Promoting the
QUALITY OF MEDICINES Plus

PQM+ Quarterly Report – Program Year 3, Quarter 3

July 31, 2022

USAID
FROM THE AMERICAN PEOPLE

usp®

Contact Information

Promoting the Quality of Medicines Plus Program
United States Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852 USA
Tel: +1-301-816-8166
Fax: +1-301-816-8374
Email: PQMplus@USP.org

This document is made possible by the generous support of the American people through the U.S. Agency for International Development (USAID) Cooperative Agreement No. AID-7200AA19CA00025. The contents are the responsibility of U.S. Pharmacopeial Convention (USP) and do not necessarily reflect the views of USAID or the United States Government.

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.

USP is an independent, scientific nonprofit public health organization and is not a part of the United States Food and Drug Administration (FDA) or any other U.S. Government agency. PQM+ is unaffiliated with, and has not been evaluated by, FDA. References to FDA or to FDA publications do not constitute FDA endorsement of the PQM+ program or of the information provided by it.

Suggested Citation

PQM+. 2022. Program Year 3 Quarter 3 Report. Submitted to the U.S. Agency for International Development by the PQM+ Program. Rockville, MD: U.S. Pharmacopeial Convention.

Contents

Acronyms

2FDC	two drug, fixed-dose combination
4FDC	four-drug, fixed-dose combination
AEFI	adverse events following immunization
ANAB	American National Standards Society National Accreditation Board
API	active pharmaceutical ingredient
CAPA	corrective and preventive action
CIP	Coalition of Interested Parties
COVID-19	novel coronavirus of 2019
CPD	continuing professional development
CRO	contract research organization
CRP	collaborative registration procedure
CSV	computerized systems validation
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
IDP	institutional development plan
IQC	internal quality control
ISO/IEC	International Organization for Standardization/ International Electrotechnical Commission
KPI	key performance indicator
LIF	laboratory information file
LMIC	low- and middle-income countries

MedRS	Medicines Risk-based Surveillance
MNCH	maternal, newborn, and child health
MOH	ministry of health
MQCL	medicines quality control laboratory
MRA	medicines regulatory authority
MTaPS	Medicines, Technologies, and Pharmaceutical Systems program
NCL	National Control Laboratory
NTD	neglected tropical disease
OpERA	Optimizing Efficiencies in Regulatory Agencies
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PMI	U.S. President's Malaria Initiative
PMS	post-marketing surveillance
PMS-TWG	post-marketing surveillance technical working group
PPE	personal protective equipment
PQM+	Promoting the Quality of Medicines Plus
QA	quality assurance
QC	quality control
QMS	quality management system
RBI	risk-based inspection
RIMS	regulatory information management system
RSS	regulatory system strengthening
SATTA	Stepwise Assessment Tool Towards Accreditation
SF	substandard or falsified
SOP	standard operating procedure
TB	tuberculosis
TRIPS	Trade-Related Aspects of Intellectual Property Rights
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

This quarterly report showcases how we structure PQM+ work plan activities to contribute to the overarching continental aspirations for improved access and regulation of medical products and – of increasing interest – vaccines.

We highlight Pakistan, where PQM+ supported the Drug Regulatory Authority to finalize guidance documents for emergency use authorization (EUA) holders on adverse events following immunization (AEFI) reporting and for risk management plans. This will enhance EUA holders' capacity to ensure quality reporting and enable the Drug Regulatory Authority of Pakistan (DRAP) to effectively monitor COVID-19 vaccine EUA holders. This guidance on risk management plans will enable COVID-19 vaccine EUA holders to fulfill their legal responsibility to highlight and report any risks associated with the vaccines and to submit their risk management plan, including vaccine safety data, to DRAP to protect at-risk/vulnerable individuals.

At the global level, an emphasis on local manufacturing of vaccines remains a priority as part of future pandemic preparedness. USAID's efforts to expand access to COVID-19 vaccines are evident through the recent obligation of $7.1 million to PQM+ through the U.S. Government's Initiative for Global Vaccine Access Initiative, which seeks to "expand assistance and enhance international coordination to identify and rapidly overcome vaccine access barriers and save lives now, with a specific emphasis on scaling up vaccination support in sub-Saharan Africa." Under this umbrella, PQM will provide support to six African countries (Ghana, Kenya, Nigeria, Rwanda, Senegal, and South Africa) that are poised to produce vaccines in Africa. This assistance will include working with manufacturers to comply with good manufacturing practices, transferring knowledge to emerging manufacturers, and supporting the development of the biomanufacturing workforce. In collaboration with other leaders in the vaccine space, PQM+ will conduct a regional competency mapping to contextualize stakeholders' priorities and gaps to build a sustainable, quality-assured biomanufacturing infrastructure.

With the Africa Union's (AU's) target of 60 percent local vaccine production by 2040 through Partnerships for African Vaccine Manufacturing (PAVM)'s Framework for Action (FFA), we are excited that the AU has made headway in selecting Rwanda to host the headquarters of the African Medicines Agency (AMA). AMA's physical presence will advance the creation of an enabling environment for Africa's manufacturing capacities for vaccines, medicines, and medical devices. Given that the AU's New Partnership for Africa's Development (AUDA-NEPAD) is a coordinating mechanism for AMA and a PQM+ core partner, the program has a unique opportunity to support the operationalization of AMA. PQM+ sees these interventions as a timely opportunity to lay a sustainable scientific, technical, and regulatory foundation to build on.

We remain dedicated to the PQM+ goal of strengthening quality assurance systems to sustainably ensure the quality and safety of medical products and protect public health. With each intervention, we aim to establish long-lasting, collaborative working relationships with our constituents and a sustainable community at the global, regional, and local levels to share experiences, challenges, and solutions.

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

Executive Summary

As of the third quarter of Program Year 3, the Promoting the Quality of Medicines Plus (PQM+) program is implementing 35 work plans, three of which are core-funded activities supporting the offices of neglected tropical diseases (NTDs), tuberculosis (TB), maternal and child health (MCH). A fourth "cross-bureau" funding stream supports the Office of Health Systems. Thirty-lne work plans are Mission buy-ins in 22 countries and the Asia Bureau, including eight COVID-19 work plans Q3. The goal of these activities is to sustainably strengthen medical product quality assurance (QA) systems in low- and middle-income countries (LMICs). As such, PQM+ helps ensure access to quality-assured medical products, including those needed for HIV/AIDS, TB, malaria, NTDs, COVID-19, other infectious diseases, and MNCH.

This report summarizes activities we conducted during Quarter 3 (April 1 to June 30, 2022) delineated by objective and funding source (USAID country Missions and USAID/Washington). All activities align with at least one of PQM+'s five program objectives, as 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. PQM+ supports national QA systems for medical products by helping countries adopt policies that promote equitable and sustainable access to quality-assured medical products and develop evidence-based strategic QA plans. The program also helps implement mechanisms to coordinate stakeholders to promote efficiency, accountability, and transparency. Through these mechanisms, stakeholders become more effective and efficient in ensuring the quality and safety of medical products, increasing public trust, and freeing up valuable resources to expand health service coverage to their populations.

During Q3, PQM+ provided governance-related technical assistance to eight countries. This work involved developing policy and strategic plans by way of consultative processes,

implementing plans, drafting regulatory frameworks, reviewing and developing standard operating procedures (SOPs), and improving institutional performance. Of note is our support to **Pakistan's** DRAP in strengthening its organizational performance and staff competencies in line with internationally recognized guidelines. At a workshop in **Guinea**, the regulatory agency and the national QC laboratory (which is independent of the regulatory authority) validated a collaborative agreement framework that delineates agreed-upon areas of collaboration and their individual responsibilities. In **Ethiopia**, in collaboration with the Ethiopian Pharmaceutical Association, PQM+ trained more than 100 private sector health professionals on good distribution, storage, and dispensing practices. These efforts seek to ensure that the quality of medical products is not compromised by poor storage and distribution conditions, to reduce errors in the handling of medicines, and to help minimize the circulation of illegal and unfit health products in the country.

Regulatory systems strengthening (RSS). PQM+ helps countries improve their regulatory systems, as assessed by the World Health Organization's Global Benchmarking Tool (GBT). WHO benchmarking allows countries to identify strengths and areas for improvement; formulate institutional development plans (IDPs) to build on strengths and address gaps; prioritize IDP interventions; and monitor progress and achievements.[1] In Q3, PQM+ assisted country medicines regulatory authorities (MRAs) in **Bangladesh, Ethiopia, Kazakhstan,** and **Pakistan** to address corrective and preventive actions plans (CAPAs) devised from their IDPs. Technical assistance has targeted eight of nine regulatory functions in these countries, including national regulatory systems, registration and market authorization, vigilance, market surveillance and control, regulatory inspection, laboratory testing, clinical trials oversight, and lot release. This work will accelerate MRA attainment of set targets for GBT indicators and sub-indicators. PQM+ is also assisting three of these MRAs (Bangladesh, Pakistan, and Kazakhstan) to become members of the Pharmaceutical Inspection Co-operation Scheme (PIC/S). In Bangladesh, we helped the new director of the Directorate General of Drug Administration (DGDA) redefine the way forward for that country's accession to PIC/S. In Pakistan, we supported government efforts to raise awareness among stakeholders in the pharmaceutical industry of the importance and benefits of PIC/S accession. In Kazakhstan, we helped develop the country's pharmaceutical inspectorate and its quality management system (QMS).

Regulatory agencies must have sufficient capacity to inspect pharmaceutical manufacturing facilities to ensure compliance with good manufacturing practices (GMP) and to grant market authorizations. PQM+ continues to develop the **online risk-based inspection (RBI) tool** and **RBI guidance document** to support GMP and good distribution practices (GDP) inspections. The tool is designed to help MRAs use a consistent RB approach, international standards, and best practices to conduct inspections. Use of the tool should reduce MRA costs associated with planning, scheduling, executing, reporting, and follow-up actions, and increase inspection efficiency and effectiveness.

This quarter, we completed 90 percent of internal user acceptance testing against parameters designed in the tool for access, operation, and functionality.

To better monitor the quality of medicines, PQM+ promotes **risk-based post-marketing surveillance (RB-PMS)** in 18 countries—**Bangladesh, Benin, Burkina Faso, DRC, Ethiopia, Ghana, Guinea, Kazakhstan, Kenya, Liberia, Madagascar, Mali, Mozambique, Nepal, Nigeria, Rwanda, Senegal,** and **Uzbekistan**. Also, the adoption of risk-based methods can

[1] WHO Global Benchmarking Tool (GBT) for evaluation of national regulatory systems. Available from https://www.who.int/tools/global-benchmarking-tools

significantly reduce both the sampling and testing costs of these programs. We are supporting **risk-based post-marketing surveillance (RB-PMS)** of medical products in 18 countries: **Bangladesh, Benin, Burkina Faso, DRC, Ethiopia, Ghana, Guinea, Kazakhstan, Kenya, Liberia, Madagascar, Mali, Mozambique, Nepal, Nigeria, Rwanda, Senegal,** and **Uzbekistan**.

This quarter, six countries (**DRC, Ghana, Guinea, Liberia, Mali,** and **Nigeria**) have continued implementing routine RB-PMS activities. Four (**Kazakhstan, Madagascar, Nepal,** and **Uzbekistan**) are in the starting phase for implementing RB-PMS activities. **Kenya, Ghana,** and **DRC** have used data from their PMS activities to inform policy changes and regulatory enforcement decisions.

In PY2, PQM+, along with the University of Washington (UW), University of North Carolina (UNC), Harvard University, WHO, and USAID, developed a generalized model to estimate the economic and health cost of substandard and falsified (SF) medicines in LMICs. This quarter, the program and stakeholders in **Kenya** piloted the model using oxytocin injection, which treats postpartum hemorrhaging. In **Pakistan**, PQM+, DRAP, and other stakeholders will conduct a second pilot of the model using amoxicillin/clavulanic acid, a childhood pneumonia treatment.

We continued providing technical assistance in other RSS areas, including regulation and quality assurance of medical devices (in **Bangladesh** and **Nigeria**); emergency use authorization (EUA) training to regulatory and expert product assessors (in **Burkina Faso**); and regulatory inspection for inspectorates (in **Ethiopia, Nigeria,** and **Rwanda**).

Assessing the quality of products accurately and efficiently throughout the lifecycle, including analyzing physicochemical and microbiological properties of products, relies greatly on the regulatory authority's capacity and competency of its national quality control laboratory (NQCL). During Q3, PQM+ continued strengthening NQCLs in 18 countries (13 in **Africa**, three in **Asia**, and two in **Central Asia**). Activities included training staff in equipment preventative maintenance and usage principles; procurement of needed testing equipment and supplies; and training in quality system control elements.

Chemistry Manufacturing and Controls. PQM+ is exploring the adoption of continuous manufacturing (CM) processes for active pharmaceutical ingredients (APIs) of critical medicines. CM is an advanced manufacturing approach aimed at lowering the cost of API production while improving quality, among other benefits. Two critical accomplishments in Q3 were: 1) the discovery of a synthetic process for an intermediate that will further lower the cost of the API for one priority medicine and 2) the development of a novel low slug-flow crystallization process compatible with the CM synthesis.

WHO accepted the dossiers of two manufacturers of NTD products — albendazole and praziquantel — for WHO PQ this quarter. This is significant, as USAID has identified both as priority NTD medicines. The manufacturers, both in **India**, have their final on-site inspections scheduled for Q4.

Two members of the PQM+ technical team and staff from the USP Ghana office participated in the West Africa Pharma and Healthcare Conference in late April to increase the pool of expression of interest (EOI) applicants for NTDs. PQM+ gave an oral presentation that included technical assistance opportunities for potential manufacturers of NTD products.

Increasing access to quality-assured NTD medicines is a key strategic response to reducing the NTD burden and is one of USAID's main priority areas. PQM+ received 12 EOI applications

from 6 manufacturers to produce seven NTD medicines. The EOIs were for ivermectin 3 mg tablet (unscored), albendazole 400 mg tablet (chewable, preferably scored), praziquantel 600 mg tablet (scored), mebendazole 500 mg tablet (chewable), diethylcarbamazine citrate 50mg (unscored) or 100 mg (scored) tablet, tetracycline eye ointment HCL 1%, azithromycin 50 mg tablet and 500 mg tablet, and azithromycin powder for oral suspension. Manufacturers submitted applications for all products except tetracycline and diethylcarbamazine and one or more applications were submitted for each product included in the EOI. PQM+ will provide technical assistance to one manufacturer of each of the six NTD products from the EOI.

PQM+ continued identifying and acquiring additional publicly available data on API and finished pharmaceutical product (FPP) for the seven priority preventive chemotherapy (PCT) NTD products featured on the NTD Medicines Information Dashboard (NTD|MID). This information—country of origin, manufacturer, supplier, distributor, dosage forms and strengths, legal status, quality, availability, shortage, and product indicative prices—will be incorporated into the dashboard. Manufacturers, suppliers, procurement agencies, and other organizations can use the information to increase the supply of quality assured PCT NTD medicinal products if the database becomes publicly available.

PQM+ is collaborating with several countries to build their **medical products manufacturing capacity**. In **Bangladesh**, PQM+ chemistry, manufacturing, and controls (CMC) and workforce development (WFD) teams conducted a training needs analysis for the Essential Drugs Company Limited (EDCL), a state-owned pharmaceutical entity. The assessment indicated a need for training in quality management systems, auditing, and documentation.

In **Nigeria**, two manufacturers submitted three dossiers for WHO prequalification. The WHO prequalification staff will visit the contract research organization (CRO) sites responsible for the zinc palatability and sulfadoxine/pyrimethamine studies after a successful dossier submission during Q3. The WHO PQ teams will also inspect the manufacturer of zinc sulfate and sulfadoxine/pyrimethamine. However, as the company is undergoing maintenance, the site inspection must be rescheduled.

PQM+ began assisting the **Ethiopian** Regional Bioequivalence Centre (RBEC) this quarter. The program hosted several virtual meetings to discuss preparatory work and future face-to-face meetings with stakeholders. The technical working group has begun working on the agenda and assessment tools to conduct a gap analysis. In **Uzbekistan**, PQM+ continued technical assistance to Nobel Pharma to produce quality levofloxacin and in Q3 conducted an on-site cGMP assessment. In all, PQM+ provided support to more than 41 manufacturers of 18 products across 10 countries during Q3.

In **Liberia**, President George Manneh Weah attended a handover ceremony and lab visit in May when USAID (via PQM+) donated laboratory equipment worth more than USD $300,000 to the Liberia Medicines and Health Products Regulatory Authority.

Liberian President George Manneh Weah, right, views the donated equipment during a lab visit in May.

Learning, Advocacy, and Awareness. In Q3, PQM+ worked to advance the use of evidence-based tools and approaches, as well as promote awareness, advocacy, and collaboration.

New tools and approaches. PQM+ continued to support counterpart use of well-established medical product quality assurance tools such as the Stepwise Assessment Tool Towards Accreditation (SATTA) to assess QC laboratories' quality management systems (in **Madagascar** and **Mozambique**) and the Medicines Risk-based Surveillance (MedRS) tool to design risk-based sampling plans for post-marketing surveillance (in **Bangladesh**, **Burkina Faso**, **Ethiopia**, and **Kazakhstan**, among others). The national medicines regulatory authorities of **Bangladesh** and **Liberia** participated in assessments of their medicines market authorization and registration functions using the Optimizing Efficiencies in Regulatory Agencies (OpERA) tool. Progress in implementing a new risk-based approach to inspection continued in **Ethiopia** and Nepal.

Of global relevance, PQM+ collaborated with the USP laboratory team to complete validation of a method to test for nitrosamine impurities in rifapentine and rifampicin, two medicines used to treat TB. Also, the Model Strategic Plan for IDP Operationalization (on which PQM+ collaborated with WHO) is now part of the Coalition of Interested Parties (CIP) RSS Global Network document package. WHO launched the CIP Global Network in **Kazakhstan**, initiating information-sharing on IDP assessment and implementation progress between the national MRA, WHO, and other relevant stakeholders, including PQM+.

Advocacy and awareness. PQM+ supported engagement of diverse stakeholders to raise awareness of the importance of manufacturer product quality assessment or advocacy for increased support, including:

- In **Liberia,** introducing the NQCL strategic plan to donors such as United Nations organizations (UNDP, UNICEF), WHO, Global Fund, and USAID to mobilize additional support for implementing the plan.
- Also in **Liberia,** disseminating new regulations that address the import, export, registration, unfit pharmaceutical, advertisement, donation, and recall of medicines and health products to importers of drugs and health products, pharmacists, non-governmental organizations (NGOs), and the Ministry of Health.
- In **Nigeria,** in liaison with the Pharmacists' Council of Nigeria (PCN), conducting sensitization workshops in Bauchi and Ebonyi states to build the capacity of community pharmacies (CPs), proprietary patent medicine vendors (PPMVs), and the

pharmaceutical inspection committees (PICs) on the process for registration and annual license renewal and selected supply chain and QA topics.

- In **Bangladesh**, with the Bangladesh Association of Pharmaceutical Industries (BAPI), conducting a stakeholders consultation workshop on prospects and challenges for API manufacturing in Bangladesh. Representatives of API manufacturers, BAPI, and the DGDA participated. At the workshop, participants discussed issues, needs, and challenges for API manufacturing in Bangladesh.

In **Pakistan**, due to a change in government, leadership of strategic planning for pharmaceutical sector development shifted to the Regulatory Modernization Initiative of the Board of Investment in the Prime Minister's Office. It includes a diverse, high-level group representing the Ministry of Commerce, the International Finance Corporation, World Bank Group, and Foreign Commonwealth Development Office (FCDO). Through multiple meetings with the Pakistan Pharmaceutical Manufacturers Association and the Pharma Bureau, 12 reform proposals for inclusion in the strategy were developed. Among other things, participants agreed to lobby for designation of the pharmaceutical sector as a priority sector.

Collaboration. Throughout the quarter, PQM+ teams collaborated closely with industry associations (in **Bangladesh, Ethiopia, Kazakhstan, Kenya,** and **Pakistan**) to improve the quality of medical product manufacturing, with universities (in **Ethiopia, Pakistan,** and **Uzbekistan**) and pharmaceutical societies (in **Kenya**) to develop and provide training, and with MRAs around the world to agree on minimum common standards for regulatory information systems.

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

Cross-Bureau Activities and Progress

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

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

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+ collaborates with USAID's Medicines, Technologies, and Pharmaceutical Systems (MTaPS) program on the common minimum standards for the regulatory information management system (RIMS) activity. This quarter, the programs analyzed 11 country (MRA), regional, and global stakeholders' responses to the standards presented during the third consultative meeting on January 26. At the fourth consultative meeting on June 2, PQM+ and MTaPS further discussed these standards and stakeholders—representatives from MRAs, ministries of health, and the WHO—agreed to their adoption. PQM+ and MTaPS are finalizing the advocacy brief outlining the importance of minimum common standards for RIMS as well as the report on the fourth consultative meeting.

PQM+ is developing with WHO a model strategic plan for national MRAs to operationalize their institutional development plans (IDP) derived from country Global Benchmarking Tool (GBT) assessments. This quarter, PQM+ and WHO finalized a concept note, "Coalition of Interested Parties (CIP) Support Plan Template." This will form part of the CIP Implementation Toolkit being developed by WHO to assist MRAs as they implement their IDPs with support from CIP members. Following communications with WHO CIP Regulatory System Strengthening (RSS) Global Network focal points, the concept note was renamed the "Model Strategic Plan for IDP Operationalization." The plan's format and structure are now in Excel format as an annex to the CIP RSS Global Network document package. The WHO CIP Global RSS Network has officially accepted PQM+ representation and the Model Strategic Plan will help facilitate information-sharing on IDP assessment and implementation among MRAs, PQM+, and WHO. The WHO CIP launched the first CIP Global Network in Kazakhstan. PQM+ technical staff were present for each of the functions it supports.

The program is also collaborating with WHO to develop a model local production and health products security strategy to strengthen local manufacturing. The strategy will help countries improve infrastructure for local production and supply of essential medical products at the local and regional levels. This quarter, PQM+ shared the concept note of the activity with WHO and both agreed on major tasks to be completed under this activity. PQM+ is conducting a desk review of the existing strategies.

Building on Q2 progress, PQM+ continued developing a risk-based inspection good manufacturing practices (GMP) and good distribution practices (GDP) framework and tool. The

framework will address key regulatory GMP and GDP inspectorate activities and is being finalized. Further testing of the tool's beta version and piloting is needed. PQM+ is identifying countries in which to pilot the tool and has begun transferring the tool to USP for hosting and maintenance.

Objective 3: Optimize and increase financial resources for medical product

In Q2, PQM+, University of Washington (UW), University of North Carolina (UNC), Harvard University, WHO and USAID developed a model to estimate the economic and health cost of SF medicines in LMICs. In Q3, the program began piloting the model in Kenya using oxytocin. The working group met on June 21 to review data for key variables to test the model. PQM+ also began planning a second pilot in Pakistan using amoxiclav. This will be conducted late in September. UNC completed the validation of the SF model and UW is reviewing the validation feedback and revising the model. Feedback acquired following completion of the two pilots will be used by PQM+ to revise the tool and its user manual for global dissemination.

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

Earlier, PQM+ and MTaPS had revised the Medicines Quality Assurance Module of USAID's Pharmaceutical Systems Strengthening Course ("PSS 101"). In Q3, both programs and USAID agreed on a delivery date (the week of September 12) for the second virtual and asynchronous session of the PSS 101 blended course, "Virtual Pharmaceutical Systems Strengthening 101." PQM+ also began developing a new module on the role of regulation during a health emergency for inclusion in the Global Health eLearning Center (GHeL) platform. The program has shared the course outline with USAID for review and comments.

Priority Activities for Next Quarter

In Q4, PQM+ plans to:

- Finalize the advocacy brief outlining the importance of minimum common standards for the RIMS.
- Test the beta version of the RBI tool, incorporate changes, and complete the online version.
- Conduct the following sub-activities for the SF modeling activity:
    - Complete orientation for the full pilot core group and working group in Pakistan.
    - Support data collection processes in Kenya and Pakistan as needed.
    - Revise the orientation materials to reflect lessons from Kenya.
    - Launch the pilot in Pakistan.
    - Complete the assessment approach and tool.
- Develop the module on product quality assurance during a health emergency.
- Finalize the model local production and health products security strategy.

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) or 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 public 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

In Q3, PQM+ supported ANCQ in implementing its roadmap toward ISO/IEC 17025 accreditation. One of ANCQ's weaknesses was poor management and maintenance of its equipment which is critical to quality testing. PQM+ trained 10 technical staff (two females, eight males) in basic preventive maintenance of 18 pieces of equipment in the laboratory and helped the maintenance team identify the spare parts required for each of these equipment. The maintenance team can now perform basic preventive maintenance to lower equipment downtime.

To further strengthen the capacity of the technical staff, PQM+ provided a two-week in-depth hands-on training on advanced analytical methods (HPLC, dissolution, and Fourier Transform Infrared Spectrometry [FTIR]) to two ANCQ staff members at USP's ISO 17025 accredited laboratory in Ghana. This training allowed the ANCQ specialists to understudy how these tests are conducted in an accredited setting.

PQM+ procured three MiniLabs to screen antimalaria samples for the 2022 RB-PMS, as well as the required tools and funds for sampling per the approved RB-PMS protocol. A total of 202 antimalaria samples have been collected from seven regions in Benin.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Supervise the screening and confirmatory testing of the antimalaria samples.

Burkina Faso

A 2018 decree created the national pharmaceutical regulatory authority, *L'Agence Nationale de Régulation Pharmaceutique* (ANRP), to strengthen the regulatory framework for 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 QA and 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, LNSP and ANRP established an official collaborative framework.

PQM+ works with the Post-Marketing Surveillance Technical Working Group (PMS-TWG) to strengthen ANRP's 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.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ helped LNSP convene two workshop and provided technical assistance to draft and validate its five-year strategic plan.

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

PQM+ trained 12 members of the PMS-TWG on the online version of the MedRS tool (the first RB-PMS utilized the offline Excel version of the tool). During the workshop, PQM+ supervised use of the tool in developing the second RB-PMS protocol for antimalarial medicines in Burkina Faso. The TWG has valided this protocol.

To close some gaps in the baseline assessment of March 2022, and as part of implementing LNSP's roadmap toward ISO 17025 accreditation, PQM+ trained 24 LNSP technical staff on internal quality control (IQC) checks. These checks are required under the ISO 17025 standard, but LNSP's DCM has not begun implementing this step. The training was theoretical, with hands-on sessions to demonstrate how to perform IQC checks in the laboratory. In addition, PQM+ helped DCM staff draft an SOP for IQC.

To sustain a quality management system, a laboratory must generate adequate resources or be heavily subsidized by the government. LNSP's current testing fee for pharmaceutical products is less than $200, which cannot sustain an ISO 17025 QMS. PQM+ met virtually with LNSP management (director general and technical staff) to relay the need to review this testing fee. Subsequently, PQM+ held a five-day workshop for 26 finance and technical LNSP staff in Ouagadougou to demonstrate how to use a new (USP-developed) costing model to arrive at realistic testing fees for an accredited laboratory.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support the training of samplers for the 2022 RB-PMS.

- In collaboration with USAID/PMI Burkina Faso, organize a roundtable to discuss the operationalization of LNSP's five-year strategic plan and support for its implementation.
- Work with LNSP to continue implementing its roadmap toward ISO 17025 accreditation.
- Support the calibration of DCM's analytical equipment and devices by a qualified calibration services provider.

Democratic Republic of Congo (DRC)

The widespread availability and distribution of non-quality-assured artemisinin combination therapies and non-artemisinin therapies[2] 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 NQCL – Pharmaceutical Laboratory of Kinshasa (*Laboratoire National de Contrôle de Qualité – Laboratoire Pharmaceutique de Kinshasa,* or LNCQ-LAPHAKI).

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+ assisted DPM and the national PMS-TWG in disseminating the results of the 2021 PMS. Of the 303 samples collected from three provinces in DRC (Kinshasa, Tsopo, and Maniema), nine (3 percent) were out of specification and 22 percent were unregistered. The out-of-specification samples were quinine sulfate tablets, quinine oral solution (drops), and artemether injection. DPM has outlined steps to determine the source of the SF and unregistered medicines and to learn how they reached market to help determine appropriate regulatory actions. MedRS ensures that products are sampled based on statistical algorithms built into the tool. Approximately 60 medicines QA stakeholders from the Ministry of Health (MOH), health programs, health inspectorate, central medical stores, the national order of pharmacists, the rural health program *Santé Rurale* (SANRU), UNICEF, and WHO were in attendance. A USAID/DRC President's Malaria Initiative (PMI) team also attended and indicated satisfaction with the work and results.

To further strengthen the capacity of the technical staff in advanced analytical methods (still new to LNCQ-LAPHAKI analysts), PQM+ gave practical training to 14 analysts on HPLC and dissolution testing using equipment in LNCQ-LAPHAKI's physico-chemical laboratory. With this training, LNCQ-LAPHAKI staff will be able to test the 2022 RB-PMS samples with minimal supervision from PQM+.

A member of the DRC PMS-TWG trained, with PQM+ supervision, 32 samplers for the second round of RB-PMS. The training addressed the requirements of the 2022 sampling protocol, sampling strategies, and best practices for documenting samples collected.

Finally, PQM+ trained 18 LNCQ-LAPHAKI technical staff on IQC checks, a requirement of the ISO 17025 standard. The training was theoretical, with hands-on sessions to demonstrate how IQC checks should be done in the laboratory. PQM+ also supervised DCM staff in drafting an

[2] ACTwatch Group., Mpanya, G., Tshefu, A. et al. The malaria testing and treatment market in Kinshasa, Democratic Republic of the Congo, 2013. Malar J 16, 94 (2017). https://doi.org/10.1186/s12936-016-1659-x.

SOP for IQC checks and followed up on implementing an analytical method verification plan (the topic of a February 2022 training). LNCQ-LAPHAKI has developed two protocols for verifying two methods for antimalaria products (artesunate injection and artemether/lumefantrine tablets). The MRA will execute these by the end of September 2022.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Work with LNCQ-LAPHAKI to continue implementing its roadmap toward ISO accreditation, including:
    - building technical capacity in equipment preventive maintenance, data integrity, and out-of-specification (OOS) medicines; and
    - supporting the calibration of analytical equipment and devices by a qualified calibration services provider.
- Supervise sampling and testing of samples for the 2022 PMS.

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 not mandated to EFDA fall under the jurisdiction of regional government and city administration regulatory bodies. However, the lack of clarity in the mandates of EFDA and the regional regulatory bodies, 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 in Ethiopia.

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

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

In Q3, PQM+ worked with the Ethiopian Pharmaceutical Association (EPA) to develop a training module and materials on GDP, GSP, and GDP to guide health professionals in private outlets. The official accreditation body, College of Health Sciences at Addis Ababa University, reviewed and accredited the course. About 100 health professionals were trained in Q3. This training will be a model for federal and regional regulatory bodies and other partners to offer training to more outlets and geographic locations. PQM+ expects that this support will reduce malpractice and the circulation of illegal and unfit products in Ethiopia.


CODE:028AAUTAHS/14/22

ጥቁር አንበሳ TIKUR ANBESSA College of Health Science

CERTIFICATE of ACCREDITATION

Ethiopian Pharmaceutical Association -Training center

Awarded with this certificate

To give the course on "Good Dispensing, Storage and Distribution Practices From Regulatory Perspectives" as an accredited course with 15 CEU after fulfilling the required standard criteria.

June, 2022

Dr. Merahi Kefyalew

CPD Coordinator

Continuous Professional Development (CPD) Center

Accreditation certificate for the CPD courses

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

EFDA used to have a national PMS technical working group, but the group was not strong and most of its members had left their organizations. In Q3, PQM+ helped re-establish the TWG with new and approved terms of reference and the election of board members. The TWG received training on the RB-PMS approach and the online MedRS tool and developed an RB-PMS protocol for MNCH medicines. About 369 MNCH products—gentamicin 40mg /mL, sulfamethoxazole/trimethoprim (200mg + 40mg)/ 5mL, cefalexin (anhydrous) 250mg /5mL, ergometrine (hydrogen maleate) 200 mcg/mL, oxytocin 10 UI/mL, and magnesium sulfate injection—will be collected from facilities identified in the MedRS risk scoring exercise. Sample collection will be finalized early next quarter. While these results may identify shortfalls and strengths in the medicines supply, they may not be nationally representative.

In Q3, PQM+ provided technical support to EFDA to benchmark its market control, inspection, and licensing functions using the GBT tool and supported development of the IDP for each function. This completed GBT tool was sent to WHO for desk review.

In addition to supporting the GBT requirements toward WHO Maturity Level 3, PQM+ helped EFDA implement an ISO 9001:2015-based QMS by developing 10 SOPs and a corporate quality manual. The program also supported identification of regulatory risks per the authority's SOP for risk management, thereby supporting one GBT requirement.

EFDA recently identified its lack of a tool to regulate packaging, labeling, and co-packing of medicines. Thus, in Q3, PQM+ supported a consultative workshop to finalize the directive on packaging, labeling, and co-packing. The directive is now ready for EFDA's review and approval.

In Q2, PQM+ supported ISO 17020:2012 accreditation of the medicine facility inspection function. To maintain the accredited function, EFDA must conduct an internal quality audit of the QMS. Hence, in Q3, PQM+ provided technical assistance to the authority to conduct that internal audit and prepare a CAPA plan.

In Q2, PQM+ helped EFDA develop an Excel template to enter data on GMP inspection findings so as to perform trend analyses. The agency can use that evidence to identify major areas of risk and develop strategies to implement more efficient risk-based inspections. In addition, this will fulfill the WHO Maturity Level 3 requirement to regularly publish inspection findings and make them publicly available.

In Q3, PQM+ supported data entry of 277 facets of the GMP inspection report in the Excel database. After analyzing and interpreting the data, the team prepared a draft report. This report will help develop strategies for risk-based GMP inspection of facilities to improve efficiency.

As part of the plan to build the technical capability of local pharmaceutical manufacturers for WHO PQ of selected products, PQM+ advertised an expression of interest (EOI) and received proposals from interested companies. PQM+ will review the proposals and identify a potential local manufacturer and product for WHO PQ next quarter.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Carry out PMS sample collection.
- Train health professionals on good distribution and storage practices, as part of the CPD requirement, in collaboration with EPA.
- Review proposals from local manufacturers and identify one to work with.
- Finalize the GMP trend analysis report and submit it to EFDA for action.
- Support preventive/corrective maintenance and calibration of the condom testing machine for EFDA.

Ghana

The Food and Drugs Authority of Ghana (GFDA) is the national body responsible for regulating 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. GFDA is ISO 9001-certified and, in 2020, attained WHO Maturity Level 3. Its Center for Laboratory Services and Research is also ISO/IEC 17025 accredited. At 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 and MNCH 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

For the second RB-PMS protocol developed for antimalaria and MNCH medicines in Ghana, PQM+ oversaw the training of 32 samplers facilitated by three FDA Ghana technical staff. The training covered best sampling practices, sampling strategies, and the 2022 RB-PMS protocol. PQM+ subject matter experts who supervised the training also evaluated the trainers, rating one above average and the other two average with respect to the quality of their facilitation.

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

As part of the process of identifying local manufacturers to produce amoxicillin-DT and packaging of the iron and folic acid tablets, PQM+ conducted a GMP gap assessment of Kinapharma Ltd. The assessment of both manufacturers has revealed GMP gaps that, to close, would require significant investment by the manufacturers. The timelines and goals for technical assistance from PQM+ will consider investment commitments from the companies.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Provide technical assistance to two local artemisinin-based combination therapy (ACT) manufacturers (Entrance Pharmaceuticals and Amponsah Efah Ltd), including training and QMS building per the roadmaps developed in PY2.
- Support the national PMS-TWG to sample antimalarial and MNCH medicines for the 2022 RB-PMS. This sampling occurs once a year.
- Organize a workshop to sensitize local manufacturers on GS1 standards. Ghana has a national GS1 office, which is engaged in this work.
- Initiate data collection of the study on MNCH commodities.

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 NQCL, *Laboratoire national de contrôle qualité des medicaments* (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 TWG to implement RB-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 1: Governance for medical product quality assurance systems improved

PQM+ convened a workshop to support LNCQM and DNPM's validation of a collaborative agreement developed in March 2022 delineating agreed-upon areas of collaboration and their individual responsibilities. Both institutions have now signed the agreement.

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

As part of the implementation of LNCQM's roadmap toward ISO 17025 accreditation, PQM+ convened a five-day workshop to familiarize staff with quality risk management principles and practices. In addition, PQM+ provided supportive supervision to LNCQM staff to develop an internal procedure and associated forms/log templates as part of their quality management system. Laboratory management has reviewed and approved the risk management procedure. The Quality Risk Management and Opportunity SOP and associated forms have been incorporated into the QMS to fulfill the ISO 17025 requirement. Fifteen staff were trained on the process for identifying and evaluating risks related to medicines quality testing.

LNCQM received three MiniLabs for screening RB-PMS antimalaria samples. LNCQ completed screening of the 183 samples but had not received reagents procured by PQM+ to proceed to confirmatory testing. To avoid delays in compendial testing, PQM+ paid for the shipment of all samples that failed screening and 20 percent of the samples that passed the MiniLab screening.

In Q3, PQM+ procured a dissolution tester, microbalance, Fourier transform infrared spectrometer, and standard weight set for LNCQM. LNCQM did not have these pieces of equipment previously; the acquisition will now allow the laboratory to expand its testing capability to include additional medicines quality parameters such as dissolution for oral solid dosage forms and identification tests.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Assist the PMS-TWG in developing the second RB-PMS protocol for antimalaria and MCH medicines.
- Validate the collaborative framework between DNPM and LNCQM.
- Complete confirmatory testing of the RB-PMS samples.

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 Q3, PQM+ focused on improving governance for medical product QA systems, strengthening regulatory systems to assure the quality of medical products, increasing the supply of quality-assured essential medical products of public health importance, and advancing the global learning and operational agenda for medical product QA in Kenya.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ worked with PPB's pharmacovigilance and post-marketing surveillance technical working group (PV/PMS TWG), DNMP, health departments of county governments and NQCL to enhance their roles in assuring the quality of medical products in the country.

- PQM+ supported the PV/PMS TWG to update PPB's PMS strategy that is undergoing review and input by stakeholders.
- PQM+ supported the PV/PMS TWG to develop their three-year costed workplan (2022 – 2024).
- PQM+ disseminated results of the rapid baseline assessment of QA systems of antimalarial medicines and other pharmaceuticals to Busia and Kisumu counties. The county health leadership, DHPT, DNMP, and PQM+ team agreed on interventions and developed action plans to address gaps identified in the assessment. PQM+ commenced implementation by holding separate virtual sessions with the two counties. The tailored interventions included strengthening QA governance mechanisms and best practices at the county and hospital levels.
- Working with DNMP, PQM+ disseminated the quality assurance framework (developed by PQM+ in PY2) for malaria commodities to 23 counties, including in the malaria-endemic counties of Bungoma, Busia, Kisii, Kisumu, Migori, and Siaya.
- PQM+ initiated the development of NQCL's strategic plan that will span the next five years. PQM+ is providing technical assistance to NQCL in developing the strategic plan.

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

PQM+ began supporting NQCL to develop a guidance document on deploying better staffing at NQCL for submission to the MOH, since the laboratory requires specialized skills and competencies.

- NQCL acted on PQM+'s recommendation from the workforce capacity assessment that PQM+ conducted in PY2, including the request that MOH post more staff at the NQCL who meet the lab's competency requirements. Consequently, the human resources guidance document PQM+ planned to develop for NQCL is no longer required.

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

PQM+ continued collaborating with PPB to strengthen local production of antimalarials and other essential medicines.

- Having delineated the challenges facing local manufacturers and proposed interventions in PY2, PQM+ supported a workshop to finalize a ministerial advisory note that seeks policy support in local manufacturing. Among stakeholders consulted were government health programs as well as public and private institutions involved in public health.

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

PQM+ collaborated with various stakeholders to advance the global learning and operational agenda for medical product QA.

- Working with the Pharmaceutical Society of Kenya (PSK), PQM+ initiated development of a competency-based curriculum on pharmaceutical regulation and QA. The proposed course will help pharmaceutical personnel in Kenya improve their skills in QA and regulation of pharmaceutical products.
- Working with PPB, PQM+ finished analyzing and synthesizing local data from previous years' PMS activities to inform policy direction for QA of antimalarial and reproductive maternal, newborn, child, and adolescent health products. As a follow-up to this, PQM+ and PPB are developing a scientific paper to share with stakeholders on the results of the PMS activities in Kenya.
- The PQM+ Kenya team shared their experience supporting the Kenya PV/PMS TWG with other global PQM+ teams through a Learning Café.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Finalize the monitoring and evaluation framework of the PV/PMS TWG work plan.
- Participate in the PV/PMS TWG quarterly meeting.
- Support implementation of county and health facility interventions to improve QA systems for antimalarials and other pharmaceuticals in Busia and Kisumu counties.
- Disseminate the results of risk-based PMS of antimalarial and reproductive/MNCH products to key stakeholders involved in QA of health commodities.
- Work with NQCL to complete the development of their strategic plan.
- Officially launch the PPB's learning management system for self-directed learning on pharmaceutical regulation and QA.
- In collaboration with PSK, complete developing the in-service course on pharmaceutical regulation and QA for pharmacists.
- Update the Federation of Kenya Pharmaceutical Manufacturers (FKPM) website to strengthen their role in coordinating and disseminating QA resources in the manufacture of antimalarials, reproductive/MNCH, and other essential medical products.

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 QC laboratory.

PQM+ supported the LMHRA to complete one round of RB-PMS. The LMHRA released the PMS results to the public on January 25. PQM+ also supported the LMHRA to clear its dossier backlog and facilitated the establishment of a technical advisory committee on medical products registration. PQM+ coordinated with the LMHRA to inspect a Liberian manufacturing site.

This quarter, PQM+ coordinated with USAID to donate laboratory equipment worth more than USD $300,000 to LMHRA. Enhanced testing capacity will enable the lab to participate in proficiency testing and perform other quality audits, making it eligible for accreditation to the International Organization for Standardization (ISO)/ International Electrotechnical Commission (IEC) for its 17025 standard. This will result in improved health system quality and a strengthened system overall.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

In PY 2, PQM+ supported LMHRA to develop a five-year strategic plan which the LMHRA Board of Directors approved in January. In April, PQM+ coordinated with the LMHRA to conduct a donors' meeting to introduce the strategic plan and mobilize additional support for implementing the plan.

Representatives of United Nations Organizations (UNDP, UNICEF), World Health Organization (WHO), Global Fund, UNICEF, USAID, and other partners attended and pledged to work with LMHRA management to achieve the objectives of the five-year strategic plan.

In May, PQM+ coordinated with the LMHRA to disseminate seven new regulations. The new regulations address the import, export, registration, unfit pharmaceutical, advertisement, donation, and recall of medicines and health products in Liberia. The dissemination took place in Monrovia on May 25 and 26 with representatives from importers of drugs and health products, pharmacists, NGOs, importers, and the Ministry of Health attending. The regulations are online here.

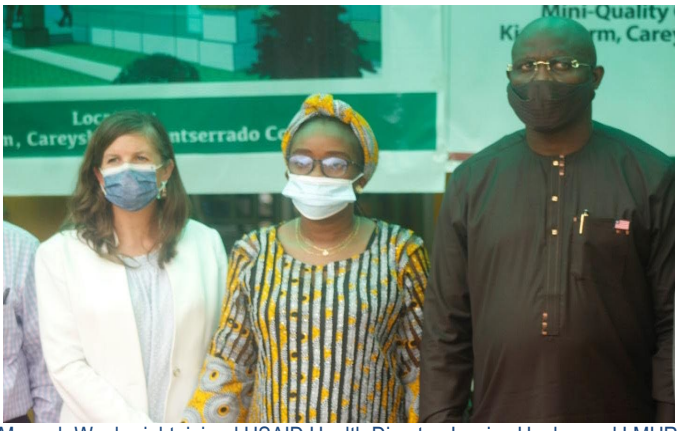
Before the dissemination meeting, PQM+ presented findings of the review of the LMHRA Act vis-à-vis the African Union model law to LMHRA management and the Ministry of Health.

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

This quarter, USAID via PQM+ donated laboratory equipment worth more than USD $300,000 to the Liberia Medicines and Health Products Regulatory Authority.

- Liberian President George Manneh Weah witnessed the handover ceremony on May 13.
- Laboratory equipment donated included a High Tech Detection Systems (HTDS) International dissolution tester, a new Waters Alliance high-performance liquid chromatography (HPLC) unit with accessories; an MES Fourier transform infrared spectroscopy (FTIR) machine with accessories; and assorted laboratory glassware, reference standards, and reagents.
- Jessica Healey, USAID's Health Office director, handed the equipment over to LMHRA. She noted that the equipment would enable Liberia to perform quality testing on medicines and other health products, instead of shipping samples out for testing in other

countries. Ensuring that medicines meet established pharmaceutical standards of internationally recognized compendia will be more efficient and cost-effective when performed in LMHRA's facility. "It means the lab is gradually moving towards sustainability because they will be able to generate funds from fees charged for sample testing," Healey noted. For more details, see the press release issued by the LMHRA:



Liberian President George Manneh Weah, right, joined USAID Health Director Jessica Healey and LMHRA Managing Director Keturah Smith-Chineh at the ceremony.

Smith-Chineh and Healey sign the handover agreement.

President Weah views the donated equipment.

PQM+ supported the LMHRA in installing and commissioning the donated Waters Alliance HPLC system at the LMHRA Quality Control Laboratory (QCL) after the donation. PQM+ also trained 13 QCL analysts on the hardware and software of the Waters Alliance HPLC System.

In Q3, PQM+ supported the LMHRA and the PMS-TWG to collect 146 samples of antimalarial and MNCH medicines. The collected samples were 31 percent MNCH medicines and 69 percent antimalarials. PQM+ gave the LMHRA a sub-award to conduct another PMS round.

PQM+ also coordinated with the LMHRA and the Center for Innovation in Regulatory Science (CIRS) to complete an assessment of the LMHRA medicines registration process using the OpERA tool. The OpERA country report from CIRS identifies gaps in the medicines registration system at the LMHRA and provides recommendations to address identified gaps.

Table 1: Status of Lab Accreditation in Liberia

Laboratory	Accreditation Sought	QMS	Initial Gap Assessment	CAPA	PT/ILC	Official Inspection/ Pre-assessment
LMHRA QC-	ISO 17025: 2017	Incomplete because the identified competence and QMS-related gaps have not yet been fully addressed	Completed	CAPA plans to be initiated and implemented	One ILC sample from WAHO to be evaluated via assay	CAPA plan against the initial gap assessment has not been addressed and submitted

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Complete drafting 10 regulations.
- Coordinate with the School of Pharmacy to complete developing a short-course curriculum to train health care workers in medical products QA in the short to medium term.
- Provide supportive supervision to LMHRA analysts for compendial testing of oxytocin.
- Support the LMHRA to review SOPs for six techniques in the LMHRA accreditation scope (HPLC, dissolution, Ultraviolet-Visible Spectroscopy (UV-Vis), FT-IR, Thin Layer Chromatography (TLC), and Uniformity of Dosage Units (UDU)).
- Conduct compendial testing of PMS samples.
- Complete the Integrated Regulatory Information Management System assessment.

Madagascar

PQM+ collaborates with Madagascar's Medicines Regulatory Authority ("the Agency," *Agence du Médicament de Madagascar*) to strengthen its capacity to assure medicines and medical product quality throughout the country. The Agency 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 QC 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 aiding the laboratory to establish and implement a quality management system to comply with international standards, PQM+ has focused on implementing a PMS

system on the quality of medicines in the country. Moving from sporadic medicines quality monitoring activities toward robust RB-PMS programs is critical for Madagascar to assure 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+ continued to strengthen the capacity of LNCQM.

- PQM+ conducted a situational analysis of LNCQM and subsequently coordinated a multi-stakeholder workshop on May 16 and 17 where the first draft of the LNCQM two-year master plan was developed.
- PQM+ assessed LCNQM's capacity using the SATTA approach to inform the laboratory development plan.
- PQM+ assisted LNCQM to revise its quality manual and SOPs per ISO/IEC 17025: 2017 accreditation and WHO prequalification requirements.
- PQM+ conducted an LNCQM workforce assessment with the aim of developing a staff competency development plan that incorporates mentorship, skills development, and motivation.
- PQM+ advanced the process of developing LNCQM's equipment maintenance plan.
- PQM+ offered technical assistance in developing LNCQ's draft risk management plan.
- PQM+ started the process of acquiring a dissolution tester, a priority equipment for LNCQM's operations.

PQM+ continued to strengthen the implementation of risk-based PMS of medicines quality in Madagascar.

- PQM+ supported the national PMS Technical Working Group (PMS-TWG) to develop the country's first PMS protocol during a workshop in Antananarivo from May 9 to 13. The protocol focused on testing three medicines: the medroxyprogesterone acetate injectable, 150mg/mL, oxytocin injectable, 10UI/mL, and artesunate-amodiaquine, fixed-dose combination antimalarial tablet, 50mg/135mg. A total of 240 samples at a rate of 80 samples per medicine will be collected. While these results may identify shortfalls and strengths in the medicines supply, they may not be nationally representative.
- PQM+ assisted the Agency to develop an SOP defining quality standards and reliable regulatory actions to be taken by the Agency based on risk-based PMS findings, to prevent poor quality medical products from reaching the people of Madagascar. The SOP in question includes a regulatory impact analysis (RIA) that involves identifying and analyzing the nonconformity problem, including the various stages of monitoring, from sampling to the output of the product test results. The regulatory decisions are motivated by and account for the sampling (modalities and information) and the steps related to the quality control of the product.
- PQM+ commenced the process of procuring reagents, reference standards, and consumables for Minilab kits located in 11 regions of Madagascar to enable rapid identification of poor-quality antimalarial, maternal and child health, and family planning

and reproductive health medical products. PQM+ trained the NQCL staff on using the Minilab kit, allowed the laboratory and the MRA to train Minilab managers throughout the country.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to provide technical assistance to LNCQM and provide instructional plans to develop staff competency, calibrate and maintain laboratory equipment, and provide laboratory development to aid the lab in complying with ISO/IEC 17025:2017.

- Validate and finalize the draft laboratory master plan.
- Finalize the laboratory risk management plan.
- Finalize procurement of a dissolution tester for the laboratory.
- Validate and finalize the SOP defining quality standards and reliable regulatory actions to be taken by the Agency based on the RB-PMS findings.
- Finalize procurement of MiniLab reagents, reference standards, and consumables.

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 1 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 both ISO/IEC 17025 accreditation and WHO prequalification.

PQM+ works with the DPM to strengthen its market surveillance function through establishing and operationalizing a PMS-TWG to implement RB-PMS and improve the capacity for medicine registration.

In addition, PQM+ has been providing tailored technical assistance to the Medicines Quality Control Laboratory within LNS to attain ISO/IEC 17025 accreditation. This would assure the reliability of testing, increase the public's confidence in test results, and help DPM take sound regulatory actions.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ encouraged LNS management to form an internal committee to develop a strategic plan, then worked closely with it to plan a five-day consultative stakeholder workshop, with PQM+ completing stakeholder interviews and collecting needed background information. PQM+ held several virtual meetings with the LNS committee to decide on the workshop's design, target audience, and agenda. LNS invited all stakeholders, but due to security threats to Bamako, the workshop was postponed.

LNS conducted the performance evaluation of its staff, but deviated from the SOPs and tool that PQM+ supported them to develop in PY2. Staff indicated that management did not take appropriate action to enable them to use the SOPs and tool. However, in a meeting convened by PQM+ with LNS staff, the director general committed to ensuring implementation of the performance assessment tool and suggested considering 2022 as a pilot phase. PQM+ then

conducted a refresher training for 30 LNS staff on the SOPs and the tool and agreed on a schedule for piloting the tool in the second half of 2022.

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

PQM+ supported LNS's Medicines Quality Control Laboratory (LCQM) to prepare for its ISO/IEC 17025 accreditation audit by addressing observations from the pre-assessment visit by the West African Accreditation System (SOAC, *Système Ouest-Africain d'Accréditation*). PQM+ supported LCQM to (a) develop new procedures (for HPLC column verification, managing external vendors, and managing chemical products); (b) update its organogram as advised by SOAC; (c) calibrate devices that were close to expiration prior to the scheduled accreditation date; (d) repeat failed proficiency testing for dissolution; and (e) conduct new proficiency testing for pH, Karl Fisher, loss on drying, and infrared spectrometry. The lab passed the proficiency testing.

At the end of June, PQM+ observed SOAC's assessment audit of LNS LCMQ and helped its quality assurance team conduct a root cause analysis of identified non-conformances to help in developing a CAPA plan for submission to SOAC.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support LNS LCQM to finalize a CAPA plan for submission to SOAC.
- Conduct a stakeholder workshop to develop LNS's laboratory strategic plan.
- Support the national PMS-TWG to conduct sampling of antimalarial and MNCH medicines for the 2022 RB-PMS.
- Provide technical assistance to the LNS microbiology laboratory as part of implementation of the roadmap toward ISO/IEC 17025 accreditation (review and finalization of QMS documents).

Mozambique

Mozambique recently established an autonomous medicines regulatory authority, ANARME (*Autoridade Nacional Reguladora de Medicamentos, Instituto Publico)*, which encompasses the Department of Quality Check (*Departamento de Comprovação da Qualidade*). PQM+ has been providing technical assistance in the transition to an autonomous national MRA and assistance moving ANARME toward attaining WHO GBT Maturity Level 3 and achieving ISO 9001:2015 certification. Additionally, PQM+ has been assisting the Department of Quality Check 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: Governance for medical product quality assurance systems improved

PQM+ provided support to ANARME toward ISO 9001:2015 certification through:

- Engaging the certification agency, Bureau Veritas (BV), to undertake an audit and certification. ANARME and BV prepared for the initial audit.
- Planning for a training on medical devices dossier review for ANARME staff, developing training materials and having ongoing discussions with ANARME to finalize dates and delivery methodology.

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

PQM+ continues to support LNCQ to address gaps identified during the PY2 assessment to attain good laboratory practices and ISO 17025:2017 accreditation. In Q3, PQM+ facilitated the development and review of key QMS documents.

1. The following documents were developed and approved, with personnel trained, and implemented: Corrective Action Risk and Opportunities, Certificate of Emission Analysis, Environmental Conditions, Good Documentation Practice/Data Integrity, and Quality Risk Management.
2. The following documents are pending implementation: Document Control, Equipment Management (Handling, Transportation, Calibration), Internal Audit, Management Review, Measurement of Uncertainty, Method Verification and Validation, Monitoring the Validity of Results, Non-Conforming Work, Out-of-Specification Procedure, Requests, Tenders and Contracts, and Sample Management.

PQM+ also provided support to LNCQ to implement actions in the updated accreditation roadmap and their operations.

- PQM+ procured a second TruScan analyzer to support PMS activities by ANARME.
- PQM+ procured MiniLab supplies for LNCQ/ANARME.
- PQM+ conducted an audit of progress on ISO 17025:2017 accreditation using the SATTA approach, which indicated good progress from 47 percent at the end of February to 91 percent in mid-May. The gap assessment identified 68 compliances, 34 partial compliances, and 12 non-compliances.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Complete pending ANARME/LNCQ activities and training as part of closing the gaps toward ISO 17025:2017 accreditation.
- Finalize the support of the ANARME ISO 9001:2015 certification process and assist in closing identified gaps.
- Finalize the medical devices dossier training with ANARME staff.

Nigeria

PQM+ is focused on helping ensure the quality of medicines and other medical products in Nigeria, with an emphasis on malaria and MNCH medicines and family planning commodities. PQM+ collaborates with stakeholders in the public and private sectors to increase local pharmaceutical manufacturing capacity and sustainably strengthen regulatory systems at the

national and state levels. PQM+ also strengthens QMS and builds laboratory capacity in QC testing in compliance with international standards.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

The Minister of Health approved the proposal to develop the strategic plan for the pharmaceutical manufacturing sector in Nigeria.

- A consultant will coordinate the project in conjunction with PQM+ and the Food and Drug Services of the Federal Ministry of Health.

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

Objective 2 activities are separated into those that relate specifically to the eight regulatory functions outside of the laboratory testing function.

Regulatory System Strengthening

- PQM+, in cooperation with the Pharmacists' Council of Nigeria (PCN), conducted sensitization workshops in Bauchi and Ebonyi states to build the capacity of operators of community pharmacies (CPs) and proprietary patient medicine vendors (PPMVs), as well as the members of the pharmaceutical inspection committees (PICs) on PCN's functions (such as the process for the registration and annual license renewal of CPs and PPMVs with PCN), and selected supply chain and QA topics.
- PQM+ partnered with PCN and other stakeholders to conduct a gap assessment to understand the regulatory and quality assurance systems (RQAS) in two new states (Benue and Kebbi) and offer solutions to the issues identified in the assessment pertaining to for-profit retail medical products sales outlets (CPs and PPMVs).
- PQM+ continued working with the PCN in Bauchi, Ebonyi and Sokoto states to strengthen the supply chain, QA, and regulatory systems by supporting the quality assurance committee meetings in these states.
- PQM+ conducted a virtual training for sample collectors from NAFDAC for the second round of RB-PMS. Sample collection for the exercise is in progress.
- PQM+ conducted capacity building/training for 22 staff across 10 NAFDAC directorates on quality risk management (QRM) to support them with needed skills t0 inspection relevant pharmaceutical manufacturing facilities.

Laboratory Support

- PQM+ conducted a gap assessment of the Medical Devices and In Vitro Diagnostics (IVD) units within the Agulu and Yaba QCLs in preparation for expanding its ISO/IEC 17025 accreditation scope to include testing of medical devices. The scope expansion covers five

devices[3] and 15 quality parameters for the Agulu Lab and six devices[4] and 22 quality parameters for the Yaba lab.

- PQM+ conducted a training/workshop for two NAFDAC Laboratories on "Introduction to Medical Devices and IVDs: Quality Management Systems and Regulatory Compliance." The workshop created awareness of global regulatory standards, frameworks, and best practices for QMS of medical devices and IVDs in preparation for the scope expansion of both laboratories in PY4.
- PQM+ supported NAFDAC to develop and review SOPs on medical devices and IVDs in preparation for the ongoing extension of scope of its ISO 17025:2017 accreditation to medical devices and IVDs by the end of 2022.
- PQM+ organized and facilitated a four-day exchange program for five National Institute for Pharmaceutical Research and Development (NIPRD) staff to the Microbiology Testing Unit of the NAFDAC's Laboratory in Lagos. The exchange program's aim is to equip NIPRD staff with relevant knowledge and skills in preparation for the scope expansion of its microbiology lab to areas such as microbial limit tests, sterility, bacterial endotoxin tests, etc.

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

JUHEL. Magnesium sulfate injection 50%w/v: PQM+ had supported Juhel to conduct tests to assess the risks of ink and adhesive migration from the label into the product. The WHO PQ team provided written confirmation accepting the results of this test in April. PQM+ expects correspondence on a date for a facility inspection from WHO in Q4.

SWIPHA. Zinc sulfate 20mg dispersible tablet: In response to conducting palatability studies for the product, the WHO PQ team scheduled an inspection of the sites. PQM+ provided technical assistance to Swipha in preparing for the inspection, which was at the end of June.

Sulfadoxine + pyrimethamine (SP) 500mg/25mg tablet: The WHO PQ team has scheduled the audit of the CRO that conducted the bioequivalence (BE) studies of Swipha's SP tablets in June. This follows initial review of the product dossier submitted to the WHO PQ team in PY2.

Artemether + lumefantrine (AL) tablets 80/480 mg: Swipha has contracted the same CRO for its SP product to conduct the BE studies of its 80/480mg AL tablets.

Priority Activities for Next Quarter

Objective 1:

- Commence meetings of the TWG to develop the strategic plan for Nigeria's pharmaceutical manufacturing sector.

Objective 2:

- Finalize the second round of RB-PMS in collaboration with NAFDAC.

[3] The five devices are condoms, hand sanitizers, hand gloves, absorbent cotton, and hypodermic syringes.
[4] The six devices are hand gloves, absorbent cotton, nose masks, isolation gowns, hypodermic syringes, and rapid diagnostic tests.

- Continue technical assistance to NAFDAC's laboratories in Yaba, Lagos, and Agulu to expand the scope of their ISO 17025:2017 accreditation on medical devices and IVDs.
- Continue supporting the NIPRD laboratory for scope expansion to microbiology testing in preparation for ISO 17025:2017 accreditation.
- Provide further support to the PCN for setting up an M&E system per the training in Q3.
- Conduct the RQAS assessment with PCN in the Federal Capital Territory (FCT).
- Disseminate findings of the RQAS assessments and develop state-level action plans.
- Build the capacity of the members of the PICs in the new states (Benue, Kebbi, and the FCT) on communication and people management to help improve the relationship between each PIC and operators of PPMVs and CPs, and encourage the operators to register with PCN.
- Conduct a one-day workshop to build the capacity of PPMVs and CPs on supply chain and QA topics and encourage improved registration with the PCN in the new states.
- Produce and distribute QA job aids to CPs and PPMVs to improve the quality of medical products at these outlets.

Objective 4: Implementation of some recommendations from the GMP roadmaps for supported manufacturers.

- Review the GMP and QMS status of manufacturers being supported for WHO PQ in preparation for PY4 planning.
- Conduct capacity building workshops on key QMS topics for professionals within the pharmaceutical manufacturing sector.
- Continue technical assistance to manufacturers of MNCH and malaria medical products to address requests for additional product data for dossiers submitted to WHO PQ.
- Follow up with Emzor on the production scale-up of its ready-to-use therapeutic foods.
- Conduct capacity building workshops for industry professionals and a local partner, the Centre for Drug Discovery, Development, and Production (CDDDP).

Table 2: Status of Lab Accreditation in Nigeria

Laboratory	Accreditation Sought	QMS	Initial Gap Assessment	CAPA	LIF	Official Inspection/ Pre-assessment
NAFDAC Main Yaba	ISO/IEC 17025:2017	Completed	Not applicable	Not applicable	Not applicable	Not applicable
NAFDAC Biologicals Yaba	ISO/IEC 17025:2017	Completed	Not applicable	Not applicable	Not applicable	Not applicable
NAFDAC Kaduna	ISO/IEC 17025:2017	Completed	Not applicable	Not applicable	Not applicable	Not applicable
NAFDAC Agulu	ISO/IEC 17025:2017	Completed	Not applicable	Not applicable	Not applicable	Not applicable
NIPRD Lab	ISO/IEC 17025:2017	Completed	Not applicable	Not applicable	Not applicable	Not applicable
*NAFDAC Agulu (New)	ISO/IEC 17025:2017 - Biologicals (Medical Devices)	Ongoing	Completed in April	Ongoing	Not applicable	Pending

Laboratory	Accreditation Sought	QMS	Initial Gap Assessment	CAPA	LIF	Official Inspection/ Pre-assessment
*NIPRD Lab	ISO/IEC 17025:2017 - Biologicals (Microbiology)	Ongoing	Not Applicable	Not Applicable	Not applicable	Pending
*NAFDAC Biologicals Yaba	ISO/IEC 17025:2017 - Biologicals (Medical Devices)	Ongoing	Completed in April	Ongoing	Not applicable	Pending

**Scope expansion for these labs for medical devices (Agulu and Yaba) and microbiology (NIPRD) for PY4*

Rwanda

As the medical products regulatory field changes, the WHO GBT requires national MRAs 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's FDA recommended developing an institutional competency framework to guide workforce capacity development. The Rwanda FDA sought support from PQM+ to undertake a training needs assessment in alignment with the WHO global regulatory competency framework.

Progress by PQM+ Objective

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

PQM+ worked with the Rwanda Food and Drugs Authority (RFDA) quality control laboratory (QCL) to by conducting an audit to identify gaps and work on a CAPA plan to address them.

- PQM+ trained 31 Rwanda FDA staff (19 male, 12 female) on ISO/IEC 17025, development of corrective actions with root cause analysis and internal audit.

Objective 2: Supply of quality-assured essential medical products of public health importance increased

PQM+ provided technical assistance to the Rwanda FDA to enhance its capacity for regulatory inspection, and for local manufacturers to apply current GMP to ensure access to quality-assured medicines by the Rwanda population. PQM+ provided technical assistance to 34 representatives from Rwanda FDA and two from local manufacturers (22 male, 14 female) to:

- Strengthen Rwanda FDA's capacity for regulatory inspection and to conduct desk reviews of antimalarial and other medical products' dossiers.
- Strengthen local manufacturers' current GMP. The regulatory authority and local manufacturers also shared their experiences to foster good relationships and facilitate promoting GMP regulatory compliance.

PQM+ provided technical assistance to the East African Community Regional Centre of Excellence for Vaccines, Immunization, and Health Supply Chain Management (RCE-VIHSCM) to carry out a rapid training needs assessment to identify gaps and map training needs that will inform curriculum design and content development. PQM+ collaborated with RCE-VIHSCM to develop course specifications and content for proposed modules of a QA/QC master's program.

PQM+ provided technical assistance to RMS Ltd. to develop 22 SOPs and one QA procurement framework. The framework includes a section on how RMS Ltd. should conduct supplier selection and prequalification to assure the quality of medical products procured and delivered to the warehouses before transporting to health facilities in the country for public use. Arising from the development of the QA procurement framework, PQM+ collaborated with RMS Ltd. to conduct a supplier selection and prequalification exercise for 23 suppliers of 280 essential medicines. Three suppliers failed the prequalification process.

Priority Activities for Next Quarter

Next quarter, PQM+ in Rwanda plans to:

- Conduct a GMP audit with five local medical product manufacturing facilities to develop a CAPA plan that the manufacturers will use to address deficiencies identified in their QA systems/GMP.
- Work with Rwanda FDA QCL to review SOPs and develop a CAPA plan and ISO 17025 accreditation/WHO prequalification roadmap.
- Work with the RCE-VIHSCM to conduct a training needs assessment and use the report findings to develop a short course on the essential aspects of quality assurance and/or quality control of medical products.
- Support RMS Ltd. to validate the developed SOPs and submit them through administrative channels for approval and implementation.

Senegal

The Government of Senegal recently developed a five-year (2019–2023) Integrated Strategic Plan for the Directorate of Pharmacy and Medicine (DPM) and the National Medicines Control Laboratory. 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 RB-PMS and to improve their capacity for medicine registration. In addition, PQM+ provides support to the National Medicines Control Laboratory to improve its capacity to test medicines.

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

PQM+ conducted a training on measurement uncertainty, an advanced requirement of the ISO/IEC 17025 standard, which LNCM had little capacity to implement. The training combined theory with case studies to help LNCM apply the basic principles to calculating uncertainties in the laboratory. Eight LNCM technical staff (four female, four male) successfully completed the training on measurement uncertainty, with five interns also participating.

In addition, in Q3, PQM+ conducted a training of trainers session on the ISO/IEC 17025 standard for LNCM technical staff. The training reached 12 people (six female, six male) and five interns. The trainees received a facilitator's guide to help them prepare to be internal trainers on this standard. At least three candidates performed well during the training and will be proposed to management to be the designated in-house trainers on the standard.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support the national PMS unit to conduct sampling of antimalarial medicines for the 2022 RB-PMS.
- Conduct a baseline assessment of DPM, per the ISO 9001 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 with 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.

Progress by PQM+ Objective

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

The PQM+ team submitted five activity implementation proposals to the ASEAN's PPWG detailing the planned technical assistance to ASEAN member states. The planned activities address the areas of marketing authorization, PMS, GMP inspection, and lot release. Once the network provides its final consent, PQM+ will move forward with activity implementation, starting with a regional workshop to disseminate findings of the regional landscape analysis and introduce topics and tools related to PQM+ planned assistance.

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

PQM+ Asia Bureau plans to conduct an analysis to assess the readiness of countries across the Asia region to expand local production and supply chain of a few shortage-prone priority essential health products. This quarter, PQM+ conducted a series of consultative meetings, including discussion with USAID's Local Manufacturing Group, to define criteria for the country selection and finalize the assessment methodology and tools for the preliminary analysis. That analysis will form the basis for an in-depth market feasibility study of two selected countries.

Priority Activities for Next Quarter

Next quarter, Asia Bureau plans to:

- Conduct a regional workshop.
- Finalize methodology for objectively evaluating countries to gauge their readiness levels for optimizing local health product manufacturing.
- Complete preliminary analysis through document analysis, key informant interviews, and focus group discussions.

Bangladesh

In Bangladesh, PQM+ works with the Directorate General of Drug Administration (DGDA), which oversees medical product quality in the country 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 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 TB medicines and good manufacturing practices.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ supported DGDA to develop a draft regulatory framework document. On May 11, PQM+ conducted a meeting at DGDA with the Regulatory System and QMS departments to form a task force committee to develop the draft regulatory framework document. Ten people (three female, seven male) attended the meeting. Based on the decision, a task force committee formed with well-defined terms of reference, then circulated notification on May 17. At a June meeting, the task force began work on a draft regulatory framework document.

PQM+ provided technical assistance to the Plasma Plus Application and Research Laboratory (PPL) to achieve international standards for medical product testing (WHO-PQ, ISO/IEC 17025:2017).

- Two technical experts, a senior technical adviser from PQM+ HQ and a technical officer for QA/QC with PQM+ Bangladesh, conducted an onsite gap assessment of the Independent University of Bangladesh (IUB) PPL from May 22 to 24 to determine capacity building areas for physical chemistry and testing of finished pharmaceutical products (FPPs), excipients, and APIs in accordance with international standards (WHO PQ, ISO/IEC 17025:2017). The team shared the draft report with PPL management on June 10.

PQM+ is supporting DGDA to prepare draft ethical marketing and promotion guidelines for pharmaceutical products.

- PQM+ supported DGDA to review the existing Code of Pharmaceutical Marketing Practices and shared that document with relevant stakeholders for review and feedback.

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

DGDA received 274 observations from the WHO formal assessment that occurred July 12 to 23, 2021. Based on those observations, PQM+ supported DGDA to develop a CAPA plan for nine functions of DGDA by:

- Updating the CAPA plan on May 14 to prepare for the WHO team meeting with nine DGDA departments.
- Providing technical support to update five SOPs and one set of guidelines to comply with the CAPA plan and meet the requirement toward WHO ML3.
    - The SOPs cover risk management; the management review process; developing guidelines; archival management; and procedures for sharing information and

regular updates to the website. The guidelines are on the recall and rapid alert system for medical products.

- Assisting the WHO South-East Asia Regional Office (SEARO) team with review of the CAPAs and the implementation process where relevant. SEARO visited DGDA May 16 to 22 to follow up the CAPA implementation.
- Providing technical support to monitor, evaluate, and update the CAPA plan on a weekly basis and conducting coordination meetings through the CIP Network.
- Delivering direct technical assistance to monitor and evaluate the CAPA plan implementation. Through June 30, about 65 percent of identified items have been closed or implemented.

PQM+ supported DGDA to develop the draft Regulatory Framework for Medical Devices:

- Held two meetings with PQM+ HQ expert Tangela Nichols to develop a strategy for the draft Regulatory Framework for Medical Devices and its implementation plan. Based on the discussion, the team developed an assessment questionnaire for stakeholders of medical device regulations.

PQM+ supported DGDA toward achieving PIC/S membership.

- On May 19, PQM+ organized an online meeting on the prospect, benefits, and challenges of PIC/S membership for DGDA. Representatives from USP HQ, DGDA, and PQM+ Bangladesh attended. Fourteen people (11 male, three female) participated. PQM+ will support DGDA to conduct an assessment against 78 PIC/S indicators and prepare a concept paper and roadmap for PIC/S accession application and membership.

PQM+ supported DGDA to introduce OpERA process mapping to integrate tracking and measuring regulatory performance and continuous improvements.

- OpERA country questionnaire responses are ongoing for completion by July. PQM+ is assisting DGDA to fill out the questionnaire.

PQM+ provided technical support to DGDA's Market Surveillance and Control department to adopt the MedRS tool for efficient implementation of RB-PMS.

- Since April, PQM+ has been working with the RB-PMS technical working group of DGDA to develop an anti-TB protocol using the MedRS tool. The draft protocol is under review to finalize. After finalization of the protocol, the National TB Program will start surveillance throughout the program's distribution chain.
- PQM+ supported the RB-PMS committee to review the SOP on RB-PMS of medicines, developed last quarter.
- PQM+ attended USAID's TB partners coordination meeting on May 19 at the Directorate General of Health Services.

PQM+ collaborated with DGDA to conduct a rapid assessment on SF anti-TB medicines in the private sector.

- In April, PQM+ met with Dr. Harun Ur Rashid, Deputy Chief of NCL, at DGDA regarding the updates of the anti-TB medicine sampling test at NCL and shared the status of the Reference Standard and discussed how the sample of TB programmatic medicines

(four- and two-drug fixed dose combinations, 4FDC and 2FDC) could be collected from anti-TB medicine DOT Centre, all public and private depots, and outlets.

- Prof. Sayedur Rahman, chair of the Pharmacology Department at Bangabandhu Sheikh Mujib Medical University, joined PQM+ in May to conduct a rapid assessment of SF anti-TB medicine in the private sector. He is developing the protocol for the assessment.

PQM+ provided technical support to DGDA to enhance the NCL's capacity for supporting the RB-PMS system for priority medicine (i.e., TB, MNCH, FP, and animal health products).

- NCL received columns for anti-TB product analysis on May 5.

PQM+ continued technical assistance to NCL to boost the vaccine testing capacity, including:

- Assisted preparation of the draft SOP for the carbon dioxide incubator on May 30.
- Assisted preparation of the draft SOP for the biosafety cabinet on May 26.
- Reviewed and updated 11 SOPs: on vendor management and vendor qualification; employee training; entry, exit, gowning, and de-gowning procedure for microbiology lab; method validation, verification, and transfer; procedure for communications with all ncl stakeholders; quality risk management; health checkup; testing and lot release procedure for vaccines; key performance indicators; laboratory safety; and management of vaccine samples.
    - As a result of the review, the team merged SOPs where applicable to address similar information like vendor management and subcontracting; incorporated more information like health status check in the microbiology laboratory for entry and exit; incorporated information about gas cylinders in the laboratory safety SOP; communicated with all stakeholders about their responsibilities as detailed in the communications SOP; and included information in the management of vaccine samples SOP about testing policy following a risk-based approach.
- A senior technical advisor from HQ visited the NCL vaccine laboratory on May 26 to meet with management and other NCL staff and oversee vaccine laboratory activities, as well as observe improvements to the laboratory's performance after receiving support from PQM+.
- Started in vivo testing for potency determination of one batch of tetanus vaccines using animals in the animal lab on April 10, completed on May 15 with satisfactory results. The team finalized the standard testing procedure for tetanus vaccine on May 15.
- Started in vivo testing for potency determination of one batch of rabies vaccine using animals in the animal lab on May 11, completed on June 8 with satisfactory results.
- Developed a standard testing procedure for rabies vaccine on May 16.
- The regulatory inspection team of DGDA conducted a cross-functional internal audit in the laboratory on June 7.

PQM+ continued technical assistance to DGDA to implement the CDTL roadmap, including:

- Completed categorization/classification of equipment for calibration for the CDTL laboratory on April 13.

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

PQM+ continued technical support to ACI Healthcare Ltd. towards prequalification of first-line TB medicines. Notable developments are:

- Batch manufacturing record of 4FDC finalized.
- ACI Healthcare Ltd. is manufacturing bio batches of the first-line anti-TB medicine 4FDC.
- PQM+ held a technical and programmatic review meeting with the company on May 26.

PQM+ provided support to capacitate the state-owned enterprise Essential Drugs Company Limited (EDCL) to implement GMP for manufacturing first-line anti-TB medicines.

- In collaboration with IntraHealth International, PQM+ completed a training needs assessment at all three EDCL sites (Dhaka, Bogura, and Gopalganj). IntraHealth prepared the first draft of the assessment report and shared it with PQM+ on June 10. The assessment report validation meeting was June 14.

PQM+ provided TA to a local CRO toward building capacity to perform bioavailability and bioequivalence (BA/BE) studies.

- A planning meeting on CRO activities took place April 28 with HQ experts to strategize the implementation process. An initial assessment questionnaire for CRO selection is under review.

PQM+ provided technical assistance to DGDA in preparation for ending the agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) flexibilities:

- Developed terms of reference for the work on TRIPS.

PQM+ initiated collaboration with the Bangladesh Association of Pharmaceutical Industries (BAPI) to raise awareness of good practices (GxP) for manufacturers of API products.

- PQM+ and BAPI conducted a stakeholders consultation workshop on prospects and challenges for API manufacturing in Bangladesh on April 21 at BAPI. The 28 participants included the CEO, secretary-general, treasurer, members, and other representatives from DGDA; officials from PQM+; and 21 technical staff from API manufacturers. Major General (Rtd.) Md. Mustafizur Rahman, CEO of BAPI, inaugurated the workshop.
- The workshop included conducting a comprehensive gap assessment to detect and diagnose issues, needs, and challenges for API manufacturing in Bangladesh.
- On May 30, PQM+ conducted a workshop at USP in Maryland with experts from the regulatory authority, academia, and manufacturers to validate identified challenges and recommendations for promoting the manufacture of quality-assured APIs in Bangladesh.
- On May 30, in collaboration with BAPI, PQM+ conducted the first training and gap assessment validation program. Participants included 40 people (36 male, four female).

Priority Activities for Next Quarter

- Finalize the draft regulatory framework document for DGDA.
- Finalize the draft ethical marketing and promotion guidelines for pharmaceutical products.

- Develop guidelines on the collaborative procedure for accelerated registration of medical products.
- Develop a draft assessment report on the preparedness of DGDA for the PIC/S accession application.
- Finalize the draft capacitation plan for promoting API manufacturing in Bangladesh.
- Conduct an assessment and develop a report on access to medical products in Bangladesh on the status of preparedness to meet challenges upon transition from least developed to developing country.
- Continue to assist DGDA in addressing CAPAs raised based on the WHO formal assessment observation in July 2021.
- Continue technical assistance to ACI in dossier review and submission of the BA/BE study report.
- Develop a draft regulatory framework for medical device regulation.
- Complete the OpERA assessment.
- Complete CRO selection.

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 a 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

PQM+ conducted the third week of metrology training at DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory.

- The training, with 15 participants attending, focused on preventative maintenance of three types of key analytical equipment: HPCL, dissolution tester, and auto titrator.
- PQM+ used instructional videos on preventive maintenance and post-preventive maintenance of equipment to facilitate the hands-on part of the training.
- PQM+ collaborated with USP Ghana to produce training videos.

PQM+ conducted measurement uncertainty training at the DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory as part of the preparations for ISO 17025:2017 reaccreditation.

- Seven participants from DFDA Nay Pyi Taw laboratory and 20 observers from DFDA Yangon and Mandalay laboratories under DFDA and YSI Pharmaceuticals QC laboratory attended the training.

- During the hybrid training, a subject matter expert joined remotely while the in-country consultant facilitated on-site.
- PQM+ collaborated with IntraHealth International to incorporate learning activities and case studies in the training.


Left: Analysts at DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory perform preventive maintenance of an HPLC system during metrology training. Right: A subject matter expert from PQM+ remotely delivered the measurement uncertainty training through Microsoft Teams while an in-country consultant facilitated the learning activities and hands-on sessions in the laboratory.

Priority Activities for Next Quarter

Next quarter, PQM+ Burma plans to:

- Organize a QMS workshop that covers ISO 17025:2017 standard, good laboratory practices, and good documentation practices at YSI Pharmaceuticals QC Laboratory
- Organize two technical webinars in collaboration with the USP General Chapters Team
- Organize an on-site GMP inspection at YSI Pharmaceuticals Factory
- Organize a data integrity training at DFDA Pharmaceutical Chemistry Laboratory

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 strengthening the public manufacturer Nepal Aushadhi Limited and introducing quality procurement guidelines for the national health insurance system.

Objective 1: Governance for Medical Product Quality Assurance Systems Improved

PQM+ is collaborating with DDA, the Ministry of Health and Population, and MTaPS to improve medicine-related legislation, policies, and regulations and promote stakeholder collaboration.

Revision of national GMP and GSDP codes: PQM+ supported the revision of the current GMP code and has supported drafting four supplemental guidelines to the GMP code. The guidelines

on biologicals; heating, ventilation, and air conditioning (HVAC); hazardous substances; and water treatment system have gone through technical review and are being translated into Nepali. PQM+ also participated in a stakeholder meeting to discuss the revised Code on Sales and Distribution of Drugs and the newly drafted Good Sales and Distribution Practices (GSDP). DDA organized the meeting with support from the MTaPS program.

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

Strengthen risk-based inspection (RBI) of DDA: PQM+ facilitated an inspection TWG meeting where the group endorsed the RBI framework and recall guideline. PQM+ worked with DDA to complete data collection of the selected 24 manufacturers and will rank them using the RBI framework. PQM+ is supporting DDA to analyze the information. Based on the analysis, PQM+ is assisting DDA to draft an RBI plan that will guide the inspection of high-risk manufacturers.

Strengthen RB-PMS of DDA: Amid the transition of leadership at DDA's Management Division that administered PMS functions, PQM+ mainly focused on the handover from DDA to NML of PMS samples collected during the RB-PMS pilot in the previous quarter. Subsequently, the program facilitated resource support to NML for testing those samples.

- PQM+ coordinated with DDA to support the lab to segregate collected medicines based on expiration date and generic name, so testing could be prioritized accordingly.
- Further, PQM+ handed over the chemicals and consumables and supported the lab to get USP reference standards to test those medicines samples.

Regulatory workforce development: PQM+ is engaging consortium partner IntraHealth to conduct three tasks related to workforce development:

- A training needs assessment and training plan for NML: PQM+ completed an internal review of the draft training assessment report and training plan and has forwarded it to NML for input.

PQM+ Nepal's chief of party delivers documentation on the FTIR equipment handover to the acting director of the NML.

- A training needs assessment and training plan for DDA: PQM+ facilitated information collection for the training needs assessment. A draft assessment report and training plan are complete and are being reviewed internally.
- Staffing needs analysis: PQM+ facilitated the formation of a working group at NML to provide input into a staffing needs analysis. IntraHealth consultants and the working

group analyzed the time inputs for NML activities with the aim of determining appropriate staffing levels for NML.

Support NML toward ISO 17025 accreditation: PQM+ Nepal NML activities remained focused on supporting areas outlined in the PY3 work plan. Similarly, PQM+ held collective discussions with NML and one-on-one discussion with NML's acting director regarding next year's plans.

- The program handed over two pieces of equipment to improve the testing capacity of NML: a Fourier transform infrared spectrophotometer (FTIR) and a pH conductivity meter.
- PQM+ continued supporting NML on drafting/ revising the QMS procedures, then reviewing and finalizing them. Through Q3, this has included drafting 21 SOPs with two implemented and 11 more finalized for implementation. Training on implementing the 11 finalized SOPs will occur in Q4.
- The program is coordinating between the lab and the service provider customizing the inventory management software for managing chemicals, reference standards, and incoming samples.
- From the PY3 work plan, the team has completed five of six outlined deliverables (83 percent), with gradual progress toward meeting ISO 17025 accreditation requirements.

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.

Manufacturers attend a training on advanced GMP.

Private manufacturers: PQM+ finalized assessment reports and drafted CAPA plans for Nepali private manufacturers to build a roadmap for obtaining WHO prequalification for selected medicines. The program discussed the CAPA plans with the manufacturers. The plans highlighted inadequacies on dossier preparation among manufacturers, for which PQM+ organized a five-day training workshop on dossier preparation to 20 technical personnel of manufacturers.

To enhance manufacturers' technical capacity on GMP, PQM+ conducted a pair of two-day trainings on advanced GMP topics. Participants totaled 91 manufacturing technical staff.

Public manufacturer: PQM+ focused on two technical components to support the country's only public pharmaceutical company, Nepal Ausadhi Limited (NAL), to achieve compliance toward national GMP. The program supported completion of upgrading NAL's water treatment facility to meet industry requirements. PQM+ and NAL are in the final stages of redesigning the microbiology section by improving the air handling unit and clean room in accordance with the regulatory standards.

Nepal pharmaceutical manufacturing strategy: PQM+ is collaborating with DDA and other national stakeholders to develop a Nepal pharmaceutical manufacturing strategy. PQM+ engaged consortium partner IQVIA to conduct a landscape analysis of the Nepali medicines market. PQM+ has completed an internal review of the report and IQVIA is finalizing it.

Quality procurement guidelines: To assure quality in the procurement process for medicines, PQM+ is assessing the medical product procurement process and developing a guideline for quality assurance at the Health Insurance Board and a local government unit. Specifically**:**

- PQM+ completed the assessment of the medical product procurement process of a local government unit and has drafted a guideline. Additionally, PQM+ is assessing the processes at the national and provincial levels, to look at broader and specific issues of quality assurance in medical commodities procurement.
- PQM+ is working with the Health Insurance Board to assess government-owned health facilities that provide health services through the insurance scheme. Through this, PQM+ will draft and submit an assessment report and guideline to the board on improving the quality assurance process in its affiliated health facilities.

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

PQM+ has worked with DDA to develop messages on SF medicines to broadcast as public service announcements through national and local radio stations. PQM+ is finalizing the compilation of audio messages after final review from DDA.

The program has developed a research proposal for pre- and post-training assessments of community pharmacists' awareness and behaviors on the identification of SF medicines. PQM+ HQ reviewed the study proposal and Nepal Health Research Council has given consent to commence the study. PQM+ trained community pharmacists in a district of Province 1 and conducted a pre-assessment of the training.

Priority Activities for Next Quarter

Next quarter will mark the end of the Nepal workplan for Year 3 and will focus on completion of remaining activities.

- PQM+ will continually advocate with the DDA on the approval of the GMP code and will finalize four supplementary guidelines for the Code in Nepali. PQM+ will work with MTaPS and DDA to review and finalize the revised draft code on sales and distribution of codes.
- PQM+ will work with DDA to organize a high-level consultative meeting in July to discuss a roadmap toward developing Nepal pharmaceutical manufacturing strategy.
- Concerning the laboratory, PQM+ will support NML on commissioning and qualification of equipment, implementing SOPs, and setting up a data management system.
- PQM+ will complete the assessments of health facilities enlisted with the National Health Insurance Board and finalize guidelines for the board and a local government unit.
- PQM+ will finalize the progress review of CAPA plans for private manufacturers. PQM+ and NAL will organize a ceremony to mark the program's technical support to NAL with participation of government stakeholders and the local USAID Mission.

- PQM+ will complete the pre-training assessment report on the visual identification of substandard and falsified medicines to the community pharmacists of Province 1.

Pakistan

In Pakistan, provision and access to quality health services is a major concern. Health regulations (particularly drug regulations), strengthening the drug testing labs network (at the federal and provincial levels), availability of centers to conduct reliable bioequivalence studies reduced confidence in the efficacy of generic medical products manufactured in the country, are some key technical areas to address for achieving long-term health targets and sustainable economic development. Inconsistent government policies for the pharmaceutical sector have undermined the private sector's potential role in improving health outcomes.

PQM+ Pakistan 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+ organized a training workshop on "Annual Performance Management System and Development of Key Performance Indicators (KPIs)" by defining organizational annual objectives and its associated key performance indicators for Drug regulatory Authority of Pakistan (DRAP) as performance evaluation criteria. This exercise would help DRAP develop its annual performance management system, a key requirement of WHO Global Benchmarking ML3 status and PIC/S accession. Thirty participants (four females, 26 males) from 13 DRAP divisions attended.

The main areas covered in this training were vision, mission, strategic priorities, fundamentals of KPIs, Global Competency Framework, and characteristics of smart approaches. In addition, the training workshop provides an overview of performance management, compliance management, and KPIs to measure the efficiency and effectiveness of various regulatory functions at DRAP.

The annual performance system and development of KPIs will help in evaluating technical and administrative DRAP staff's performance, resulting in better achievement of annual and biannual targets. This training workshop will help DRAP's organizational restructuring for better reporting compliance and standardization of practices among its divisions. PQM+

- Developed training materials (including methodology, agenda, and relevant forms) for DRAP's KPI capacity building program. PQM+ trained assistant directors at DRAP.
- Organized a training workshop on "Annual Performance Management System and developing KPIs" for DRAP.

Activity 1.2: Develop a National Medicines Policy (NMP) implementation plan and guidelines for quality assurance of medical products (including antimicrobials): PQM+ is developing an NMP implementation plan to implement the NMP. In this regard, PQM+ has reviewed the details of the National Medicines Policy (NMP) and worked on a matrix of six elements. PQM+ drafted an implementation plan for National Medicines Policy (NMP), which is under review.

Activity 1.3: Support DRAP for Provincial Coordination and Cross-cutting tasks in Global Benchmarking Tool (GBT): With PQM+ support, DRAP is pursuing international accreditation to provide better regulatory oversight and better ensure the availability of quality-assured medicines and boost exports.

WHO auditors planned to conduct a formal assessment on the benchmarking tool of the national regulatory system in two phases: a July 17 field visit for pharmacovigilance and regulatory inspection and the October 25 final audit. This benchmarking contains nine regulatory functions covering legislation, guidelines, procedures, human and financial resources, and performance outputs. DRAP identified various gaps during self-assessment and developed its IDPs, a few activities of which are cross-cutting with provinces and other organizations. PQM+ continued technical support to DRAP for developing the IDPs.

In this context, PQM+ met with representatives of relevant stakeholders, Drug Control Organization, and health departments in provinces, Islamabad Capital Territory, Gilgit-Baltistan and Azad Jammu, and Kashmir.

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+ supported the Public Health Laboratory (PHL) at the Institute of Public Health (IPH) in Lahore toward achievement of ISO 15189 accreditation, an international standard for QMS at medical diagnostic laboratories. As a result of PQM+ assistance, Pakistan National Accreditation Council (PNAC) completed the final assessment for ISO 15189. During the reporting quarter, IPH is working to develop a CAPA plan to submit to PNAC for closure of the final assessment observations. ISO 15189 accreditation would enable PHL to improve its lab testing reliability going forward. The key achievements are:

- Provided technical assistance on the preparation of CAPA against PNAC final-assessment observations.
- Submission of CAPA.

PQM+ support to Drug Testing Laboratory (DTL) Lahore

WHO Peer Audit: During Q3, PQM+ assisted DTL, Lahore to prepare a CAPA plan against WHO peer audit observations. Afterward, DTL, Lahore submitted its CAPA to WHO for comments and further action. Currently, the final WHO PQ inspection date is pending from WHO, with scheduling expected in Q4. PQM+ assisted in the preparation of the CAPA against WHO peer audit observations.

PQM+ support to Drug Testing Lab (DTL), Multan

WHO PQ Peer Audit: PQM+ and the WHO PQ team established a partnership for peer audits to strengthen the quality control lab system in Pakistan. PQM+ visited DTL, Multan to prepare for the peer audit CAPA. Key achievements of the reporting quarter are:

- Peer audit CAPA submitted to WHO for review; PQM+ evaluated the CAPA and returned it for conversion and reporting in the WHO-specified format.

ISO 17043 (PT): PQM+ supported DTL, Multan in developing a QMS against the ISO 17043 standard. PQM+ performed the initial gap assessment and PNAC carried out the pre-assessment. Afterward, PQM+ supported the development of the CAPA plan against the pre-assessment and the final assessment date is pending.

PQM+ support to Drug Testing Lab (DTL), Bahawalpur

WHO PQ Peer Audit: PQM+ assisted Bahawalpur DTL to review and submit the laboratory information file (LIF) for WHO prequalification, which WHO has accepted and approved. Key achievements are:

- Peer audit CAPA has been submitted to WHO PQ for review.
- Date of inspection is pending from WHO PQ.

PQM+ support to Drug Testing Lab (DTL), Rawalpindi

WHO PQ Audit: PQM+ provided technical assistance to Rawalpindi DTL during the WHO prequalification audit. As a follow-up activity, PQM+ assisted the DTL with CAPA preparation and submission to WHO. Key achievements during the quarter are:

- Reviewed CAPA report.
- Delivered guidance on preparing the laboratory for a follow-up visit; date is pending from WHO.
- A follow-up visit by WHO is planned for the last week of July.

PQM+ support to Central Drug Laboratory (CDL), Karachi

WHO PQ Peer Audit: In the initial phases, the CDL was assessed for QMS certification and is continuously engaged with WHO for its PQ accreditation as one of the quality control laboratories in Pakistan. In this regard, PQM+ collaborated with the WHO PQ team to conduct a peer audit. Earlier, Karachi's CDL CAPA WHO peer audit report was reviewed and submitted to WHO headquarters for onward communication to CDL Karachi.

Key achievements are:

- CAPA plan against peer audit submitted to WHO PQ for review.
- WHO PQ inspection will be carried out in the last week of July.

Table 3: Status of Labs Accreditation in Pakistan

Laboratory	Accreditation Sought	Initial Gap Assessment	CAPA (Corrective & Preventive Action)	Quality Management System (QMS)	Proficiency Testing (PT)/ Laboratory Testing (LT)	Official Inspection/ Pre-Assessment
IPH Lab	ISO 15189	Completed	Completed	Completed	Completed	Final assessment and CAPA completed. To be submitted to PNAC.
Appellate lab	ISO 17025	Completed	Ongoing	Developed, under implementation through training	One PT sample performed and reported. Result pending.	Lab is in the renovation phase. Pre-assessment application will be submitted as soon as PT results are received.

Laboratory	Accreditation Sought	Quality Management System (QMS)	Initial Gap Assessment	CAPA (Corrective & Preventive Action)	Laboratory Information File (LIF)	Official Inspection/ Pre-Assessment
DTL, Rawalpindi	WHO Prequalification	Completed	Completed	Under review		CAPA is submitted and reviewed by Inspector, WHO. Follow-up visit by WHO is planned in last week of July.
	WHO Prequalification	Completed	Completed	Completed	Submitted and approved	Completed. Peer audit CAPA submitted to WHO for review. (CAPA evaluated by PQM+ and reverted back to convert to on WHO-specified format.)
	ISO 17043 (PT)	Completed	Completed	Completed (Reviewed by PQM+ after pre-assessment by PNAC)	Completed	Final assessment date pending from PNAC
DTL, Lahore	WHO Prequalification	Completed	Completed	Completed and submitted	Submitted and approved	Completed Peer audit CAPA submitted to WHO for review; CAPA report reviewed by PQM+ prior to submission and provided guidance to lab on its development. WHO PQ date pending from WHO.
	ISO 17025:2017 (Calibration)	Completed	Initial gap assessment by PQM completed	Completed	N/A	Application for scope extension to include calibration laboratory in accordance with ISO/IEC 17025:2017 submitted to PNAC.

Laboratory	Accreditation Sought	Quality Management System (QMS)	Initial Gap Assessment	CAPA (Corrective & Preventive Action)	Laboratory Information File (LIF)	Official Inspection/ Pre-Assessment
CDL, Karachi	WHO Prequalification	Completed	Completed	Completed and submitted	Submitted and approved	CAPA plan against Peer audit submitted to WHO PQ for review. WHO PQ inspection will be carried out in Last week of July.
DTL, Bahawalpur	WHO prequalification	Completed	Completed	CAPA plan is under review	Submitted and approved (Reviewed and revised by PQM+)	Peer audit CAPA submitted to WHO PQ for review. Date of inspection pending from WHO PQ.

Activity 2.3: Developing a roadmap for stepwise implementation of BE studies: Pakistan is among the few countries where BE studies are not mandatory for marketing authorizations. This is a key requirement for PIC/S membership, WHO PQ, and the GBT tool.

Background

The main aim of this activity was to develop a roadmap for a stepwise implementation of BE studies in Pakistan. Earlier, in a meeting with DRAP officials, PQM+ presented a draft roadmap for implementing BE studies. Considering the dynamics of Pakistan, PQM+ proposed several steps for a smooth and phase-wise implementation of BE studies. The final guidelines document has been uploaded to DRAP's web portal for stakeholder consultation. PQM+ will organize a virtual meeting with DRAP and stakeholders. After incorporating comments and feedback from stakeholders, these guidelines will be ready for adoption.

Key achievements during the reporting quarter are:

- The final guidelines document is on DRAP's web portal for stakeholder consultation.
- PQM+ has selected two BE centers for technical assistance to conduct BE studies per international best practices. The letters of understanding were reviewed by the selected centers and shared with USP HQ for legal review. The centers are the Institute of Biological, Biochemical, and Pharmaceutical Sciences at Dow University of Health Sciences in Karachi and the Center for Bioequivalence Studies and Bioassay Research at University of Karachi.
- PQM+ conducted a meeting with DRAP management to develop an appropriate BE policy implementation strategy that considers challenges of the local pharma industry.

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

Activity 3.1: Private sector engagement to increase the supply of quality-assured priority medical products: PQM+ Pakistan continued to support the country's pharmaceutical manufacturing industry by monitoring progress through the implementation of CAPA plans for amoxicillin-DT and zinc manufacturers. PQM+ planned to assist the manufacturers to develop CAPA plans to address observations/findings from their GMP gap assessment in relation to QMS, current GMP at the production floor, GLP in the quality control lab, and product dossiers.

PQM+ visited three manufacturers and provided technical assistance toward WHO PQ: Next Pharmaceuticals for zinc DT; CSH Pharma for amoxicillin-DT; and PharmEvo for zinc DT.

PQM + carried out a gap assessment at Next Pharmaceuticals for zinc DT from May 15 to 17, evaluating whole plant operations and the quality system in line with WHO GMP guidelines.

PQM+ also visited CSH Pharma for amoxicillin-DT on May 19, conducting a gap assessment for WHO prequalification.

PQM+ also carried out a gap assessment visit at PharmEvo to prepare for the upcoming inspection by the WHO PQ team. During the visit, PQM+ reviewed the last WHO PQ CAPA report and thoroughly evaluated the plant facility.

Table 4: Status of WHO PQ of Medicines in Pakistan

Manufacturers	Accreditation sought	Initial Gap Assessment	CAPA	Product Development	Dossier compilation	Dossier Submission /Acceptance	Official Inspection (WHO PQ)
M/s Macter for	WHO Prequalification	Complete	In process	Complete	In process	To be done	To be done
M/s Dynatis for zinc (DT/oral liquid)	WHO Prequalification	Complete	In process	Compete	In process	To be done	To be done
M/s Schazoo Zaka for (4FDC anti-TB product)	WHO Prequalification	Complete	Complete	Complete	Complete	To be done	To be done
M/s CSH for amoxicillin-dispersible tablet (amox-DT)	WHO Prequalification	Complete	Preparing report with PQM+	Not started	To be done	To be done	To be done
M/s Next Pharma for zinc DT/oral liquid	WHO Prequalification	Complete	Report to be shared by PQM+	Started	To be done	To be done	To be done
M/s PharmEvo for zinc DT/oral liquid	WHO Prequalification	Complete	Complete	Complete	Complete	Complete	To be done

Activity 3.2: Development of a National Pharmaceutical Strategy: A focus of PQM+ is to help foster a business enabling environment that encourages private sector investment in pharmaceutical manufacturing. Pakistan currently exports approximately $230 million in pharmaceutical products, which is a very small percentage of the approximately $1 trillion+ global market for pharmaceuticals.

During the reporting quarter, the key achievements include:

Formation of a new working group for strategy development: The first working group had been formed as an initiative of the Ministry of Planning led by the minister and chief economist. However, with the expected change in government PQM+ focused on developing a parallel strong relationship

with the Regulatory Modernization Initiative of the Board of Investment in the Prime Minister's Office for championing this work.

As a result, a new Strategy Working Group was notified by the Board of Investment on April 26 to take the strategy development exercise forward within a few weeks of the change in government. While this new working group will result in a delay in achieving some planned deliverables, the approach focuses on ensuring ownership and traction of the strategy's implementation. Ensuring that will require the team to delay the draft strategy by a few weeks and make sure all members of the working group own the process and each of the strategy recommendations.

In preparation for the first meeting of the working group planned on May 11, PQM+ engaged with all key stakeholders to sensitize them to the purpose of the working group and ensure alignment of objectives. Key stakeholders who met to prepare include representatives from the public sector, private sector, and development partners. Stakeholders engaged included director general for non-agro at the Ministry of Commerce, representatives from the International Finance Corporation, World Bank Group, and Foreign Commonwealth Development Office (FCDO). Multiple meetings took place with representatives from the industry associations Pakistan Pharmaceutical Manufacturers Association (PPMA) and the Pharma Bureau, where 12 reform proposals for inclusion in the strategy were developed. These proposals were shared with the Board of Investment and other development partners directly supporting the government for the development of the FY2022 budget.

Key discussion points from the first working group meeting: At the first meeting of the Working Group on Strategy on May 11, participants acknowledged the need for a consolidated strategy to grow the pharmaceutical sector given its vast export potential and public health significance. They decided on key action items: that all participants would lobby for designation as a priority sector and taking the strategy recommendations to the Cabinet to be formalized into implementation plans with SMART[5] targets.

One key area for consultation with the private sector identified was the API policy. A Board of Investment-led public-private dialogue took place in Lahore June 3 with representation from the industry, regulator, and relevant public sector entities. PQM+ actively participated in the dialogue, sharing various best practices for the promotion of domestic production of APIs.

Dedicated session with industry on Regulatory Environment and Policy Framework: During meetings with Pharma Bureau (industry association), PQM+ received a request for a dedicated session with key association members on regulatory and policy pain points and reform proposals. The session took place June 1 at the Pharma Bureau office in Karachi with senior leadership from GlaxoSmithKline, Novartis, Sanofi, Pfizer, Reckitt Benckiser, and the executive director of Pharma Bureau. The participants outlined key challenges they faced in working with the regulator, obstacles to increasing investment, and expanding the country's production of innovative therapies. These included DRAP's technical capacity, weak intellectual property rights protection, variable enforcement of quality standards, and with an opaque and unpredictable pricing policy.

PQM+ included these challenges and associated reform proposals in the draft strategy, shared the draft with participants for validation, and received feedback on it.

[5] Specific, Measurable, Achievable/Attributable, Relevant, Time-bound.

Private sector engagement (PSE): As part of the PSE, the PQM+ team continued developing relationships with industry associations and conducted meetings with the PPMA, Pharma Bureau and Healthcare Devices Association of Pakistan to identify regulatory challenges and bottlenecks for industry to grow in the domestic and export markets.

PQM+ focused its efforts on expanding partnerships with knowledge leaders in the global pharmaceutical industry. The aim of this exercise is to develop a strong relationship and leverage partners' technical expertise to offer training and capacity building to DRAP.

Preparation for training on lot release of biologicals for DRAP: In response to a request from DRAP for capacity building on the lot release of biologicals, PQM+ is working with the Biopharmaceutical Analysis Training Laboratory (BATL) at Northeastern University to design a training for the regulator. PQM+ developed a preliminary draft agenda and content for a training in early Q4.

PQM+ continues to work closely with DRAP to address their training needs and identify new private sector partners to leverage their technical expertise through in-kind contributions for addressing DRAP's capacity building needs.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Carry out training at DRAP's request on the lot release of biologicals.
- Review the preparation of WHO final audit for DRAP regarding IDPs.
- Support adoption of two data standards (ISO 11615 and ISO 11238).
- Perform two case studies documenting best practices from countries that have successfully promoted their pharmaceutical sectors for the government/regulator.

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), as well as to support the NCEM in establishing a risk-based post-marketing surveillance system.

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 Q3, 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 the PQM+ peer audit. In accordance with recommendations of the WHO PQ team, PQM+ assisted Almaty MQCL in preparation of additional information requested by the WHO PQ team. PQM+ reviewed and improved several additional SOPs requested by the WHO from the Almaty MQCL. Almaty MQCL submitted the CAPA plan and additional documents to the WHO.
- PQM+ reviewed and improved Almaty MQCL's updated LIF before submission to the WHO.
- The WHO PQ team confirmed the inspection of Almaty MQCL for July 19 to 22.
- On May 16 to 20, Almaty MQCL was audited by the European Directorate for the Quality of Medicines (EDQM) for accreditation status and membership in the European Network of Official Drug Control Laboratories (OMCL). EDQM confirmed accreditation and membership of the Almaty MQCL to the European network of the OMCL.
- PQM+ assisted Karaganda and Almaty MQCLs to develop their capacity in computerized systems validation (CSV). WHO and PQM+ have identified a need for further support in this area. In Q3, laboratories had several technical consultations with the CSV expert for discussion of validation protocols and reports for the laboratory equipment. CSV consultant visited Almaty MQCL June 13-16 and provided technical assistance on practical validation of computerized systems.

PQM+ is supporting Kazakhstan in strengthening the pharmaceutical inspectorate and preparing for ascension to PIC/S. That achievement will facilitate reliance and open access to

the GMP inspection mechanism with other PIC/S member countries; resources for capacity development; and access to quality-assured medicines in the country. PQM+ continued technical assistance to advancing on the PIC/S ascension roadmap. In PY3, Q3 PQM+ helped the GMP inspectorate prepare its newly developed quality management system for launch.

PQM+ continued technical assistance to NCEM in strengthening the post-marketing surveillance (PMS) system by building on the work conducted in the previous quarters. PQM+ provided an onsite training April 13 to 22 for the NCEM staff on MedRS as a follow-up of the initial introduction to the tool. The purpose of this training was to provide technical assistance to strengthen the PMS program of TB medicines in the country using effective RB-PMS. In addition to the training on the RB-PMS approach using the MedRS tool, PQM+ assisted the PMS working group with an RB-PMS protocol for anti-TB medicines and selecting medicines and facilities based on risk scoring for 2022. The 25 participants represented the Committee, the Ministry of Health of the Republic of Kazakhstan, NCEM, and SK-Pharmacy LLP.

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 medicine's regulatory workforce in Kazakhstan. In Q3, PQM+ continued to work on training materials on how to prepare and administer tests. This training is planned for Q4.

PQM+ signed a terms of reference document that outlines PQM+ as the technical assistance provider to the NCEM in meeting select gaps identified during the WHO GBT audit in Q3. The TOR was initiated by WHO with PQM+ and NCEM as the signatory parties. PQM+ also participated in the remote WHO GBT follow-up by WHO. PQM+ is working with NCEM to complete a matrix that outlines the support plan for WHO GBT assessment findings.

One gap identified during the WHO GBT assessment was that the Committee needs to establish the QMS according to ISO 9001, as they are involved in regulatory function. In Q3, PQM+ provided technical assistance to the Committee in establishing QMS according to ISO 9001. PQM+ provided a virtual training for the Committee and the NCEM on ISO 9001:2015 QMS. Attending were 27 participants from the Committee, the Ministry of Health, and NCEM. In additional to the general ISO 9001:2015 training, PQM+ provided a short, intensive three-hour course on ISO 9001 to the Committee's chairman and deputy chairman and provided highlights on the role of top management in ISO 9001:2015 QMS.

PQM+ organized an initial audit on the Committee's management system for conformance with the ISO 9001:2015 requirements. PQM+ conducted interviews with the heads and key staff of all structural units of the Committee's Central Office affecting the quality of pharmaceutical control, as well as two regional departments. Based on the results of the audit, PQM+ developed a report, including evaluation of the level of conformance with the requirements of all sections of the ISO 9001:2015 standard and describing all identified non-conformities.

Based on the audit results, PQM+ developed a detailed action plan to improve the management system in accordance with the ISO 9001:2015 standard and to prepare for certification according to this standard. This action plan covers the period from late May to December. PQM+ submitted the action plan to the committee.

PQM+ developed and presented two Committee management structure scenarios that meet the ISO 9001:2015 requirements and cover all areas that affect pharmaceutical control quality. The Committee management selected one structural scenario and agreed on the process owners. PQM+ also developed templates for the management system manual and SOP.

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' Association to understand the training needs of the manufacturers specifically in terms of improving their GMP compliance. PQM+ developed a questionnaire to assess the training needs of the local manufacturers and provided it to the SEC for review. SEC is reviewing the questionnaire. When the questionnaire is finalized, PQM+ and SEC will work with the manufacturers to conduct a survey that will inform the priorities for GMP trainings to be prepared by SEC with PQM technical assistance.

Priority Activities for Next Quarter

- Assist Almaty MQCL with the 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.
- Assist the Committee in establishing ISO 9001 QMS.
- Assess the training needs of the local manufacturers.
- Continue technical assistance to the NCEM in preparation for the next WHO GBT assessment.

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 the medicines quality control laboratory (MQCL) to be able to test the quality of medicines reliably and accurately in accordance with the international standards.

Progress by PQM+ Objective

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

In Q3, PQM+ developed an assessment report and action plan for addressing identified gaps at the Dushanbe MQCL. The Laboratory is currently accredited to the previous version of the international standard for general requirements on the competence of testing and calibration laboratories, ISO/IEC 17025:2005. The aim of the assessment was to identify areas of system strengthening needs for the MQCL to meet the requirement of the revised standard as well as WHO good practices for pharmaceutical quality control laboratories (GPPQCL) and good practices for pharmaceutical microbiology laboratories.

PQM+ identified and documented system deficiencies and shared them with MQCL management. One deficiency noted during the assessment was the lack of understanding and implementation of root cause analysis within the MQCL QMS. Root cause analysis is important to help address any identified gaps within the QMS and technical operations of the laboratory.

To address this issue, PQM+ developed and delivered a one-day training on root cause analysis in April to MQCL representatives and staff, presenting several methods. MQCL will select to continue addressing the analysis of existing problems.

As the MQCL is required to be accredited according to ISO 17025:2017 by the National Accreditation Centre in 2022, it was jointly agreed to start technical assistance with the training on that standard. Thus, a virtual training that spanned nine days in April compared the old and new versions of ISO 17025. In collaboration with the Dushanbe MQCL, PQM+ developed the CAPA plan. The capacity of the MQCL staff on physio-chemical and microbiological methods and QMS will be developed in accordance with this plan.

State service and PQM+ agreed that improvement of the regulatory process and communication to improve the efficiency in the registration system is a priority. The TWG on registration from the state service agreed to concentrate on developing two SOPs on the screening application and evaluation of assessment.

To encourage the manufacturers that have achieved WHO prequalification to apply for registration of their products in Tajikistan, PQM+ selected the local company Shifoi Sino that will work with these manufacturers and, on their behalf, compile and submit dossiers for registration in Tajikistan.

In parallel, PQM+ coordinated closely with the Global Drug Facility (GDF) to identify potential manufacturers of WHO-prequalified TB medicines that will be interested in registration of their products for Tajikistan. After several meetings with the GDF technical team, two WHO-prequalified TB drug manufacturers expressed interest in registering their products in Tajikistan. PQM+ started communication with both companies and outlined a plan for registration of their TB medicines.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Implement activities with MQCL according to the CAPA plan.
- Develop and submit SOPs for review for registration.
- Prepare and submit dossiers of WHO-prequalified manufacturers for approval in Tajikistan.

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 MOH in developing the "pharmaceuticals and medical devices" strategic block of the ministry's Health Strategy 2030. In Q2, PQM+ launched the strategy development by organizing a working group and meeting with various public and private sector stakeholders to gather information for the pharmaceutical and medical devices situational analysis that will inform the strategy development. In Q3, based on the information obtained during the meetings, as well as through the desk review of many documents, PQM+ identified major findings from the situation analyses, challenges, and strategy recommendations for pharmaceutical strategy and medical devices block.

In May, PQM+ (including the strategy experts) participated in a workshop with World Bank consultants from various other health strategy blocks to refine situational analysis findings and align recommendations. During the visit, PQM+ and other blocks presented challenges and recommendations to the Minister of Health and deputy ministers. The minister engaged extensively in all the presentations but did mention that he felt pharmaceuticals pose the biggest challenge to health care in Uzbekistan, underscoring the importance of this work.

In June, the PQM+ strategy advisor traveled to Uzbekistan again to participate in the first international pharmaceutical forum of Uzbekistan. PQM+ was invited to facilitate a plenary session on the strategy for development of a new Uzbekistan for 2022 to 2026 and the development of the pharmaceutical industry of the Republic of Uzbekistan. The Minister of Health attended the presentation, as did several other ministries and the Agency. PQM+ also asked to present the strategy recommendations at a session on pricing of medicines in Uzbekistan and neighboring countries. PQM+ met with several other stakeholders, including the Agency, to further clarify and refine the strategy recommendations. The strategy document will be finalized, incorporated into the larger Health Strategy 2030 document, and submitted to the Government of Uzbekistan for approval in Q4.

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

In Q2, PQM+ continued to provide technical assistance to strengthen the medicines registration system. Through its COVID funding, PQM+ had initiated the concept of EUA, which was included in the updated draft version of Cabinet Resolution #213. PQM+ reviewed the EUA provisions in Resolution #213 and provided feedback for improvement. In Q3, PQM+ continued technical assistance to the Agency to help them to advocate to the Cabinet of Ministers to adopt the EUA clause.

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. In Q2, four additional dossiers were submitted to the Agency for the first-line WHO-prequalified TB medicines. In Q3, the Agency is reviewing the dossier for these four first-line TB medicines for registration for WHO CRP. The decision on registration is anticipated soon.

In Q3, PQM+ continued to work with the newly established GxP Center, which is responsible for the GMP inspection. PQM+ continued to engage with the working group on the development of an updated version of the GMP guideline, training programs for inspectors, and SOPs on the QMS and inspection process. In Q3, PQM+ facilitated three meetings with the working group; reviewed and finalized six QMS SOPs; and assisted the MRA in developing an annual inspection plan for the GxP center.

In Q3, the PQM+ technical advisor for the laboratory visited the Andijan and Tashkent MQCLs and conducted internal audits of both laboratories. In addition to evaluating the current level of compliance of both laboratories with WHO prequalification requirements, the internal audits were used as capacity building opportunities for MQCL staff. By observing and discussing with PQM+, the MQCL staff learned about good audit practices and the technical competence expectations and soft skills requirements of auditors. Key staff of the Tashkent MQCL accompanied PQM+ to the Andijan MQCL to act as audit observers and strengthen collaboration and coordination mechanisms between the two laboratories. PQM+ staff also followed up with the Andijan Testing Center on the status of recommendations that were previously provided related to the control of nonconforming work and CAPA processes.

In Q3, PQM+ completed a review of the floor plans and designs for the Urgench MQCL. PQM+ provided feedback and recommendations on the laboratory design to comply with the best practices for laboratory design.

This quarter, PQM+ hired and oriented an expert who will develop the capacity of the QMS group to help support the Agency, including the state center, in developing a QMS according to ISO 9001.

In Q2, a presidential decree on development of the pharmaceutical industry was issued with a provision on the introduction of PMS to the country's regulatory system. This is an important milestone as the first time a concept of PMS was introduced; PQM+ advocacy efforts and familiarizing the Agency staff with PMS were crucial. As a result, a working group was established for PMS. In Q3, PQM+ guided the working group to draft regulations for PMS. PQM+ reviewed the regulation and provided feedback for improvement. The regulation is in the final stages of approval, after which PQM+ will help the working group draft the SOP and build capacity of the Agency on PMS and implementation of the PMS approach in the country.

In Q2, PQM+ started working with Purdue University to provide technical assistance to the University of Pharmaceutical Technology at the Tashkent Pharma Park. In Q3, Purdue conducted an electronic survey using Qualtrics to gather information from the Tashkent university and other stakeholders on their priority for important modules. Purdue is using the summary response to design the first course for the Tashkent university.

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

In Q3, PQM+ continued technical assistance to Nobel Pharmsanoat toward prequalification of its TB product levofloxacin. Nobel is working on laboratory scale lots and developed a batch manufacturing report jointly with PQM+. Nobel has also started the stability study. The PQM+

technical advisor conducted an onsite GMP assessment of Nobel on Levofloxacin finished product manufacturing. This assessment is to identify gaps and opportunities toward prequalification of levofloxacin 500mg tablet for compliance with current GMP requirements. PQM+ The technical advisor also followed up on discussion around product development and dossier preparation in CTD for WHO prequalification submission.

In Q2, PQM+ discussed internally the approach for improving GMP compliance of the local pharmaceutical industry in Uzbekistan. The local pharmaceutical industry should be GMP compliant before accession to PIC/S, and training will assist the local industry in understanding GMP requirements and facilitate achievement of GMP compliance. To address this need, PQM+ will identify and hire a company to develop and deliver GMP training materials to the local industry. In Q2, PQM+ also developed a scope of work for potential vendor. In Q3, PQM+ completed the procurement and is finalizing the vendor to train manufacturers on GMP.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Finalize the situational analysis and recommendations to inform the Health Strategy 2030 pharmaceutical and medical devices block.
- Review the SOPs to support strengthening of the medicines registration system and advocacy and approval for EUA.
- 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 work with Tashkent and Andijan MQCLs to bring their CAPA and internal audit in line with WHO PQ requirements.
- Continue technical assistance to the Agency on compliance to QMS 90001:2015.
- Continue technical assistance to the RB-PMS working group to operationalize RB-PMS in Uzbekistan following the approval of the decree.
- Complete course design and initiate the course for the Tashkent pharma university.
- Continue technical assistance to Nobel Pharmsanoat for product development and dossier preparation.
- Initiate GMP training for local Uzbekistan pharmaceutical manufacturers.

COVID-19

Bangladesh

Coordination and Operations

PQM+ is working with the DGDA to strengthen regulation for licensing oxygen manufacturing plants and registration of medical oxygen production. This quarter, with technical support from PQM+, DGDA formed a consultation group for the development of medical oxygen regulation guidelines. The consultation group has 17 members representing regulators, academia, relevant physicians groups, and eight observer manufacturers and distributors. On April 18, PQM+ organized a second workshop with the group to review and assess Bangladesh's regulatory system for medical oxygen. In that workshop, PQM+ shared initial draft guidelines for feedback from the consultation group, chaired by the DGDA director general. Sixteen participants (14 males, two females) joined the workshop and provided inputs on the initial draft of medical oxygen guidelines. The following month, PQM+ organized the third consultation workshop and developed the final draft guideline for the regulation of medical oxygen in Bangladesh. PQM+ will work to finalize the guideline DGDA's working committee for medical oxygen, organize a dissemination workshop among relevant stakeholders, and upload it to DGDA's website.

PQM+ is also working to establish and strengthen the relationship among key stakeholders monitoring the roll-out of COVID-19 vaccines. Key stakeholders include the Ministry of Health and Family Welfare, DGDA, the Expanded Program on Immunization (EPI), Institute of Epidemiology Disease Control and Research (IEDCR), Vaccine Quality Assurance Committee, adverse events following immunization (AEFI) expert review committee, National Immunization Technical Advisory Group (NITAG), and development partners (e.g., WHO, UNICEF, World Bank, USAID). On June 8, DGDA hosted a vaccine quality assurance committee meeting on "Risk-Based Post-Marketing Surveillance of COVID -19 Vaccines." At this meeting, the committee members emphasized the need for DGDA to implement RB-PMS of vaccines in cooperation with PQM+. At the meeting, PQM+ presented the context and importance of vaccine RB-PMS, as well as two critical activities related to country capacity building for the safety surveillance of vaccines. These are pharmacovigilance (PV) and testing for the identity and potency of vaccines as a medical product.

PQM+ also noted that for the Vaccine Quality Assurance Committee to oversee the implementation of RB-PMS, it will need to form a technical working group. RB-PMS needs to be implemented in collaboration with the Directorate General of Health Services, EPI, IEDCR, WHO and UNICEF. Fourteen participants (10 males; four females) attended the meeting from DGDA, the Bangladesh Medical Research Council (BMRC), IEDCR, EPI, the National Control Laboratory (NCL), and PQM+. As an outcome of the meeting, participants agreed on the necessity and importance of implementing RB-PMS of COVID-19 vaccines. From this meeting, the Vaccine Quality Assurance Committee decided to form the technical working group under the DGDA Market Control Department (MC) with representation from EPI, IEDCR, WHO, UNICEF, GAVI, PQM+, the MC & PV Dept. of DGDA and BMRC to implement RB-PMS. This TWG will be responsible for reviewing the RB-PMS implementation plan and identifying roles and responsibilities of key stakeholders.

Immunization Readiness and Implementation

PQM+ is supporting DGDA in vaccine testing and RB-PMS. Based on the feedback from a workshop in February, PQM+ updated two draft documents to implement RB-PMS for COVID-19 vaccines: (1) Guideline on Risk-Based Post-Marketing Surveillance of Vaccines in Bangladesh and (2) RB-PMS Sampling and Testing Protocol for COVID-19 Vaccines 2021 – Round 1.

Laboratory Systems

PQM+ is working with DGDA's National Control Laboratory (NCL) to establish a personal protective equipment (PPE) testing laboratory to ensure quality-assured PPE. PQM+ procured and set up two items of testing equipment [*I. Medical Mask Gas Exchange Pressure Difference Tester and II. Particulate filtration efficiency (PFE) tester*] for the NCL's new premises for PPE testing. On June 14, PQM+ organized a hands-on training on how to use the new PPE equipment and conduct tests with NCL analysts. Seventeen participants (11 males, six females) attended the training – 12 from NCL (eight males, four females) and five from PQM+ (three males, two females).

PQM+ is also supporting DGDA to build the capacity of the NCL in vaccine testing. In April, PQM+ conducted a gap analysis to understand the NCL's vaccine testing capacity. The key areas of the analysis were: cell culture laboratory facility, cleanliness, cell culture-related instruments, and qualification status. This quarter, PQM+ received three pieces of equipment it procured for the NCL's Vaccine Laboratory, including the carbon dioxide cylinder, liquid nitrogen tank, and hemocytometer. The remaining piece of equipment is expected by July. After the equipment arrived, PQM+ developed an equipment qualification/calibration guideline for NCL. PQM+ also reviewed and prepared the following testing methods for the Covidshield vaccine:

- Virus content determination and Adenoviral vector backbone identity by qPCR in ChAdOx1nCoV-19 samples.
- Virus content by infectivity assay in ChAdOx1nCoV-19 samples.
- Spectrophotometric analysis for determination of adenovirus particle concentration using DNA and Protein ratio
- Extractable volume of COVID-19 vaccine
- Determination of the ratio of VP in ChAdOx1nCoV-19 samples
- Container or closure integrity test

This quarter, PQM+ also worked on drafting the assessment report of private laboratories' vaccine testing capacity and the NCL plan for building laboratory testing capacity which will be finalized during the next quarter.

Burkina Faso

Immunization Readiness and Implementation

PQM+ is working to support the MRA *Autorité National de Regulation Pharmaceutique* (ANRP) to strengthen its AEFI surveillance system and build its capacity to grant regulatory approval for COVID-19 vaccines in alignment with the country's National Vaccine Deployment Plan. Following the AEFI training of trainers (ToT) session (organized by PQM+ in Q2) for 26 health

care workers from the *Direction de la Prévention par la Vaccination* (DPV) and the national immunization program, PQM+ supported the cascade of this training to other health care workers in Burkina Faso's Central and South-Central regions. While PQM+ oversaw the trainings and provided the needed logistics, staff from DPV and ANRP delivered these cascaded trainings. In the Central region, the cascaded training was delivered by three health care professionals (two from the regional health directorate and one from ANRP). The topics for the training were: general information about COVID-19 vaccines, pharmacovigilance of COVID-19 vaccines, immunization errors, notification of adverse reactions, AEFI notification circuit and tools in Burkina Faso, serious AEFI investigation and ended with a practical exercise filling in notification tools. Thirty-four (34) health care professionals participated (13 female and 21 male) at the *Direction Régionale de la Santé du Centre* (Central Regional Health Directorate) in Ouagadougou. In the South-Central region, the cascaded training covered the same topics and was also facilitated by health care professionals from ANRP and DPV trained during the ToT session. Twenty-two (22) health care professionals (four female, 18 male) received training. The session improved participants' knowledge about AEFIs and strengthened their capacity on AEFI notifications and the use of notification tools. This is expected to lead to improvement in AEFI notifications for COVID-19 vaccines being administered in Burkina Faso.

PQM+ is also working with ANRP to build its capacity in emergency use authorization (EUA). Based on the findings of the Q2 training needs assessment on EUA, PQM+ developed new training curriculum which was used to train ANRP staff on EUA. The training, which took place in June, enabled ANRP regulatory personnel to determine the importance of reliable EUA mandates and flexible regulatory environment with the required laws, legislations, and regulations to establish EUA systems. It built their capacity to analyze Good Review Practices for major key categories of health product for emergency use: vaccines, health products related to the emergency situations, and diagnostics and devices used to protect or diagnose diseases and finally enabled them to be able to identify effective post EUA follow-up on supplementary information required for full authorization. 23 participants attended the training [9 Female: 14 Male] from ANRP, LNSP and other departments in the ministry of health such as *Direction Générale de l'Accès aux Produits de Santé* (DGAP). The trainees, at the end of the training, developed a roadmap that would lead to EUA approval procedures in-country and scheduled a working session to develop this EUA procedure for Burkina Faso.

PQM+ is also supporting ANRP to improve its lot release function, for which there is currently no procedure in place. This quarter, PQM+ convened two virtual sessions to: (1) guide ANRP on identifying a strategy to adopt for conducting lot release based on their current regulatory context and (2) to train them on lot summary protocols. For the lot summary protocol training, seven ANRP, LNSP, and DPV technical staff (five female and two male) received training. Participants gained knowledge on how to review lot summary protocols for individual lots of vaccines to be imported into the country.

Laboratory Systems

PQM+ is working to build the capacity of the national quality control lab, *Laboratoire National de Santé Publique* (LNSP), to test COVID-19 vaccines. This quarter, PQM+ received the quotation from the lab for the 25 items of equipment and 25 types of consumables it needs to test vaccines, which exceeded $600,000. Given limited funds for this procurement, PQM+ worked with LNSP to prioritize this procurement in alignment with the available budget. As a result, 12 items of equipment and 26 types of consumables were prioritized for procurement. PQM+ submitted the approval request for seven items of equipment requiring prior approval to USAID.

Ethiopia

Immunization Readiness and Implementation

PQM+ is supporting EFDA to conduct risk-based inspection of cold chain facilities across the country. In Q2, PQM+ completed the assessment of Ethiopia's cold chain system for COVID-19 vaccine products and generated the report. Once the report was finalized, in Q3, PQM+ organized a dissemination workshop with all relevant stakeholders including EFDA, USAID, regional regulatory bodies, and the central procurement agencies at which results of the assessment were communicated, discussed, and participants provided their inputs to the report. A total of 31 participants (one female and 30 male) attended the dissemination workshop. After the workshop, EFDA communicated the results of the assessment to stakeholders for relevant actions. Some of these actions include trainings for health care facilities on immunization handling and storage, plans for the Ethiopian Pharmaceuticals Supply Agency to conduct audits at all immunization sites, and support from the Expanded Program on Immunization to health facilities and immunization sites. PQM+ is also supporting EFDA's Market Surveillance Directorate to map the overall circulation of substandard and falsified vaccines in Ethiopia. In May, PQM+ provided logistical support for a training hosted by EFDA and Interpol on basic principles and techniques of conducting market surveillance through its intelligent approach for of 59 (six female and 53 male) inspectors. Based on this training, inspectors will be able to assess the overall marketing of the COVID-19 vaccines in the country and provide evidence of illegal marketing and distribution to the regulatory body for evidence-based decision making. The inspectors were deployed to conduct the surveillance aimed at identifying the illegal marketing and distribution of COVID-19 vaccines in the country. After the surveillance, the team developed a surveillance report based on which EFDA started taking relevant regulatory measures.

Surveillance, Case Finding, Rapid Response Teams, Case Investigation, and Contact Tracing

PQM+ is working to strengthen product defect reporting through Adverse Drug Reaction (ADR) reports. Recent data gathered from EFDA indicates that the monitoring of the safety and quality of COVID-19 vaccines is inadequate. The practice of reporting AEFIs through the passive safety reporting system is still very low, which can potentially overlook serious AEFIs. Because of this, the number and type of AEFI reports received, investigated, and analyzed are small when compared to the number of people that are vaccinated. In the EFDA report, one of the interesting results reported during the last six months was the "dramatic improvement in spontaneous reporting of AEFIs" during the second-round vaccination (9,046) in comparison to that of the first round (1,493). But the causality assessment /investigation rates are still low and out of 29,416,307 doses administered as of June, only 711 AEFI reports were received through the passive safety reporting system as of June 25. More strikingly, before PQM+ support, causality analysis was performed for only eight of the cases from the total of 36 serious AEFIs. This indicated the need to build capacity of the national pharmacovigilance system to be able to reactivate the passive safety reporting system and strengthen casualty analysis. Because of the absence of causality analysis for the remaining serious cases, cause and effect relationship couldn't be established. To continue to improve EFDA's vaccine reporting, in Q3, PQM+ worked with EFDA and WHO to train the National Safety Advisory Committee on advanced causality assessment to review COVID-19 vaccine safety data. The training was conducted from May 25 to May 27 for 23 members (five female, 18 male). Training topics included AEFI basic concepts, AEFI surveillance in Ethiopia, AEFI reporting and recording, investigation and adverse events

following immunization causality assessment- case definition and case studies, and a demonstration of WHO's Causality Assessment electronic tool. After the training, the committee members were able to perform causality assessment on a real case of serious AEFI using the demonstrated electronic causality assessment tool. This quarter, PQM+ also supported the National Safety Advisory Committee to perform causality analyses for two serious adverse events, bringing the total to 32 causality analyses performed with PQM+ support.

Ghana

Immunization Readiness and Implementation

PQM+ is supporting the Ghana Food and Drug Authority (Ghana FDA) with its cohort event monitoring (CEM) of COVID-19 vaccine distribution, expected to last eight months. A total of approximately 10,000 participants are expected to be enrolled and followed on predetermined days post the first and second doses of the COVID-19 vaccine. As of June 21, Ghana had 164,612 confirmed cases of COVID-19, including 1,448 deaths, with 16,752,032 doses of the five COVID-19 vaccines (a combination of the AstraZeneca, Pfizer, Moderna, Johnson and Johnson and Sputnik V) administered in Ghana.[6]

The joint COVID-19 vaccine safety review committee (JCVSRC) reviewed all safety reports received from the vaccinations in Ghana as well as reports from international sources and found that generally, reports on side effects received in Ghana are rare and consistent with what is expected from the vaccinations. The commonly reported side effects continue to include headache, fever, chills, pain at injection site and body pains, are usually minor and resolved within a day or two.

In Q3, PQM+ continued to support the enrollment of CEM study participants and the follow-up of enrolled participants vaccinated with Pfizer and Moderna vaccines from April to June. A total of about 7,146 participants out of the target of 10,000 have been enrolled since March 2021. Close to 5,000 of these participants were enrolled with support from PQM+ since November 2021. A reduced vaccine uptake has been noted in Ghana. The country has attained only 21.4 percent fully vaccinated of the country's mid-2022 target of 70 percent. This impacted enrollment in Q2, with most CEM enrollment resulting from national vaccination campaigns. The breakdown of CEM enrollments is below:

- Ashanti Region: 599 participants
- Central Region: 746 participants
- Volta Region: 423 participants
- Bono East Region: 650 participants
- Northern Region: 1000 participants
- Greater Accra (Mamprobi Site): 968 participants
- Greater Accra (Tema General Hospital Site): 732 participants
- Total Enrolled: 7,418 participants (74.2% of target)
- Total Enrolled with direct PQM+ Support: 5,118 participants

[6] https://data.covid19taskforce.com/data/countries/Ghana; http://www.ghs.gov.gh/covid19

Kazakhstan

Immunization Readiness and Implementation

PQM+ is supporting the National Center for Expertise for Medicines, Medical Devices, and Medical Equipment (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. Under this activity, PQM+ has been tasked with conducting a situational analysis of the pharmacovigilance (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 ML3, specifically in its vigilance functions. In the previous quarter, PQM+ completed the situational analysis of the PV system in Kazakhstan. The report highlighted gaps, specifically the need for PV processes to be organized between the NCEM and the Committee for Medical and Pharmaceutical Control (the Committee), NCEM staff training needs, and SOPs that need to be developed. In Q3, PQM+ translated the situational analysis report to Russian and disseminated it to stakeholders.

In Q2, PQM+, in partnership with the WHO Collaborating Center for Pharmacovigilance based in Morocco, provided a virtual training on the PV process to staff from NCEM's PV department to familiarize them on implementation and management of a PV system. In Q3, from May 11 to 13, PQM+ held a hybrid workshop on the development of a three-year PV roadmap for Kazakhstan. Participants from the Committee, NCEM, and representatives from the National Immunization Program (NIP) discussed the development of a PV system in the country. The WHO Collaborating Center facilitated the workshop virtually. A total of 23 participants, including representatives of the NIP, attended the seminar. The outcome of this workshop was a draft three-year PV roadmap for Kazakhstan.

In June, the WHO Collaborating Center team visited Nur-Sultan and held an in-person workshop to finalize the three-year PV roadmap and develop an action plan as part of the roadmap. During the workshop, the 11 participants from NCEM discussed the importance of PV developing regulation; implementing a human resources analysis of the national PV system; and integrating PV in national health programs, including the immunization program. Integration of PV into national health programs would include pathways for reporting; validation of reporting forms; adverse event reporting forms, and PV curriculum for staff at the national, regional, and local level. These topics were included into the roadmap. Currently, PQM+ is finalizing the three-year PV roadmap based on inputs from the workshop.

PQM+ is also providing technical assistance to NCEM in strengthening its lot release systems, which allow for the continuous quality and safety monitoring of biological products through a regulatory release system on a lot-by-lot basis. This is a relatively new area for NCEM, as it has not been assessed by the WHO team as a part of the WHO GBT process. In Q2, PQM+ completed the review of several Kazakhstan specific lot release documents and identified the need for lot release legal provisions, regulations, and guidelines. PQM+ suggested action items such as: review of WHO guidance document on vaccines lot release, development of detailed lot release procedure, development of criteria for recognition of results from external testing laboratories and others.

In Q3, based on PQM+'s recommendations, NCEM continued its revision of Kazakhstan's Order 282 on quality assessment of medicines and medical devices. The revised Order will include detailed information on quality assessment of vaccines, which is directly related to the lot release function. PQM+ also held several meetings with NCEM staff to discuss lot release

function indicators and provided specific recommendations for improvement. WHO is expecting all of NCEM's documents related to this function by the end of July so it can prepare for the assessment of NCEM this December.

In Q3, PQM+ also delivered an online training on lot summary protocol review for 36 staff from NCEM, the Committee for Medical and Pharmaceutical Control (CMPhC), the Ministry of Health of the Republic of Kazakhstan, and representatives of local vaccine manufacturers from June 6 to 8 to familiarize participants on how to conduct a summary protocol review for the continuous quality and safety monitoring of vaccines through a regulatory release system on a lot-by-lot basis.

In Q3, PQM+ also initiated technical assistance to NCEM on vaccine testing capacity building. PQM+ provided NCEM different options for organizing vaccine testing required for lot release in Kazakhstan. These options include developing the biosafety level three capacity at the Almaty laboratory in Kazakhstan; contracting another private laboratory in Kazakhstan; or sending this outside the country. These options are currently being discussed within NCEM. PQM+ also met with Almaty laboratory staff for discussion of laboratory testing indicators included in the WHO GBT. A PQM+ expert will travel to Kazakhstan in July to conduct an onsite assessment of the Almaty lab's testing center (TC) and another potential lab for vaccine testing capacity. Following the travel, PQM+ will identify gaps and action items in relation to the TC's infrastructure (facilities, equipment, personnel) and vaccine testing to advise on the possible vaccine-testing strategy for the future.

Pakistan

Coordination and Operations

PQM+ is supporting the Drug Regulatory Authority of Pakistan (DRAP) to strengthen its COVID-19 vaccine vigilance. This quarter, PQM+ finalized the guidance documents for emergency use authorization (EUA) holders on adverse events following immunization (AEFI) and for risk management plans, based on feedback DRAP provided the previous quarter. PQM+ shared the finalized guidance documents with DRAP, who will share the documents with other stakeholders, such as vaccine manufacturers and EUA holders. The finalized guidance document on AEFI reporting will enhance EUA holders' capacity to ensure quality reporting and enable DRAP to effectively monitor COVID-19 vaccine EUA holders. The guidance document on risk-management plans will enable COVID-19 vaccines EUA holders to fulfill their legal responsibility, as per best international practices, to highlight and report any risks associated with vaccines and submit their risk management plan, including vaccine safety data, to DRAP in order to protect at-risk/vulnerable individuals.

PQM+ is also working with DRAP to formally establish a Pharmacovigilance Risk Assessment Expert Committee (PRAEC) at DRAP for strengthening AEFI reporting for COVID-19 vaccines. In April, PQM+ had a formal consultation with DRAP and proposed the establishment of the PRAEC. DRAP, after thorough deliberation with their technical team, has codified PRAEC in the rules and included the committee composition and roles and responsibilities as suggested by PQM+. This committee will play a critical role in keeping EUA products safe by evaluating the safety signals and quality issues on a priority basis and sharing recommendations with stakeholders on safety and quality matters.

Finally, PQM+ is working to ensure that DRAP collects quality AEFI data and is able to react from it in a timely manner. PQM+ developed a guidance document and SOP for AEFI handling

and management. The routine surveillance of AEFI is an important tool to monitor vaccine safety and maintain public confidence in vaccines. The guidance document will enable DRAP to enhance the monitoring of pre-specified adverse events of special interest (AESI) for COVID-19 vaccines in the context of overall AEFI surveillance. Regarding the SOP, it lays out the process for the receipt, handling, and reporting of AEFI at the Pakistan National Pharmacovigilance Centre (PNPC) via the National Pharmacovigilance System. This SOP will help DRAP effectively monitor and handle AEFI cases following COVID-19 vaccination. Both the documents will strengthen the system of COVID-19 vaccine vigilance reporting and AEFI surveillance and will help to harmonize the AEFI data management and evaluation using standardized tools. They will also help DRAP preserve the functionality of its AEFI surveillance system at all levels.

PQM+ also held a meeting with DRAP in April, to discuss the development of an AEFI reporting dashboard in DRAP's Pakistan Integrated Regulatory Information Management System (PIRIMS) and the development of an interface for facilitating the digital transfer of AEFI data in VigiFlow – an international, web-based PV management system. As an outcome of this meeting, DRAP coordinated with Uppsala Monitoring Center (UMC), the owner of VigiFlow, and now plans to integrate VigiFlow with the National Immunization Management System (NIMS) in the last quarter of 2022.

In the meantime, the PQM+ team hired an Information Technology (IT) consultant for the development of an online application and portal in DRAP's PIRIMS for the digital transfer of AEFI data and AEFI reporting. DRAP has shared the User Requirement Specifications (URS) and discussed them with PQM+. The IT consultant is working with DRAP's Pharmacy Services Division, which is responsible for pharmacovigilance activities. This interface will help DRAP to digitally transfer AEFI data from NIMS to VigiFlow which would enhance the reporting of accurate AEFI data, ultimately saving time wasted in manual entries.

In parallel to creating the online portal, PQM+ conducted an extensive two-day training from April 14 to 15 for DRAP's core pharmacovigilance (PV) staff on AEFI data collection and analysis. The topics discussed during the training session included an Overview of the PV Process, the Anatomical Therapeutic Chemical (ATC)[7] classification system, VigiFlow: data entry and extraction, signal detection in pharmacovigilance, qualitative and quantitative detection and management, and the pharmacovigilance reports. The training facilitators apprised the participants that pharmacovigilance is a science that involves data collection, data validation and analysis, database feeding/data entry, signal detection and validation, risk quantification and alert generation, root cause analysis, and risk minimization actions. The training was attended by 13 participants (2 female, 11 male) from DRAP's Biological Evaluation and Research & Pharmacy Services divisions. This training built the capacity of DRAP staff and will help DRAP to analyze 88,000 AEFI reports entered in VigiFlow. The training also enhanced the participants' knowledge of the basics of ATC classification and its importance in pharmacovigilance.

Immunization Readiness and Implementation

In collaboration with national stakeholders in Pakistan, PQM+ is working to develop a National Action Plan for adverse events following immunization (AEFI) surveillance for COVID-19

[7] In the Anatomical Therapeutic Chemical (ATC) classification system, the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological, and chemical properties. Drugs are classified in groups at five levels.

vaccines. In Q3, the Federal Directorate of Immunization (FDI), in coordination with PQM+, sought the feedback of the provinces on the draft AEFI guidelines and National Action Plan. After incorporating the feedback from provinces in both documents, PQM+ shared the documents with the Ministry of National Health Services Regulations and Coordination (MoNHSR&C) for approval and endorsement, which was received in June. After the necessary formatting, PQM+ sent the final versions to FDI for dissemination. The implementation of these guidelines will lead to an increase in the overall vaccine safety in Pakistan with efficient and real-time AEFI reporting. This is an immense accomplishment for all involved as these national AEFI Guidelines and Action Plan formally define the roles and responsibilities of key AEFI stakeholders and improve vaccine vigilance and safety ultimately enhancing immunization efforts in Pakistan.

PQM+ is also working with stakeholders in Pakistani provinces to ensure private sector healthcare facilities are engaged in vaccine vigilance and AEFI surveillance, including establishing or revitalizing AEFI Committees. As of Q3, all Provincial AEFI Committees have been established, however, they are struggling to operationalize and play a larger role in COVID-19 vaccine data review at the provincial level. During the quarter, PQM+ worked with the World Health Organization (WHO) to strengthen the Provincial AEFI Committees for COVID-19 vaccination, included clinical experts in the committees, and revise their terms of reference. The final version of the terms has been shared with the respective provinces. The objective of revising the terms is to harmonize the operations of Provincial AEFI Committees in all provinces. As a result of the revised terms of reference, reporting of AEFI cases is expected to increase, and all stakeholders will be responsible to respond to AEFI cases. In addition to terms of reference, PQM+ developed comprehensive SOPs for coordination mechanisms amongst key stakeholders of AEFI surveillance systems at the provincial level, such as the Ministry of Health, FDI, the DRAP, COVID-19 vaccine EUA holders, provincial healthcare commissions, and healthcare facilities. Implementation of these SOPs will help to establish/reinforce vaccine safety surveillance systems at the provincial level and improve coordination with provincial AEFI committees.

In Q3, PQM+ held a hybrid training workshop on AEFI investigation and causality assessment for the Provincial AEFI Investigation Committees of four provinces (Punjab, Sindh, Khyber Pakhtunkhwa, and Baluchistan) on May 30-31. PQM+ presented on general principles of AEFI investigation and causality assessment; investigation of adverse events (AE) clusters; investigation of specific AE clusters following COVID-19 immunization; WHO key resources for AEFI investigation and AEFI causality assessment; and WHO methods for AEFI causality assessment. PQM+ also demonstrated causality assessment software application during the workshop. The training was attended by 41 participants (in person: 34/virtual: seven; two females/39 males) from all four provincial AEFI committees including participants from EPI and UNICEF. The Director General of Health Services in Sindh also participated in the training. The participants shared excellent remarks regarding the training and had good interactive sessions on both training days.

The PQM+ team also held a training on AEFI reporting for COVID-19 vaccines on June 7 in Islamabad for key stakeholders from Gilgit-Baltistan (GB), Islamabad Capital Territory (ICT), and Azad Jammu and Kashmir (AJK). The training was well attended by 32 participants (seven females, 25 males). For this training session, PQM+ developed a draft desk guide for AEFI reporting (in line with the National AEFI Guidelines) for private healthcare providers. This AEFI desk guide will act as a reference for the public and private field staff who are involved in AEFI reporting. PQM+ facilitated the training along with a WHO representative. The participants learned that it is crucial to report any event of any kind that has occurred at our institutions through a proper channel, and it should be implemented in institutions. At the end of the training

session, all participants were motivated to report on AEFI and were eager to have the reporting system in place at their organizations. Also, the participants were willing to train their institutional staff on the AEFI guidelines.

Uzbekistan

Surveillance, Case Finding, Rapid Response Teams, Case Investigation, and Contact Tracing

PQM+ is supporting the Agency in strengthening pharmacovigilance and vaccine surveillance systems. PQM+ is working with the Services for Sanitary and Epidemiological Well-being (SSEW) which oversees the National Immunization Program (NIP), the Agency (Uzbekistan's medicines regulatory authority), and its State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment (the State Center) and other national and international stakeholders. In the previous quarters, PQM+ initiated collaboration with the WHO Collaborating Center (RCC) in Morocco. PQM+ also established connections with the NIP, with whom PQM+ had not worked before. PQM+ with the RCC introduced several overview and training sessions on pharmacovigilance and vaccine safety surveillance systems for the Agency as well as the NIP. There was also no designated group within the Agency on PV, so PQM+ advocated for the Agency to establish a PV department. PQM+ completed the review of the national standard of the good pharmacovigilance practice (GVP) developed by the Agency and provided feedback with recommendations on improvement of the GVP standard.

One of the challenges identified during the initial interactions with the Agency and NIP was that there was no coordination and collaboration on vaccine safety surveillance activities. In addition, there was no commitment from either side to initiate this kind of collaboration. To initiate a dialogue between the two sides and to expose them to the best practices in terms of vaccines safety surveillance and collaboration, PQM+ organized a study tour to the WHO Collaborating Center in Morocco (RCC) from June 1 to 8 for five participants (two from the Agency, two from NIP, and one from PQM+). Uzbekistan participants visited the Moroccan immunization program and the Moroccan medicines regulatory authority to discuss and learn from the best practices of collaborative work on vaccine safety surveillance. The participants also attended a training hosted by the RCC on general principles on PV and vaccine safety surveillance. The Uzbekistan team also prepared and delivered an overview of the PV and immunization program work in Uzbekistan. RCC facilitated a discussion between the PV and NIP teams to develop an implementation plan on establishing interconnection between the PV and NIP in Uzbekistan. This study tour and related work is important because it is a step toward collaboration between the two organizations (Agency and the NIP) who have not worked together to date. This builds the ground for work on AEFI that requires participation from both agencies.

The RCC team of experts visited Uzbekistan from June 20-22. They met with the leadership from the Agency and the immunization program. PQM+ organized a workshop between the Agency's PV team and NIP. During the workshop, PQM+, the Agency, and NIP developed the first draft of responsibilities for both parties on identifying and analyzing AEFIs. As a next step, both parties will formalize and approve the roles and responsibilities in vaccines safety surveillance.

As a result of PQM+ advocacy, the Agency director signed the Order of MOH #102 on June 8 approving a pharmacovigilance department with six staff units. The new department will sit within the State Center. The Cabinet of Ministers also approved an updated resolution that approves establishing a training center for healthcare providers on addressing and identification

of AEFIs within the Immunization Program. These very important decisions will help in strengthening the vaccines safety system in Uzbekistan.

Progress by Health Elements

Maternal and Child Health (MCH)

PQM+'s support to USAID's directed core MCH work focuses on assisting medicine regulatory authorities and manufacturers to improve their systems. PQM+ also supports global leadership efforts in collaboration with other MCH partners to continue to advance USAID's, global, and country MCH agendas and to increase access to quality-assured life-saving 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

In Q4, PQM+ replaced the development of an operational guidance document on quality test requirements for priority MNCH medical devices activity given the limited information available on the landscape of medical devices regulation and testing in LMICs. This activity has been replaced with the development of a product information report (PIR) for gentamicin injection and related job aids to support product registration and inspection functions of the national MRA. PQM+ began the subaward process with Purdue University to develop the PIR.

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

PQM+ finalized a technical brief describing impurities in chlorhexidine and how manufacturers can address them during production. The brief's goal is to share information with local manufacturers to increase the supply of quality-assured sources of the product. The brief was submitted for USAID review and the final document is being translated into French. Upon completion, PQM+ will share the brief with PQM+ in Pakistan, Nepal, and Bangladesh to disseminate to their local manufacturing associations and make it available online.

PQM+ met with USAID and Global Health Supply Chain – Procurement and Supply Management (GHSC-PSM) in late April to discuss plans for how both programs will support the Every Newborn Action Plan (ENAP). The first meeting with ENAP took place June 2, at which PQM+ agreed to join both the medicines and medical device sub-working groups.

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

PQM+ collaborated with MTaPS and GHSC-PSM to organize a series of consultative meetings to identify actions to increase access to and use of quality-assured medicines for newborn and child health. The consultative meetings were convened by the commodities subgroup of the Child Health Task Force, co-chaired by UNICEF and USAID, to validate evidence and prioritize solutions to address bottlenecks. The meetings took place May 10, 17, and 24. PQM+ led the second meeting on the lack of quality pediatric child health products. PQM+, MTaPS, and GHSC-PSM are now developing the call-to-action paper.

PQM+ began development of an e-learning course on MNCH medical device quality assurance for manufacturers and regulators. This online course is intended to describe basic regulatory frameworks and important QA requirements and concepts to inform programmatic and funding

decisions to advance the delivery and safe use of MNCH devices. PQM+ shared the course outline for USAID review. Once finalized this course will be hosted on the USP learning management system and linked to the GHeL platform and USAID University.

Priority Activities for Next Quarter

In Q3, PQM+ plans to:

- Engage Purdue University via a subaward to develop a gentamicin injection PIR.
- Finalize work on the call-to-action paper with MTaPS and GHSC-PSM.
- Translate the technical brief on the importance of 4-chloroaniline (4CA) impurities in chlorhexidine into French.
- Continue developing the online course on quality assurance of medical devices focusing on MNCH.

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 NTDs 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 patients in need.

Progress This Quarter

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

To increase the availability of quality assured NTD medicines, PQM+ continues to support manufacturers with direct technical assistance and to raise awareness of the WHO prequalification program. This quarter, PQM+ continued to support two manufacturers toward WHO PQ for two NTD products: albendazole 400mg tablets and praziquantel 600mg tablets.

- For albendazole, PQM+ submitted additional data to WHO on the dossier as requested; it is at the final stage of acceptance. The manufacturer's WHO GMP inspection is scheduled for mid-August and PQM+ is preparing for a mock GMP assessment from July 4 to 8 as part of the technical support milestone toward full prequalification. To prepare for the mock audit, PQM+ submitted the India Mission concurrence request to USAID and is awaiting approval.
- For praziquantel, WHO issued a conditional PQ approval in April 2021 for the product pending onsite inspection and repeat BE study. This quarter, PQM+ completed the subaward for partial financial support to the manufacturer to cover the cost of the BE study. PQM+ continues to work with the CRO to finalize the BE study protocol, after which it will be submitted to the independent ethics committee for approval.

PQM+ attended the West Africa Pharma Healthcare Show, an international medical, pharmaceutical, and health care industry trade fair in Ghana, from April 27 to 29. PQM+ organized a booth and presented "PQM+ Advancing Access to Quality-Assured Health Products." The presentation highlighted the program's objectives, impact, the NTD landscape analysis and key findings, the EOI, and an upcoming WHO PQ advocacy workshop in Kenya. PQM+ shared the trip report with USAID and will soon respond to USAID's comments.

PQM+ continued development and enhancement efforts of the publicly available NTD Medicines Information Dashboard and database (NTD | MID) for regulators, manufacturers, procurement agencies, suppliers, donor communities, and other interested parties in planning for procurement, supply, and use of NTD medical products. PQM+ also completed adding approved NTD finished pharmaceutical product data from six stringent regulatory authorities (Ireland, Malta, Latvia, Netherlands, Norway, and Portugal). PQM+ began procurement to engage a contractor to make the tool Section 508 compliant and continues to test the tool and troubleshoot issues as they arise. PQM+ also gave an NTD | MID dashboard demo to Expanded Special Project for Elimination of Neglected Tropical Diseases (ESPEN).

PQM+ continued efforts to promote and disseminate the repackaged GMP e-learning course. In Q3, PQM+ began drafting the GMP course information handout and dissemination strategy to promote the course uptake.

Priority Activities for Next Quarter

In Q4, PQM+ plans to:

- Continue ongoing technical assistance to supported manufacturers until full WHO PQ is attained.
    - For albendazole, PQM+ will perform a GMP mock audit and address CAPAs as needed.
    - For praziquantel, PQM+ plans to finalize the BE study.
- Inform the selected manufacturers of PQM+ technical support following the review of the EOI applications.
- 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 pipeline of new TB medicines and regimens are in varying stages of clinical research. In this evolving situation, it is important for national MRAs to stay engaged and ensure timely review and approval of new TB medicines to enable access to these lifesaving products. In recent years, national MRAs in some countries occasionally have faced challenges to timely reviews and approvals 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 (FDA) to organize a virtual workshop for representatives of MRAs and manufacturers from high-burden TB countries, at which FDA will share experiences on the regulatory review of new TB medicines. Previously, PQM+ identified and submitted topics of interest and draft agenda for the workshop to the FDA. In Q2, PQM+ continued to meet with the FDA to prepare for a webinar planned for August 16 to 18. PQM+ is broadening the agenda to include regulatory experience and learnings beyond TB medicines. FDA and PQM+ are collaborating to develop and release a promotional video for the webinar to generate wider interest and a larger audience for the webinar. PQM+ submitted a draft agenda of the webinar with preliminary speakers and worked with FDA to finalize the agency's subject matter experts for the webinar. PQM+ met with the subject matter experts and addressed their questions related to the webinar topic. PQM+ is also working with FDA and USAID to identify keynote speakers for the event.

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

In Q2, 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 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 Schazoo has been submitted to WHO, which accepted it for full assessment. In Q1, PQM+ provided technical assistance to Schazoo in responding to the first-round additional data requested and comments from WHO. In Q2 and Q3, PQM+ continued working with Schazoo and submitted the pending dossier question to WHO on March 11. Further additional data was clarified in April and the dossier is now at the final stage of approval. As part of full prequalification, PQM+ has been planning to conduct an onsite mock GMP assessment for Schazoo in Q3 as part of the site preparation for WHO inspection. This trip had to be postponed due to the unstable political situation in Pakistan. The trip is now planned for Q4, during the last week of July. Schazoo is still waiting for an inspection date from WHO between September 10 and 23.

Another Pakistani manufacturer, Pacific Pharmaceutical, has submitted an updated dossier along with stability studies of the 4FDC product. PQM+ has reviewed the updated dossier and met with Pacific, which is correcting missing information and will submit the updated dossier along with the stability data for review by PQM+ prior to submission to WHO. PQM+ will continue to provide technical assistance through full prequalification of the product by Pacific.

During Q3, PQM+ collaborated with USP's laboratory team to complete validation of a liquid chromatography with tandem mass spectrometry (LC-MS/MS) test method for nitrosamines impurities in rifapentine and rifampicin TB medicines. The USP laboratory has finalized both the development and validation reports.

In Q3, PQM+ provided ongoing technical guidance and monitoring of the Virginia Commonwealth University (VCU) subaward for phase 2 on optimization, scale-up, and integration of the synthesis process on developing an alternative route to produce API for a priority TB product. During the laboratory phase, in PY2 Q4, a synthesis route was identified and demonstrated to qualify for the target continuous manufacturing process. In Q3, PQM+ was looking for a manufacturer for technology transfer. During Q4, PQM+ aims to evaluate, recommend, and select a manufacturer for technology transfer.

In Q2, PQM+ signed a non-disclosure agreement with a pharmaceutical manufacturer in Africa, which currently produces two TB APIs. Based on the initial review, the manufacturer has the potential to implement innovative approaches for manufacturing TB APIs. Under the current Core TB workplan, PQM+ plans to provide technical assistance to the manufacturer to work toward prequalification of the TB API product, which will be an important step toward diversification of the global supply of TB APIs. In Q3, PQM+ completed a visit to the manufacturer to assess facilities, personnel, equipment for batch and continuous manufacturing, and volume capacity, as well as answer questions and discuss the isoniazid technical assistance status and more.

A BE study report is a critical document used as evidence to justify the interchangeability and effectiveness between two products in the dossier submitted for marketing authorization. The Regional Bioequivalence Centre Sh. Co. (RBEC) in Ethiopia is a public-private partnership organization established in 2012 to serve as a CRO for East African pharmaceutical manufacturers to improve the quality and effectiveness of essential medicines. Through the clinical and bio-analytical laboratory services provided by RBEC, the center could play a fundamental role in the region to fulfill the continent's unmet needs for the supply of safe, effective, and quality-assured medicines that are accessible to people of the continent. PQM+ will work with RBEC through a TWG to identify bottlenecks that hinder RBEC from delivering BE studies for Ethiopia and the rest of the continent. In Q3, PQM+ facilitated the first TWG meeting and with RBEC laid out a plan of action for the assessment, identification of gaps, and action planning to address the gaps. The TWG plans to conduct face-to-face consultative meetings in the presence of subject matter experts from the ACDIMA BioCenter for Bioequivalence and Pharmaceutical Studies in Jordan to share experience addressing the challenges facing RBEC. The TWG is working on the agenda and assessment tools to conduct a gap analysis to produce the technical reports.

Priority Activities for Next Quarter

Next quarter, PQM+ will:

- Follow up with the manufacturer in Pakistan to review the updated dossier along with the stability data for review by PQM+ prior to submitting to WHO.
- Follow up with the manufacturer in Pakistan to respond to WHO questions and queries as needed while WHO reviews the dossier and plan for mock assessment.
- Continue joint work with VCU on Phase 2 of the manufacturing process optimization for a priority TB product.

- Continue to map out the collaboration with CPT in South Africa following the assessment visit.
- Continue to prepare for the U.S. FDA workshop with the pharmaceutical regulatory authorities to share the agency's experience on the review and registration of new TB medicines.
- The TWG for the RBEC support will have consultative meetings with experts from ACDIMA in Jordan and produce a draft of the agenda and assessment tools for technical reports.

Program Support

Communications

Social media: PQM+ shared 30 posts this quarter via Twitter and LinkedIn highlighting program activities around the world. Our posts earned 825 "engagements," with LinkedIn posts about work with the Rwanda FDA topping the list for the most interactions (retweets/shares, replies, quotes, and likes). LinkedIn content continues to perform especially well, with posts there earning up to 77 likes. Collectively, our posts earned more than 54,000 impressions during the third quarter.

Webinars: The communications team is working closely with the Core TB team and the FDA Small Business and Industry Assistance's team to develop the *Regulatory Best Practices for Global Access to Medicines, Including Anti-TB Medicines Conference,* which will take place virtually August 16 to 18.

Newsletter: PQM+ disseminated its seventh newsletter this quarter, which had a 50 percent open rate. This issue spotlighted PQM+'s support to the Liberia Medicines and Health Products Regulatory Authority (LMHRA) and its quality control laboratory. Recently, USAID through PQM+ donated several pieces of critical medicines testing equipment to the LMHRA. Liberian President George Manneh Weah attended the handover ceremony. The newsletter also featured Nigeria's National Agency for Food and Drug Administration and Control (NAFDAC) and its achieving ML3, and Uzbekistan's registration of two WHO-prequalified anti-TB medicines, cycloserine and prothionamide, using the Collaborative Procedure Accelerated Registration (CPAR) process.

Website: In January, at USAID's request, PQM+ resubmitted the privacy and Section 508 compliance forms for approval, which are required for Governance Board review. This quarter, USAID approved both forms. The agreement officer's representative submitted the website for security testing.

Staff: PQM+ continues to recruit applicants for two full-time communications positions, which were posted in March. In the meantime, several experienced writer consultants have joined support communications activities on a part-time basis until those positions are filled.