for introduction of PMS into the Presidential Decree. This is a good development because this indicates the government's desire to transition into a PMS system. In Q1, the approval for the decree is pending, PQM+ will begin work on PMS as soon as the decree is approved.

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

PQM+ officially launched the Quality Club, which will provide a mechanism for continuous dialogue between the Agency and local pharmaceutical manufacturers to discuss updates, challenges, and solutions related to medicines and medical products regulation in Uzbekistan. This is important because this is the first time in Uzbekistan, a forum for formal dialogue between the Agency and the manufacturer, took place. Representatives of the USAID Mission to Uzbekistan, the Agency, State Center, the Association of Pharmaceutical Industries of Uzbekistan, the National Chamber of Innovative Health under the Ministry of Health, and participants from about 20 manufacturers attended the event.

PQM+ continued technical assistance to Nobel Pharmsanoat towards prequalification of their TB product levofloxacin. In Q1, PQM+ technical assistance included training of the staff on specific topics related to dossier development in common technical document (CTD) format. Also, guidance was provided on specific topics related to product development, as well as on biowaiver, product formulation, dissolution profile, and bio batch production. In addition, with PQM+ technical assistance, several CTD module documents were prepared. CTD format is the format required by WHO for dossier submission for prequalification.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Review the newly developed SOPs to support strengthening of the medicine's registration system.

- Provide technical assistance to develop the integrated information management system for medicines registration.
- Continue facilitation of registration of WHO-prequalified TB medicines through the WHO CRP mechanism.
- Assess at least one additional regional MQCL.
- 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.
- Continue technical assistance on strengthening the PMS including finalization and approval of the roadmap.
- Continue technical assistance to Nobel Pharmsanoat in its preparation for WHO PQ for levofloxacin production.
- Launch the PQM+ contribution to the Development of The Health Strategy 2030.
- Conduct the second Quality Club session with topic on Track and Trace system and GMP requirements

COVID-19

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: to improve the country and regional regulatory systems to assure the quality of medical products in the public and private sectors. The two main activities implemented in this workplan included:

- Develop an operational guide for Emergency Regulatory Procedures for COVID-19 Medical Products.
- Disseminate the USP quality control toolkit for COVID-19 vaccines.

PQM+ engaged its partners – the University of Washington, the Global Health Impact Group (GHIG), and the London School of Hygiene and Tropical Medicine (LSHTM) – to implement the emergency regulatory procedure activity. PQM+ also collaborated with USP and African Medicines Regulatory Harmonization (AMRH) to plan and host the second activity on quality control toolkits for vaccines.

PQM+ hosted a webinar titled “Model Practical Emergency Use Authorization (EUA) Guidance to Expedite Availability of COVID-19 Vaccines and Diagnostics” on October 18. The draft documents for both vaccines and diagnostics were circulated to the participants before the webinar. The main purpose of the webinar was to conduct a soft launch of the EUA guidance for vaccines and diagnostics and to solicit feedback from stakeholders that participated for content improvement.

The webinar, with 42 participants from around the world, provided an overview of the draft guides and tools and gave an opportunity for key stakeholders to express feedback before finalization. During the webinar, participants were asked to join one of two breakout rooms. One room focused on EUAs for vaccines and the other focused on EUAs for diagnostics. Feedback from the event informed finalization of the EUA guidance documents for vaccines and diagnostics.

Both documents were translated into French and disseminated widely to PQM+ offices, country NMRAs, and the PQM+ stakeholder contact list, as well as on Twitter and LinkedIn. The final English and French documents are available on the [PQM+ website](#). PQM+ also developed a one-page description of the guidance document for dissemination.

This activity was completed in December 2021.

Bangladesh

PQM+ is supporting the Directorate General for Drug Administration (DGDA) in vaccine testing and RB-PMS. In Q1, PQM+ reviewed DGDA’s existing EUA/no-objection certificate (NOC) systems. PQM+ also held consultative meetings with 20 experts from the Public Health Emergency Committee (PHEC), DGDA, and other relevant stakeholders to discuss the EUA guideline for COVID-19 vaccines in Bangladesh. Based on information from these consultative meetings, PQM+ developed an EUA Guideline for DGDA, which the program finalized in late November. In collaboration with DGDA, PQM+ conducted a training of trainers (TOT) in late November, launched by the DGDA’s director general and attended by DGDA senior officials, the

PQM+ activity manager, and the USP Global Health and Manufacturing Vaccine Program director. Fifteen people participated.

PQM+ also worked with DGDA to draft an RB-PMS Guideline for Vaccines, based on input from the Federal Expanded Program on Immunization. The guideline was finalized in November and disseminated in December. PQM+ also compiled a list of COVID-19 vaccine distribution and administration sites, including vaccination centers, storage facilities, and temporary centers for mass vaccination campaigns. DGDA will update this list regularly as information changes and upload it into the Medicines Risk-based Surveillance (MedRS) tool to help determine sampling. PQM+ also worked with the vaccine division of the National Quality Control Lab (NQCL) in Dhaka to build its capacity in vaccine testing. In Q1, PQM+ Bangladesh developed a protocol for COVID-19 vaccines RB-PMS sample collection and testing.

To advance its work around vaccine safety surveillance, PQM+ visited two private sector laboratories in December to assess the level of analytical capability for COVID-19 vaccines testing in-country. The team assessed each lab's capacity to test the vaccines based on human resource competencies, lab environment, and necessary equipment. This information will support DGDA in deciding whether to use private/autonomous labs for regulatory testing of medical products, based on existing legal provisions.

PQM+ is also working with DGDA's NCL to establish a PPE testing laboratory to ensure quality-assured PPE. In December, PQM+ started to develop specifications for particulate filtration efficiency, a medical mask differential pressure tester machine, and other PPE testing equipment to procure the needed equipment for the lab. These specifications were validated by DGDA, NCL, and a Bangladesh University of Engineering and Technology expert.

Burkina Faso

PQM+ is working to support the medicines regulatory authority (MRA), *Autorité Nationale de Régulation Pharmaceutique* (ANRP), to strengthen its adverse events following immunization (AEFI) surveillance system, build its capacity to grant regulatory approval for COVID-19 vaccines in alignment with the country's National Vaccine Deployment Plan, and improve its lot release functions. In Q1, PQM+ met with other USAID implementing partners (the Health Policy Plus (HP+) and MtaPS programs) to understand their AEFI-related activities and strategize on how to better coordinate and collaborate during implementation. As a result of this conversation, the programs agreed to convene bimonthly meetings with ANRP's safety committee to review AEFI notifications and draft a report of findings.

At the request of the USAID/Burkina Faso Mission, following an urgent call for support from the Ministry of Health, PQM+ contributed to a national vaccination campaign targeting four regions, aimed at increasing the vaccination uptake in the country. The uptake rate was at about 2 percent nationally in November after six months of vaccine deployment. PQM+ joined the USAID/Burkina Faso Mission team to supervise the vaccination campaign and in the process was able to observe the recording of AEFI at vaccination sites. In one of the four regions targeted, PQM+ contributed to vaccinating 1,303 people with doses of the Pfizer vaccine. Other USAID implementing partners also supported the campaign. PQM+ noted a lack of AEFI notifications during the supervisory visits. To help with uptake in AEFI surveillance, PQM+ will collaborate with HP+ and MTaPs in Q2 to provide a refresher training in Ouagadougou for vaccination staff on AEFI notifications for COVID-19 vaccines.

PQM+ is also supporting ANRP to grant regulatory approval for COVID-19 vaccines in alignment with the priorities of Burkina Faso (outlined in the National Vaccine Deployment Plan).

In December, PQM+ participated in and supported the dossier evaluation for the Moderna vaccine by ANRP's committee of 20 technical experts to establish its safety, efficacy, and quality for the Burkina Faso population. The Technical Commission for the Approval of Health Products (CHPS, *Commission technique d'Homologation des Produits de Santé à l'usage humain*) reviewed the evaluation and recommended the issuance of an EUA for the Moderna vaccine by ANRP. Participating in this session, PQM+ observed gaps and can now tailor its capacity building plans to strengthen ANRP's EUA process. During the session, PQM+ also provided feedback on best practices per the new guidance developed by PQM+ with Cross Bureau COVID-19 funding: *A Proposed Model to Build Capacity for Emergency Use Authorization for Vaccines and Diagnostics: Guidance for National Regulatory Authorities*. Based on this session, PQM+ will plan and host a formal training on emergency use listing (EUL) and this new EUA guidance for ANRP's technical committee. PQM+ will also plan a general training on the evaluation of vaccines and other biologics based on recommendations from ANRP's technical committee.

PQM+ is also working to build the capacity of LNSP to test COVID-19 vaccines. In November, PQM+ assessed LNSP's microbiological laboratory to ascertain its QMS level of readiness, competency of its personnel, and adequacy of equipment, accessories, and lab consumables available for testing these vaccines. PQM+ noted that the facilities of the microbiology laboratory did not conform with the required clean room classification per WHO's good practices for pharmaceutical microbiology. Also, lab analysts had experience in basic microbiological testing such as pH, sterility, and endotoxin, but had no experience in more advanced tests such as potency or identity tests. While the lab had some equipment for the basic microbiology tests, they did not have many consumables, accessories, and equipment required for identification and potency testing of the COVID-19 vaccines.

PQM+ introduced LNSP's microbiology personnel to the COVID-19 vaccine testing toolkit developed by USP. As the analysts at LNSP have never tested vaccines/biologicals, this training provided a good introductory overview of the types of vaccine platforms that exist, the tests required to ascertain their quality and where to find information on the process. PQM+ is also working with LNSP to procure the necessary supplies and equipment for LNSP to perform these tests.

Ethiopia

PQM+ is working to support EFDA to prevent SF vaccine distribution/ administration through risk-based inspection. Specifically, PQM+ will work with health offices in Woreda to inspect 100 sites involved in the storage, handling, and delivery of COVID-19 vaccines. The Ethiopia COVID-19 work plan was approved in late October and PQM+ dedicated the rest of that month to starting up the project, as well as providing training to 30 EFDA branch inspectors and regional regulators. The training focused on an overview of vaccine regulation and regulatory requirements of cold chain management. As a follow-up, PQM+ developed a checklist for cold chain inspection. PQM+ met with EFDA, its branch offices, and regional/Woreda regulators to define the plan for inspection of cold chain facilities for COVID-19 vaccines, conducted by regional/Woreda regulators in December.

PQM+ provided support to EFDA in its inspection of cold chain facilities for proper handling, storage, and delivery of COVID-19 vaccines per regulatory requirements. Regional regulators conducted inspections at more than 200 sites (including the Harari, Sidamama, Gonder, Gojam, and Gambella regions) using inspection checklists and knowledge from the November PQM+ training. This inspection of cold chain facilities will continue in the Addis Ababa and Oromia

regions in January. PQM+ will continue to support this inspection in its next phase, including data entry and reporting.

In November, PQM+ supported EFDA to strengthen COVID-19 vaccine registration and market authorization by building its capacity to review dossiers. Review of COVID-19 vaccine dossiers requires specialized knowledge and experience, but only three assessors at EFDA had the needed experience, which is inadequate. To enhance the capacity of EFDA to review the growing number of new applications in a timely fashion, PQM+ planned to support the training of additional assessors. PQM+ met with the Medicine Registration Directorate and identified three assessors to train on dossier review of COVID-19 vaccines.

In addition to registering vaccines, PQM+ is supporting EFDA to strengthen product defect reporting through adverse drug reaction (ADR) reports. PQM+ will provide training to health workers at COVID-19 active surveillance sites to promote the detection and notification of product defects through the passive ADR report. PQM+ developed a proposal for training health workers and other stakeholders on monitoring product quality defects of COVID-19 vaccines through the spontaneous reporting system, to ensure that all relevant stakeholders are aware of the requirements and exercise their own responsibilities.

PQM+ is also helping EFDA's national safety advisory committee improve its review of AEFI data. EFDA does not have the capacity to monitor AEFI. The number of AEFI reports received, investigated, and analyzed is small compared to the number of people who are vaccinated. More strikingly, causality analysis was performed for only eight cases of the 36 serious AEFIs. To strengthen casualty analysis, PQM+ trained 33 participants (seven female) on COVID-19 safety data review in November and December. In addition to the safety advisory committee, the EFDA pharmacovigilance staff at headquarters and branch locations, staff from the decentralized pharmacovigilance centers at regional university hospitals, the task force members of National Novel Oral Polio Vaccine (NOPV), and staff of the immunization program at the Ministry of Health participated in the virtual training program. The training covered a range of topics on AEFI, including surveillance, monitoring and responding to adverse events, causality assessment, and the use of the new electronic tool developed by WHO for causality assessment.

This training was important, as causality assessments are a crucial part of AEFI surveillance and decision-making in terms of action taken on serious adverse events (SAEs). Causality assessment helps to determine the likelihood of a causal association between the event and the vaccine(s) received. Once the result of causality analysis is determined, the EFDA can use this information to take the necessary enforcement actions, thereby protecting the public from unnecessary vaccine-related harms and increasing confidence and uptake of the vaccines themselves. By building the capacity of the safety advisory committee, PQM+ is enabling EFDA to carry out effective and timely causality assessments and follow-up regulatory actions that are critical to vaccine safety.

PQM+ also provided technical assistance to EFDA with the investigations of six cases with SAEs to facilitate timely causality analysis. The National Safety Advisory Committee completed its causality analysis for three SAE cases, two of which were categorized as indeterminate and one as coincidental. One of the SAE cases was the first Ethiopian case assessed using WHO's online causality assessment tool, which PQM+ had trained the committee on in early December. For all cases, the National Safety Advisory Committee recommended strong post-vaccination monitoring to the MOH and Expanded Program for Immunization (EPI).

Ghana

Immunization Readiness and Implementation

PQM+ is supporting the Ghana FDA with its cohort event monitoring (CEM) of COVID-19 vaccine distribution, expected to last eight months. Approximately 10,000 people are expected to enroll in the study and be followed on predetermined days after they receive first and second doses of a COVID-19 vaccine. In October, PQM+ co-facilitated a training of 15 health care professionals and 29 Ghana FDA staff (totaling 44 participants: 32 male and 12 female) on AEFI, the revised CEM protocol and its importance, and the use of the Open Data Kit (ODK) platform for data collection. Ghana FDA hosted the event, with facilitation by experts from PQM+, EPI, and the World Health Organization Regional Office for Africa (WHO-AFRO).

As part of the CEM study implementation in seven sites across six regions, a team of monitors and supervisors from FDA Ghana and EPI have oversight of the study to monitor the progress of the study and identify challenges for quick redress. Throughout the quarter, PQM+ procured two tablets per region (14 total) to use during the CEM study for downloading the ODK software needed for data entry. In addition, PQM+ provided the study team allowances to procure internet data and call credit for communication between the teams and to enable follow-up with enrolled participants to gather AEFI information. PQM+ also supported printing the aids (posters and leaflets) for team members and study sites. PQM+ accompanied monitors and supervisors to observe enrollment in the Ashanti and Greater Accra regions.

The study recorded the following number of participants enrolled in December:

Ashanti Region	466
Central Region	176
Volta Region	101
Bono East	596
Northern Region	
Greater Accra (Mamprobi Site)	548
Greater Accra (Tema General Hospital Site)	385
Total Enrolled in December	2,772
Total Enrolled to Date (March-December)	5,272 (53% of target)

FDA Ghana and EPI updated the target to 750 to 1,000 people per site for the study period with a monthly target of 188 to 250 per site to be enrolled across four months, with follow-up spanning three months. They also noted that performance is based mainly on vaccine availability at the sites.

PQM+ worked with Ghana FDA to enable the quality control laboratory to conduct all tests required for COVID-19 vaccines. PQM+ purchased 35 items required by the quality control laboratory for the testing of COVID-19 viral vector vaccines (those from Johnson and Johnson and AstraZeneca). These items are required to train Ghana FDA on conducting the potency testing of COVID-19 vaccines and will be used by the laboratory for routine potency testing after the training. PQM+ has ensured Ghana FDA will include these same consumables in its 2022 budget so that they are able to procure more of these consumables for routine testing of the vaccines going forward.

In Q1, PQM+ also conducted an assessment of the Ghana FDA microbiology laboratory, which is currently at Biosafety Level (BSL) 2; however, vaccine testing should be conducted in a

BSL 3 environment. The assessment identified requirements for the laboratory to upgrade to BSL 3. While the laboratory has a Class II biosafety cabinet in its sterility testing room, where the testing of the COVID-19 vaccines occurs, this cabinet is not qualified by the equipment vendor, therefore its functionality/effectiveness as a Class II A cabinet cannot be guaranteed. In addition, the facility's environment is not a classified clean room (free of dust, mold, or microorganisms) and is therefore rated at BSL 1.

PQM+ recommends: a facility upgrade (architectural and civil works) to meet the facility design requirements of a BSL 3 laboratory; procurement of a new Class II C biosafety cabinet providing better protection for the product and the personnel; procurement of PPE for lab personnel; and dedicated basic equipment for testing COVID-19 vaccines. The technical report for the assessment has been drafted and is under review. The final report will include estimated costing of the requirements for the upgrade of the laboratory from BSL 1 to BSL 3 to enable FDA Ghana to advocate internally and externally for funding. In the meantime, FDA Ghana will continue to test in this facility.

Kazakhstan

PQM+ is supporting the NCEM in strengthening vaccine surveillance systems to ensure the system can detect, investigate, and analyze AEFI and adverse events of special interest (AESI) to ensure an appropriate and rapid response. This activity tasks PQM+ with conducting a situational analysis of the PV system in Kazakhstan in alignment with the WHO's recent GBT assessment and providing related technical assistance in support of Kazakhstan's effort to reach Maturity Level 3 (ML3), specifically in its vigilance functions. During the quarter, PQM+ developed, conducted, and reviewed findings from a PV assessment, as well as related SOPs and legislative acts on PV that NCEM provided.

PQM+ conducted a workshop on strengthening PV development in Kazakhstan for 11 staff in NCEM's PV department to present and discuss initial findings from the PV assessment and further technical assistance. PQM+ discussed roles of the PV center, national PV technical committee, and pharmaceutical industry PV. PQM+ walked the participants through structural, process, and impact indicators of a PV system, discussed areas for improvement, and determined next steps. PQM+ will finalize its assessment of the PV system in Kazakhstan in January. In addition to assessing Kazakhstan's PV capabilities, PQM+ is providing technical assistance to NCEM to strengthen its lot release function. In December, PQM+ reviewed an NCEM self-assessment on lot release function as part of the WHO GBT.

Pakistan

In Q1, the PQM+ COVID-19 program supported DRAP, pharmaceutical industry (manufacturers and importers), CROs, and BE centers through the following major activities:

Lessons Learned on Global Regulatory Reliance Pathways during COVID-19

In October, PQM+ organized a panel of expert trainers, with support from a U.S.-based pharmaceutical manufacturer (Roche), who have worked with regulators such as the Singapore Health Sciences Authority and cross-industry collaborative platforms such as the European Federation of Pharmaceutical Industries and Associations, the Middle East Regulatory Network, the International Federation of Pharmaceutical Manufacturers and Associations, and the Advisory Committee of the Drug Information Association. The trainers shared processes and practices that enabled regulatory agencies to optimize their resources, implement collaborative

review and reliance procedures to enhance their overall capacity, while maintaining high-quality standards of the review process during the COVID-19 pandemic.

The training session took place in Islamabad with 39 participants (12 females and 27 males) from DRAP participating. Training objectives included:

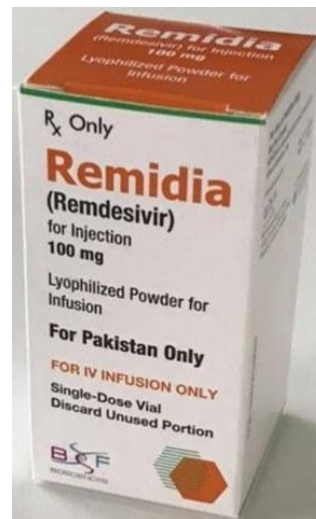
- Provide an overview on global regulatory convergence.
- Introduce WHO good reliance practice and benchmarking tools.
- Share insights into global initiatives to promote regulatory convergence and accelerate patient access.
- Discuss lessons learned from the COVID-19 pandemic on utilizing regulatory reliance practices.
- Enable an exchange on processes and practices that enable regulatory agencies to optimize their resources while maintaining high-quality standards of the review process.

Engaging Local Private Sector to Manufacture Quality-Assured Remdesivir

PQM+ supported BF Biosciences (Pvt.) Ltd. (Ferozsons) to build their capacity for compliance with GMP, in line with Pharmaceutical Inspection Cooperation Scheme (PIC/S) standards, International Organization for Standardization (ISO) 17025:2017 standards for quality control testing laboratory, and a supply chain assessment for products, to ensure end to end quality of the product, while also providing support to increase Remdesivir production for local use and exports.

Regarding Ferozsons' compliance with GMP under PIC/s standards, PQM+ led a detailed five-day onsite audit visit to conduct a gap assessment of the facility. The assessment included the manufacturing site, its ancillary areas, and the pharmaceutical QMS against the PIC/s standards and has identified and documented areas for improvement.

In Q1, PQM+ undertook an on-site visit to BF Biosciences (Pvt.) Ltd (Ferozsons) in order to finalize its corrective and preventive action (CAPA) plan, and to also conduct a Gap Assessment of its microbiology lab - for improving BF Biosciences' system for sterile manufacturing of COVID-19 medicine (Remdesivir Injection) and other microbiological testing as per Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) requirements. PQM+ has shared findings and observations regarding the lab with BF Biosciences, in addition to recommendations for making improvements going forward – this workplan activity has been completed accordingly.



Engaging Local Private Sector to Manufacture Quality-Assured PPE

To cope with and control the spread of the COVID-19 pandemic for the government, it is necessary to ensure the proper tools and measures are available and in place. One of the most crucial tools is the supply and use of quality personal protective equipment (PPE) for the public. Moreover, the better the quality of PPE, such as masks, the more effective they are at containing the pandemic and at saving lives. The use of quality-assured PPE will also contribute towards infection prevention and control (IPC) accordingly.

PQM+ assisted nine PPE manufacturers to produce high quality PPE per international standards, for both local use and export. PPE manufacturers were selected through an advertised expression of interest (EOI) 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 (EU)).

PQM+ team visited PPE manufacturers to identify the gaps related to environment, health, and safety (EHS) and compliance issues in manufacturing practices. Following the gap analysis, the team provided support to develop a CAPA Plan in order to address existing gaps at the facility, in addition to providing technical assistance for ISO 13485 accreditation and CE mark certification for one product.



The CE mark and ISO-13485 accreditations would allow PPE manufacturers in Pakistan to design quality management systems and maintain the effectiveness of their processes as per international standards, as well as export PPE globally.

In Q1, PQM+ conducted on-site visits to five local PPE manufacturers to provide technical assistance on ISO 13485 certification:

- Mundia Exports, Karachi, on November 19;
- BlitzKrieg Defense Solution, Islamabad, on November 19;
- Samad Rubbers, Lahore, on November 24;
- Techno Trend, Lahore, on November 26; and
- Maheen Textile Mills Pvt Ltd., Faisalabad, on November 27.

PQM+ held a two-day training session on ISO 13485 in November in Lahore for PPE manufacturers and DRAP staff. The training session was conducted by a leading inspection, verification, testing and certification company, Société Générale de Surveillance (SGS) (Pvt) Ltd, who shared guidance regarding ISO 13485 standard requirements for manufacturing PPE. A total of 13 participants attended the session (10 in-person, 3 virtually) from DRAP and PQM+ supported PPE manufacturers including Mundia Exports, American Safety, Samad group, Techno trends, Wilshire industries, Maheen Textile, and BlitzKrieg Defence Solution.

PQM+ also partnered with SGS (Pvt) Ltd to conduct a two-day training session on the CE Mark for PPE manufacturers and DRAP from November 29-30, 2021. A total of 41 participants (08 in-person, 33- virtual) attended the training. Products with CE marking indicate they comply with EU's requirements for General Safety and Performance Requirements (GSPR) and are thus a legal requirement for PPE manufacturers to export to the EU. PQM+ support will thus help to equip local PPE manufacturers in Pakistan to export their products to the EU.



Regulatory support to DRAP to reduce the risk of shortages of quality-assured and evidence-based COVID-19 medical products and supplies

In public-health emergencies, such as the COVID-19 pandemic, the pharmaceutical supply chains are badly impacted. It often is necessary to identify and arrange for alternative sources of Active Pharmaceutical Ingredients (API) and finished pharmaceutical products (FPP) to prevent medicine shortages and guarantee timely access to both COVID-19 medicines and regular supplies of essential medicines. In PY2, PQM+ supported DRAP in preparing to monitor and respond to shortages.

PQM+ provided support to the Drug Regulatory Authority of Pakistan (DRAP) to develop a guidance document and a National Drug Shortages Policy, in order to help equip DRAP to effectively monitor and prevent drug shortages. PQM+ presented, discussed, and handed over this policy to DRAP staff for review and final approval for implementation, after incorporation of all discussed amendments on October 20, 2021. This policy and guidance document were shared with DRAP for final review by the DRAP drug shortages committee.

The DRAP Drug Shortages Control Monitoring Committee held a meeting with PQM+ on December 8, 2021, regarding its review of the draft Drug Shortages Policy/Guidance document, developed with PQM+ support. The committee shared its comments and inputs on the draft document, which will be finalized during December. The final guidance document on drug shortages policy will accordingly be published on DRAP's official website after necessary approvals.

Implementation of this policy document, coupled with DRAP's subscription⁹ to the online API global database provided by PQM+ in the previous quarter, along with the API dashboard (also developed earlier by PQM+) will help DRAP to monitor and prevent drug shortages in emergencies such as the COVID-19 pandemic and in future.

Provision of PPE testing equipment for public sector PPE testing lab

During the COVID-19 pandemic, there is a greater demand for masks and other PPE in Pakistan. Due to the increase in demand, there is subsequently an increased risk of poor-quality PPE circulating in the local market. In Pakistan, the public sector lacks the capacity to conduct quality testing and post-marketing surveillance of PPE.

By the end of the quarter, Central Drug Testing Laboratory (CDL) Karachi received PPE testing equipment procured by the PQM+ program. PQM+ completed the installation, Equipment Qualification (IQ), Operational Qualification (OQ), and development of Standard operating procedures (SOPs) (Operations, Calibration and Maintenance) for the all PPE testing equipment. Examples of this equipment include:

- Differential Pressure Tester
- Wet microbial Penetration Resistance Tester
- Mask Respiratory/Breathability Resistance tester
- Bacterial Filtration Efficiency Tester with accessories (Weighing Balance and Oscillating Orbital Shaker)

⁹ PQM+ is purchasing this annual subscription and is providing support to develop a database dashboard for DRAP to monitor API shortages. After PQM+ ends, DRAP will pay the subscription charges to ensure sustainability.

The PPE testing equipment provider conducted a hands-on training on the installed equipment for PQM+ and CDL staff. In addition, the PQM+ team conducted a training for CDL staff on Bacterial Gram Staining Technique.¹⁰

The CDL Karachi PPE testing lab was formally inaugurated by Special Assistant to the Prime Minister (SAPM) on Health, Dr. Faisal Sultan on November 8, 2021. The DRAP Chief Executive Officer (CEO) and CDL Director were also present at the event and briefed the SAPM about the functions of CDL's different high-tech departments.

Dr. Faisal Sultan appreciated the support and efforts of PQM+ to support CDL in its journey to become a standard international laboratory, which would greatly help in regulating the medicine market – from manufacturing to the consumers.

Implementation of QMS at Pakistan Institute of Medical Science (PIMS)'s public diagnostic laboratory

PQM+ is strengthening public sector hospitals diagnostic laboratories' testing quality by implementing a QMS at public sector PIMS hospital laboratory for International Organization for Standards (ISO) 15189 accreditation.

PQM+ conducted a gap assessment of the PIMS lab and implemented all major standard operating procedures (SOPs) developed for the laboratory quality management system (LQMS) at PIMS, in addition to implementation of Quality Management System (QMS) forms, in order to ensure the lab's compliance with ISO 15189 standards.

PQM+ provided support to PIMS for the acquisition of proficiency testing and equipment calibration services. PQM+ also supported PIMS to update its application to the Pakistan National Accreditation Council (PNAC) for ISO 15189 accreditation, in line with changes in its scope of accreditation, with submission of the application Laboratory Information File (LIF) to PNAC.

PQM+ conducted the following trainings at PIMS for ISO 15189 accreditation:

1. Awareness Session
2. Advanced Training on ISO 15189, which covered the following key topics:
 - Implementation of SOPs
 - Risk Management
 - Corrective Action
 - Participation in PT
 - Measurement Uncertainty

The PQM+ team, along with the USAID local mission, visited the PIMS diagnostic lab in December. The USAID Mission Activity Manager, Mr. Khalid Mehmood appreciated the efforts made by PQM+ and progress towards lab improvement. Dr. Ijaz Qadeer, Joint Executive Director, PIMS was also present and extended his gratitude to the PQM+ program for its support to PIMS's diagnostic lab and requested to extend PQM+ support in the future.

¹⁰ This technique is used to identify bacterial stains as Gram negative and Gram positive classification.

At the end of Q1, PQM+ supported PIMS in submitting its pre-assessment application for lab ISO 15189 accreditation to the Pakistan National Accreditation Council (PNAC). The PIMS lab is waiting for the final audit for ISO 15189 accreditation by PNAC.

As of the end of Q1, PQM+ completed all activities originally set out in its COVID-19 work plan.

Vaccine Activities

In Pakistan, there is very limited safety data available for current COVID-19 vaccines, as DRAP has issued EUA for COVID-19 vaccines, in response to applications received from importers in Pakistan (with limited clinical trial data). Thus, there is an increasing chance of adverse events following immunization (AEFI) occurring with limited safety data available for COVID-19 vaccines. In this scenario, 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 for AEFI reporting for effective use of data for decision-making.

While the Ministry of National Health Services, Regulations & Coordination (MoNHSR&C) has developed national guidelines for surveillance of adverse events following immunization (AEFI) for COVID-19 vaccines, these guidelines have not been officially announced by the Pakistan Government through any statutory regulatory order (SRO), nor do the existing guidelines include roles/responsibilities for key AEFI stakeholders such as DRAP,

Provincial Healthcare Commissions, and the Expanded Program on Immunization (EPI). To address this issue, and to ensure effective pharmacovigilance of AEFI data, PQM+ collaborated with national stakeholders (federal and provincial government representatives, WHO, and others) through a consultative meeting to support the revision of existing AEFI guidelines, in order to formulate and disseminate a National Action Plan for AEFI surveillance for COVID-19 vaccines.

In preparation for this consultative activity, PQM+ conducted a joint meeting with Federal EPI, WHO, and DRAP on October 5, 2021, for reviewing AEFI guidelines and discussing arrangements for the Joint Consultative Meeting on Review of National Adverse Effects following Immunization (AEFI) Guidelines and Formulation of the National Action Plan for COVID-19 Vaccine. PQM+ updated and shared the AEFI guidelines and draft National Action Plan for AEFI with Federal EPI, WHO, and DRAP for further feedback.

PQM+ also held a meeting with the CEO of Sindh Healthcare Commission on October 15, 2021, to discuss inputs on the AEFI national action plan and AEFI guidelines. In addition, the PQM+ team coordinated with the CEO of Islamabad Health Regulatory Authority (IHRA) to brief him about the AEFI program and the upcoming consultative meeting.

The PQM+ program then held a Joint Consultative Meeting on Review of National Adverse Effects Following Immunization (AEFI) Guidelines and Formulation of the National Action Plan for COVID-19 Vaccines on October 21-22 in Islamabad in collaboration with WHO and Federal EPI. All key AEFI stakeholders actively participated in the event, including Federal EPI,



PQM+ held a joint consultative meeting for review of the National AEFI Guidelines and formulation of the National Action Plan for COVID-19 vaccines in October in Islamabad, in collaboration with the WHO and Federal EPI.

representatives from Provincial EPI, Provincial & Regional Director General Health Services, WHO, DRAP, UNICEF, NCOC, NADRA, 1166 Helpline, provincial & federal Healthcare Commissions, Coronavirus Expert Advisory Board (CEAG) Punjab, hospitals, and universities, with a total of 67 participants attending the meeting. During the two-day consultative meeting, partners and stakeholders presented and discussed the following topics/areas:

- Technology as Enabler in Healthcare by National Database and Registration Authority (NADRA)
- AEFI Surveillance structure in Pakistan by Federal EPI
- Strengthening Vaccine Vigilance System (AEFI) by USAID/PQM+
- COVID-19 Vaccine update by National Command & Operation Centre (NCOC)
- Pharmacovigilance Rules- AEFI practices by DRAP
- COVID-19 AEFI Surveillance Challenges and Hurdles by WHO
- COVID-19/ National Immunization Management System (NIMS) Information & Grievances by NADRA 1166 helpline representative
- AEFI Challenges and Obstacles faced by provincial AEFI stakeholders (Healthcare Commissions, WHO provincial consultants, provincial EPI, Corona Expert Advisory Board (CEAG) Punjab)
- Review of AEFI guidelines
- Components of National Action Plan for AEFI

During the meeting, stakeholders and partners discussed challenges under the current AEFI surveillance system for COVID-19 vaccines, as well as how to strengthen and improve the system. PQM+ coordinated with the federal EPI and WHO to update the draft National Action Plan for AEFI, incorporate stakeholders' feedback, and shared it with key stakeholders and partners for review and approval. PQM+ also sought UNICEF's input on the risk communication portion of the National AEFI Guidelines. PQM+ has shared the updated draft National Action Plan for AEFI, AEFI Guidelines, and the AEFI training plan with WHO for review and feedback.

The PQM+ national AEFI expert visited Sindh in November to meet with the Sindh Director General (DG) of Health, provincial EPI manager and team, and Sindh Healthcare Commission to discuss PQM+ AEFI activities.

In addition, PQM+ closely coordinated with DRAP for AEFI data reporting to the WHO Program for International Drug Monitoring's VigiFlow.¹¹ WHO acknowledged that Pakistan's AEFI data reporting rate is one of the best in the WHO Eastern Mediterranean region. PQM+ also met with DRAP, NADRA, and 1166 Helpline to discuss the integration of AEFI reporting software (VigiFlow and NIMS) to improve the AEFI reporting system. DRAP and NADRA responded positively to PQM+'s suggestions, and PQM+ will discuss and plan further with all stakeholders.

¹¹ VigiFlow supports the collection, processing, and sharing of data of individual case safety reports to facilitate effective data analysis.

Uzbekistan

Immunization Readiness and Implementation

PQM+ is working with the medical regulatory authority, the Agency on Development of the Pharmaceutical Industry (the Agency), to establish a system for EUA. In Q1, the Agency officially established a designated working group to support EUA activities. To kick off the working group, PQM+ provided an overview of the EUA procedure for the eight members and shared the “Guidance for National Regulatory Authorities on EUA” and the “Summary of Global EUAs for Stringent Regulatory Authorities (SRAs), WHO, and Other Countries” developed by the PQM+ Cross-Bureau COVID-19 team.

PQM+ supports the Agency in ensuring that the vaccine surveillance system can detect, investigate, and analyze AEFI and AESI to enable an appropriate and rapid response. In October, PQM+ met with the Agency and the PV working group and provided an overview of PV systems and how to assess them, as well as introduced the PV assessment questionnaire. During the quarter, PQM+ and the PV working group completed the assessment. Based on the findings, PQM+ and Agency will begin planning interventions, such as training, SOPs, etc. In December, PQM+ met with the deputy director of the National Immunization Program (NIP) and introduced PQM+ program activities in Uzbekistan and ways for the NIP to collaborate with the PV center and be involved in strengthening vaccine safety surveillance and AEFI.

PQM+ completed a five-day training for 12 experts from the Agency’s PV center and from NIP (including the deputy director) on COVID-19 vaccines and AEFI in December. The training provided an overview on pharmacovigilance; notions of vaccine vigilance; COVID-19 vaccines and AEFIs; and case studies. By the end of the training, the NIP deputy director and other participants understood the importance of collaboration between the two entities to ensure vaccine safety surveillance.

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.

Progress This Quarter

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

PQM+ commenced activity planning for the development of a guidance document on quality test methods for medical devices targeting regulators and manufacturers to increase the knowledge and practices for testing priority MNCH medical devices circulating in the country markets. This quarter, PQM+ is working with MTaPS and USAID's MNCH team to gather information needed to develop the guidance document.

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

With support from Muhimbili University in Tanzania, PQM+ finalized the amoxicillin dispersible tablet (DT) manufacturing landscape analysis report in Africa. The final report will be disseminated next quarter. In PY3, PQM+ plans to collaborate with MTaPS and Global Health Supply Chain Pharmaceutical Supply Management (GHSC-PSM) programs to plan a stakeholder consultative meeting on access to and use of quality-assured medicines for newborns where findings will be presented.

WHO and UNICEF launched the global Every Newborn Action Plan (ENAP) in 2014 in an effort to end preventable newborn deaths and reduce maternal deaths and morbidity. The results framework for ENAP was revised and approved in April 2021, highlighting revised coverage targets and milestones for 2025. PQM+ was invited to participate in the commodities sub-group formed to monitor progress towards targets and milestones. PQM+ participated in the first meeting in September 2021. This quarter, PQM+ collaborated with two USAID partner programs (MTaPS and GHSC-PSM) to review and provide input for the revision of the sub-group's terms of reference document. PQM+ will continue to participate in meetings and contribute to technical deliverables as required.

Objective 5: Advance a global medical products QA learning and operational agenda

PQM+ is collaborating with two USAID partner programs – MTaPS and GHSC-PSM – to organize a consultative meeting on access to and use of quality-assured amoxicillin for newborn health. This quarter, the MTaPS program shared a draft concept note, outline for evidence brief, and a matrix for data collection from members of the child health group. These documents were reviewed and planning for the consultative meeting commenced. The group agreed that a total

of three consultative meetings will be held each focusing on the three main bottleneck areas identified that are:

- Inaccurate quantification at all levels and/or inadequate financing of pediatric amoxicillin and gentamicin formulations
- Quality of child health products not guaranteed
- Inappropriate use of medicines for treatment of pneumonia and possible serious bacterial infection (PSBI) by providers and caregivers.

The group also agreed to expand the scope of the activity to include gentamycin formulations. By next quarter, the group plans to engage USAID and UNICEF to send out announcements for the consultative meeting to stakeholders for their participation.

PQM+ was invited to participate in the [Newborn and Child Health Commodities Sub-Group](#). The goal of this group is to improve availability, accessibility, affordability and safe use of quality child and newborn commodities for high impact public health interventions. USAID and UNICEF chair this working group with participation of implementing partners working in the child health and newborn commodity space. The next meeting is planned for January 2022.

Priority Activities for Next Quarter

In Q2, PQM+ plans to:

- Commence development of the guidance document on quality test methods for medical devices once the list of MNCH devices of focus has been finalized.
- Finalize and disseminate the amoxicillin DT manufacturer landscape analysis report for the Africa region.
- Continue to participate and provide technical advice at the ENAP and in the newborn and child health commodities sub-group meetings.
- Continue planning with the two USAID partner programs to execute the first of three planned consultative meetings on access to and use of quality-assured medicines for newborn.

Neglected Tropical Diseases (NTDs)

The November 2020 WHO NTD global roadmap, [Ending the Neglect to Attain the Sustainable Development Goals: A Roadmap for Neglected Tropical Diseases 2021 – 2030](#), sets goals for an integrated approach across all NTD diseases and sets targets to reduce the number of people requiring treatments for NTDs by 90 percent. WHO has been instrumental in coordinating NTD medicine donations from manufacturers for use in affected populations globally. However, shortfalls remain compared to the demand for some medicines. The USAID NTD program targets the most prevalent NTDs that also have proven, cost-effective health interventions: lymphatic filariasis, blinding trachoma, onchocerciasis, schistosomiasis, and soil-transmitted helminths. The overall goal of the PQM+ NTD work is to ensure the availability of affordable, quality assured NTD medicines for the patients in need.

Progress This Quarter

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

PQM+ continues to support two manufacturers toward WHO PQ for two NTD products- albendazole 400mg tablets and praziquantel 600mg tablets. For albendazole 400mg tablets, the product dossier has undergone full assessment by WHO. WHO requested additional information and PQM+ provided technical support in the preparation of the feedback and review of the requested documents through a meeting held with the company to clarify and review WHO request and generate a response. The completed feedback was successfully submitted to WHO on January 07, 2022.

For praziquantel 600mg film-coated tablets, WHO issued a conditional PQ approval in April 2021 for the product pending onsite inspection and a repeat bioequivalence (BE) study. PQM+ conducted a mock inspection of the manufacturing site in October 2021 and provided in-person technical assistance to get the manufacturing site ready for the WHO PQ onsite inspection that was conducted November 8 – 12, 2021. After the inspection, PQM+ provided technical assistance to the manufacturer to address the corrective and preventive actions (CAPA) identified from the WHO PQ team inspection. The WHO PQ team accepted the CAPA responses and found the manufacturing site compliant with the standards of Good Manufacturing Practices (GMP). PQM+ is also providing technical assistance for the BE study. A new contract research organization (CRO) was identified for the study with PQM+ support and the manufacturer is working on finalizing the contract agreement. PQM+ is currently undergoing procurement to recruit a BE specialist that will provide ongoing support to the manufacturer. USAID also provided partial financial support to the manufacturer to cover the cost of the study.

To identify and provide support to newly identified manufacturers of NTD medical products toward increased global supply of quality-assured products in quarter 4, PQM+ published an [expression of interest \(EOI\)](#) for eight NTD products for local manufacturers. The EOI was initially published with Federation of African Pharmaceutical Manufacturers' Associations (FAPMA), The Federation of East African Pharmaceutical Manufacturers (FEAPM), and West African Pharmaceuticals Manufacturing Association (WAPMA). In quarter 1, the EOI was posted on the PQM+ website with a link shared with PQM+ country representatives to disseminate to manufacturers in their respective countries. PQM+ has received three EOI applications for albendazole and azithromycin.

PQM+ engaged two core flex partners Muhimbili University in Tanzania and Mahidol University in Thailand to conduct an NTD market landscape analysis in Africa and Asia to better understand the local supply and demands of NTD API and FPP in the two regions. This quarter, PQM+ concluded the data collection and analysis of the survey of manufacturing and procurement of selected NTD products manufacturing in Africa and Asia. The draft report was finalized this quarter for review and feedback. The final report will be completed by next quarter.

PQM+ commenced the development of a publicly available NTD database and dashboard for regulators, manufacturers, procurement agencies, suppliers, donor communities, and other interested parties in planning for procurement, supply, and use of NTD medical products in project year 2. This quarter, a functional draft version of the NTD Dashboard was completed. This draft was presented to USAID and PQM+ management in November 2021. Feedback with suggestions for improvement was received and are being incorporated in addition to new options. Currently PQM+ is working to include available WHO Listed Authorities (WLA)

approved FPP product information into the dashboard. Internal consultations are underway on how to source or utilize commercially available information to supplement relevant API and FPP information that are not publicly available but are deemed important to anticipated users of this dashboard tool.

PQM+ continued efforts to promote and disseminate the repackaged GMP e-learning course. During this quarter, PQM+ conducted an analysis (October to December 2021) of eCourse uptake and completion. The findings showed that out of 92 registrants for the quarter, approximately 40 percent (37) completed at least one of the course modules. PQM+ has been sending out monthly reminders since June 2021 to all course registrants to complete course modules. It has been observed that registrants take up to two to three months to complete a course module. During the quarter, however, all course registrants who completed their modules did so within the same month of registration. PQM+ will continue to promote course uptake and completion.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Continue ongoing technical assistance to supported manufacturers until full WHO PQ is attained.
 - For albendazole, PQM+ expects to receive feedback on the submitted additional data to WHO PQ team by end of February 2022. PQM+ has commenced discussions on the GMP mock audit planning and execution with the manufacturer and expects to finalize plans by next quarter.
 - For praziquantel, PQM+ will provide technical assistance to manufacturer to develop the BE study protocol for submission to WHO PQ. PQM+ also plans to conduct a remote or an in-person audit of the CRO site based on travel restrictions and feasibility.
- Expand advertising to receive additional applicants by directly mailing EOI to respondents from NTD product landscape analysis, Chiefs of Party, others and follow up notification of FAPMA, FEAPM, WAPMA.
- Finalize report for the NTD landscape market analysis.
- Finalize and launch the NTD dashboard for public users and collect feedback for improvement.
- Continue to promote uptake and module completion for the GMP eLearning course.

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.

Progress This Quarter

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. Recent years saw the introduction of three new TB medicines (bedaquiline, delamanid, and pretomanid), while a large pipeline of new TB medicines and regimens are in varying stages of clinical research. In this evolving situation, it is important for national medicines regulatory agencies (NMRAs) to stay engaged and ensure timely review and approval of new TB medicines to enable access to these life-saving products. In recent years, NMRAs in some countries occasionally have faced challenges in timely reviews and approval of new products due a lack of corresponding experience and procedures.

To address this, PQM+ started collaborating with the U.S. Food and Drug Administration (U.S. FDA) to organize a virtual workshop for representatives of MRAs and manufacturers from high-burden TB countries, at which the agency will share experiences on the regulatory review of new TB medicines. Previously, PQM+ identified and submitted topics of interest and a draft agenda for the workshop to US FDA. In Q1, PQM+ met with US FDA to prepare for the webinar, which is tentatively planned for August 2022. PQM+ is broadening the agenda to include regulatory experience and learnings beyond TB medicines. US FDA and PQM+ are also collaborating to develop a promotional video for the webinar to generate wider interest and a larger audience.

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

In Q1, PQM+ continued to support two pharmaceutical manufacturers of first line, fixed-dose combination (4FDC) TB medicines in Pakistan. Previously, PQM+'s technical assistance to one manufacturer enabled the finalized compilation of a dossier, including the report on a completed stability study and bioequivalence study. This was an important milestone toward prequalification of the product and ensuring that TB patients in Pakistan have access to locally produced quality-assured TB medicines. As a result, the 4FDC dossier of the manufacturer has been submitted to WHO and accepted by WHO for full assessment. In Q1, PQM+ continued to provide technical assistance to the manufacturer in responding to the first-round additional data and comments requested from WHO. The first-round additional data has been successfully submitted and the company has addressed most of the questions, only few questions are left to be clarified. Currently the manufacturer is working on the remaining additional queries received from WHO on December 7, 2021, that is scheduled to be finalized by the second week of January 2022.

Another Pakistani manufacturer has submitted and updated stability studies on the 4FDC product. PQM+ has reviewed the stability data at three-month station and requested the manufacturer provide the six months stability data with additional updates on the specification of the product based on the three months data review. The manufacturer will submit the results, the updated dossier along with the stability data for review by PQM+ prior to submitting to WHO. The PQM+ team will continue to provide technical assistance through full prequalification of the product.

During Q1, work progressed in the validation of methods to test for nitrosamines impurities in rifapentine and rifampicin TB medicines. Previously, USP laboratory identified issues in accuracy and sensitivity with the selected gas chromatography-mass spectroscopy/mass spectroscopy (GC-MS/MS) method. As a result, the USP lab is investigating an alternative method utilizing liquid chromatography-mass spectroscopy/mass spectroscopy (LC-MS/MS) was found to have acceptable sensitivity and accuracy. The latter method is under further evaluation and will also be assessed on similar instruments. In Q1, efforts continued using the GC-MS/MS method to resolve the accuracy and sensitivity issues identified, which could result in two validated methods and provide more flexibility to stakeholders.

In Q1, PQM+ provided ongoing technical guidance and monitoring of the Virginia Commonwealth University (VCU) subaward for the laboratory phase on developing an alternative route to produce Active Pharmaceutical Ingredient (API) for a priority TB product. During the laboratory phase, which ended Q4, the team successfully identified a synthesis route and demonstrated each step of the target continuous manufacturing process. During Phase II, further development will take place to optimize, scale up, and integrate the steps of the synthesis process. PQM+ developed a concept note and outlined budgetary needs for the next phase; USAID has approved the concept note. PQM+ extended the VCU agreement through September 2022 (the end of PY3) to include Phase 2. In Q1, PQM+ also worked on developing the criteria to identify a manufacturer for technology transfer, the next step after Phase 2.

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 respond to WHO questions and queries as needed while WHO reviews the dossier.
- Continue joint work with VCU on Phase 2 the manufacturing process optimization for a priority TB product. Continue to refine the criteria for technology transfer, on scaling up the proposed synthetic process.
- Continue to prepare for the US FDA workshop with the pharmaceutical regulatory authorities to share the agency's experience on the review and registration of new TB medicines.

Program Support

Communications

Newsletter: In December, PQM+ sent its fifth newsletter, which featured key M&E findings about PQM+ support to local manufacturers, the webinar on how stronger regulatory systems can better respond to the pandemic, and Bangladesh's efforts to address findings from their GBT assessment. The open rate was 60 percent, which is very high for the industry. According to Constant Contact, "an open rate of 30 percent is, in practice, a top-tier score, and most people average 10-15 percent per campaign." The click rate was 3 percent, consistent with an industry average range between 2 percent to 5 percent. Clearly, the audience is interested in PQM+'s content and work.

Social media: This quarter, PQM+ continued to reach a broad global audience with news about our activities. The program shared 36 posts on Twitter ([@USPGlobal Health](#) and [@USPharmacopeia](#) handles) and 10 posts on LinkedIn. Engagement levels were high even during the holiday season. On Twitter, the program garnered more than 15,000 impressions. Engagement on LinkedIn was even higher at 57,802, in part due to USP's large audience of followers on that platform: 98,000.

Success stories: This quarter, PQM+ Pakistan submitted a success story on PPE production to USAID'S Global Health Front Office and Agency leadership. Subsequently, Jeremy Konyndyk (executive director of USAID's COVID-19 Task Force) picked the story up as part of a National Security Council update on broader COVID-19 commitments and expanding PPE production. The U.S. Embassy Islamabad's [Khabr-o-Nazar Magazine](#) also published a story on the PPE success in Pakistan in its January 2022 issue.

In Uzbekistan, PQM+ oversaw the launch of the new Quality Club, which USAID captured in a [success story](#). PQM+ has written a story expanding on this work, which will be shared for review in Q2. The Pakistan team has drafted a success story about remdesivir, which HQ is reviewing before sharing with USAID for review.

Webinars: On November 4, PQM+ hosted a webinar titled "Playing the Long Game: How Can Strengthening Medical Product Regulatory and Manufacturing Systems Help Countries Respond to COVID-19 and Future Health Crises?" Several PQM+ portfolios shared their experiences implementing regulatory strategies to help countries pivot during the pandemic and ensure access to quality-assured medical products. Khalid Mahmood, PQM+ activity manager at the USAID/Pakistan Mission, provided the welcome and the PQM+ Pakistan chief of party presented on EUA and the broader registration of medical products related to COVID-19. The session drew 110 participants.