Promoting the
QUALITY OF MEDICINES Plus

PQM+ Quarterly Report – Program Year 4, Quarter 3

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About PQM+

The Promoting the Quality of Medicines Plus (PQM+) Program is a six-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 medical products for HIV/AIDS, tuberculosis, malaria, neglected tropical diseases, and other infectious diseases as well as for reproductive, maternal, newborn, and child health.

USP establishes quality standards for medicines the United States Food and Drug Administration (U.S. FDA) is legally mandated to enforce. USP is an independent, scientific nonprofit public health organization and is not a part of the U.S. 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's endorsement of the PQM+ program or of the information provided by it.

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Contents

Acronyms

2FDC	two drug, fixed-dose combination
4FDC	four-drug, fixed-dose combination
ADR	adverse drug reaction
AEFI	adverse events following immunization
AMA	African Medicines Agency
AMQF	African Medicines Quality Forum
AMR	antimicrobial resistance
AMRH	African Medicines Regulatory Harmonization
ANAB	American National Standards Society National Accreditation Board
API	active pharmaceutical ingredient
ARV	antiretroviral drugs
AUDA-NEPAD	African Union Development Agency- New Partnership for Africa's Development
CAPA	corrective and preventive action
cGMP	current good manufacturing practices
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
DMF	drug master file
DT	dispersible tablets (amoxicillin)
EAC	East African Community
EPI	Expanded Program on Immunization
EUA	emergency use authorization
FP	family planning
FPP	finished pharmaceutical product
FTIR	Fourier-transform infrared spectroscopy
GBT	WHO Global Benchmarking Tool to evaluate national regulatory systems
GCP	good clinical practices
GDSP	good storage and distribution practices

Global VAX	U.S. Government's Initiative for Global Vaccine Access
GLP	good laboratory practices
GMP	good manufacturing practice
HPHC	High-Performing Health Care tool
HPLC	high-performance liquid chromatography
HPT	health product technology
HR	human resources
IDP	institutional development plan
IGAD	Intergovernmental Authority on Development (Africa)
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
mRDT	malaria rapid diagnostic test
MOH	ministry of health
MQCL	medicines quality control laboratory
MRA	medicines regulatory authority
MTaPS	Medicines, Technologies, and Pharmaceutical Systems program
NCL	National Control Laboratory
NGO	non-governmental organization
NTD	neglected tropical disease
OHS	Office of Health Systems (USAID)
OpERA	Optimizing Efficiencies in Regulatory Agencies
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PIR	product information report
PIRIMS	Pakistan Integrated Regulatory Information Management System
PMI	(U.S.) President's Malaria Initiative
PMS	post-marketing surveillance
POC	point of contact
PPE	personal protective equipment

PQM+	Promoting the Quality of Medicines Plus
PSS101	Pharmaceutical Systems Strengthening course
PV	pharmacovigilance
QA	quality assurance
QC	quality control
QMS	quality management system
RBI	risk-based inspection
RB-PMS	risk-based post-marketing surveillance
RIMS	regulatory information management system
RRB	regional regulatory body
RSS	regulatory system strengthening
RUTF	ready-to-use therapeutic food
SADC	Southern African Development Community
SATTA	Stepwise Assessment Tool Towards Accreditation
SBCC	social and behavior change communication
SF	substandard or falsified
SOP	standard operating procedure
T2T	Test-to-Treat
TB	tuberculosis
TOR	terms of reference
TRIPS	Trade-Related Aspects of Intellectual Property Rights
TWG	technical working group
TXA	tranexamic acid
UDU	uniformity of dosage units
UEMOA	*Union Economique et Monétaire Ouest Africaine* (West African Economic and Monetary Union)
USAID	U.S. Agency for International Development
USP	U.S. Pharmacopeia
UV-vis	ultraviolet-visible spectrophotometry or spectroscopy
WHO	World Health Organization
WHO PQ	World Health Organization prequalification

Letter from the Director

With USAID funding, PQM+ continues to work to increase the supply of quality essential medical products by supporting candidate manufacturers to pursue marketing authorization for specific priority medicines. Currently, PQM+ is providing technical assistance to 35 manufacturers across 11 countries to attain local authorization or WHO prequalification (WHO PQ) for their medicines. Sixteen of these manufacturers are in Africa (in Burkina Faso, Ghana, Kenya, Nigeria, and South Africa) and 19 are in Asia (in Bangladesh, Burma, India, Nepal, Pakistan, and Uzbekistan).

We are proud to acknowledge that over time, the country of origin of pharmaceutical manufacturers supported by PQM+ has intentionally shifted, positioning the program to contribute to USAID's goal for regionalization—including procuring significant quantities of antiretrovirals (ARVs) and other medical products from African sources.

A recent success and testament to realizing that local and regional manufacturing objective is the Nigerian Swiss Pharma Limited (Swipha) achievement of World Health Organization (WHO) prequalification for zinc sulfate 20mg dispersible tablet, a medicine to treat diarrhea in children. Swipha received technical support from PQM+ as well as its predecessor program, PQM, throughout its journey. This is a significant accomplishment for the continent, as the approval signifies the first pharmaceutical product and manufacturer to receive WHO prequalification in West Africa. As this quarterly report was being finalized, PQM+ received news of the WHO prequalification of two zinc sulfate products from PharmEvo, a manufacturer we support in Pakistan. With this additional quality-assured source, PQM+ and its predecessor have provided support to four of the seven WHO-prequalified sources of zinc sulfate for diarrheal diseases.

Equally exciting, the PQM+ program received a 12-month no-cost extension of the cooperative agreement's period of performance (originally September 27, 2019, to September 26, 2024), shifting its end date to September 26, 2025. With this extension, PQM+ will continue to work in current as well as potential future countries and across all technical areas covered in the original award. Specifically, it allows us to continue providing technical assistance to hundreds of pharmaceutical manufacturers across Africa and Asia that are producing priority medicines to prevent or treat malaria, tuberculosis (TB), neglected tropical diseases (NTDs), and other infections, as well as support treatments for maternal, newborn, and child health (MNCH). Additional time enables us to assist more manufacturers in finishing their journey to WHO prequalification or, at a minimum, in mapping an expedited way forward as they diversify their product portfolios using innovative tools and approaches developed or customized by PQM+. Nearly 30 countries and regional economic communities are currently receiving technical assistance from PQM+ to strengthen their regulatory systems. This program extension will help scale up regulatory capacity development and ensure that many of those national and regional authorities progress in their maturity level according to the WHO benchmarking.

These anticipated achievements will help address the global interest in regionalization, that is, diversification of sources for essential medical products, and stronger regulatory systems for pandemic preparedness. As we remain at the forefront of these efforts with our partners, please continue following our progress toward ensuring that quality-assured medicines are available globally and equitably.

Jude I. Nwokike
PQM+ Director

Executive Summary

During the third quarter of Program Year 4, the USAID-funded Promoting the Quality of Medicines Plus (PQM+) program worked in 25 countries[1] and four regional portfolios and implemented 50 work plans.[2] Active work plans included:

- 24 Mission buy-ins,[3]
- Three core-funded activities supporting the USAID Bureau for Global Health's Office of Infectious Disease for neglected tropical diseases (NTDs) and tuberculosis (TB) and the Office of Maternal and Child Health and Nutrition;
- Four regional buy-ins from USAID's Africa, Asia, Latin America and Caribbean (LAC) bureaus, and East Africa regions;
- One "cross-bureau" funding stream supporting the Office of Health Systems;
- Six funded by the U.S. Government's Initiative for Global Vaccine Access (Global VAX);
- Seven active other COVID-19 buy-ins;[4] and
- One funded by USAID's COVID-19 test-to-treat initiative to promote access to safe and effective oral COVID-19 therapeutics in low- and middle-income countries (LMICs).

The goal of all the 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, reproductive health, and maternal, newborn, and child health (MNCH).

This report summarizes activities conducted during the third quarter of Program Year 4 (April 1 to June 30, 2023). The activities are 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).

[1] Bangladesh, Benin, Burkina Faso, Burma, DRC, Ethiopia, Ghana, Guinea, Kazakhstan, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mozambique, Nepal, Nigeria, Pakistan, Panama, Rwanda, Senegal, South Africa, Tajikistan, Uzbekistan

[2] A few countries are implementing more than one work plan, such as a Global VAX country work plan.

[3] The 24 countries include the list of buy-ins in footnote 1 minus South Africa, which is a Global VAX buy-in.

[4] One each from Bangladesh, Burkina Faso, Ethiopia, Ghana, and Uzbekistan, and two from Mozambique.

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

Technical Areas

Governance

Improving regulatory governance requires the effective and efficient establishment and implementation of quality assurance systems for medical products. PQM+ supports national pharmaceutical QA systems by facilitating the adoption of sound policies and aiding in the development of strategic plans. The program aims to help establish adequate coordination mechanisms that promote sound governance as well as efficiency, accountability, transparency, and alignment of partners. Through PQM+ support, program beneficiaries are becoming more effective in ensuring the quality and safety of medical products, increasing public trust, and freeing up valuable resources that can be used to expand health service coverage to their populations. PQM+'s objective in supporting countries to develop strategic plans enables public organizations in multiple countries, including Bangladesh, Malawi, and Mali, to define their strategic goals, identify necessary strategies and interventions to reach those goals, allocate adequate resources, and implement a monitoring and evaluation system to measure progress of regulatory oversight and plan implementation. All together, these governance efforts help ensure more timely access to quality-assured essential medical products and protection from substandard and falsified (SF) products.

Asia Bureau. This quarter, USAID tasked PQM+ with implementing a venture in support of the "Diversifying the Asia Pharmaceutical Supply Chain (DAPSC)" initiative. PQM+ Asia Bureau analysis supported selection of two countries—Uzbekistan and Kazakhstan—as centers for the two-year project to strengthen the countries' local capacities in competitive manufacturing, procurement, regulatory systems, technology development and investment, and workforce development. Additionally, it will help improve business readiness and the commercial viability of the local pharmaceutical industry to attract investment. One goal for this endeavor is to

develop or strengthen local production of key starting materials (KSMs) and active pharmaceutical ingredients (APIs) to avoid exposure to any supply chain disruptions, minimize overdependence on one supplying country, and support diversification of the supply chain.

Regulatory Systems Strengthening (RSS)

A strong regulatory system helps ensure access to safe, effective, and quality-assured medical products, including essential medicines, and protects public health by preventing the distribution of SF medical products. SF medical products can cause serious health problems, waste scarce resources, and undermine trust in a health system. PQM+ provides support in various areas of RSS. Highlights include the following activities.

The World Health Organization (WHO) shared a list of countries that will undergo Global Benchmarking Tool (GBT) evaluation this year and invited PQM+ to observe the self- or formal benchmarking of specific countries. PQM+ asked to observe the GBT process for **South Africa** and **Ghana**. By participating in these benchmarking exercises, PQM+ will not only ensure that appropriate responses to relevant GBT sub-indicators are provided by NMRAs, but also support the development and implementation of institutional development plans (IDPs). This will help MRAs accelerate progress toward their targeted maturity level. PQM+ supports two regional portfolios and 17 countries in RSS activities linked to GBT sub-indicators.

In support of the African Medicines Regulatory Harmonization (AMRH) Initiative, PQM+ prepared a concept note for the formation of a continental technical working group (TWG), under the evaluation of the medicinal products technical committee (EMP-TC). This TWG would focus on harmonizing requirements for bioavailability and bioequivalence (BA/BE) studies to support approvals of generic products. The concept note was presented at the 4th EMP-TC meeting held in Nairobi, Kenya in May. EMP-TC members and supporting partners provided comments and, after the presentation and discussion, EMP-TC members voted to form the TWG. PQM+ drafted the terms of reference (ToR) for the TWG based on both the concept note and comments. The EMP-TC leadership is in the process of formally adopting the ToR, which will then be disseminated to partners/stakeholders for additional funding and support of activities.

Bangladesh. In collaboration with the national Expanded Program on Immunization (EPI) project, PQM+ supported the “Cold Chain Management of Vaccines” training for 23 inspectors. This training focused on how best to store, handle, and transport vaccines. Also, during the quarter, the Directorate General of Drug Administration (DGDA) issued a request letter to the Line Director of the National Tuberculosis Program (NTP) to provide support to conduct risk-based post-marketing surveillance (RB-PMS) of first-line anti-TB medicines. In response, the Line Director of NTP issued an official memo enabling DGDA inspectors to collect drug samples from NTP outlets/directly observed therapy, short-course centers. This is the first time DGDA is conducting quality surveillance of programmatic anti-TB medicines in the country using the MedRS tool. Surveillance of the quality of medicines is critical to ensuring the treatment outcome of TB patients.

Ethiopia. To address gaps identified during the WHO GBT assessment, PQM+ supported the Ethiopian Food and Drug Administration (EFDA) in finalizing Clinical Trial Directive No. 964/2023. The directive will assist the authority in outlining the legal requirements under each activity of the clinical trial process. Other key benefits include improved information sharing and increased transparency among all stakeholders involved in clinical trial activities. Making this clinical trial directive available and implementing it is part of EFDA’s IDP.

Kazakhstan. PQM+ is assisting Kazakhstan in strengthening its inspectorate and preparing for accession to Pharmaceutical Inspection Co-operation Scheme (PIC/S). Its PIC/S application is scheduled for submission in January 2024. PIC/S membership will provide access to good manufacturing practice (GMP) inspection mechanisms, capacity development resources, and quality-assured medicines. Developments this quarter included amending regulatory documents to meet PIC/S requirements, assessing indicators, and conducting thorough reviews of key procedures. PQM+ visited Astana this quarter and provided training on inspection methodology to 144 participants.

Nigeria. PQM+ collaborated with the Pharmacy Council of Nigeria (PCN) to conduct multiple one-day capacity building workshops for Pharmaceutical Inspectorate Committee (PIC) members, community pharmacists (CPs), and patent and proprietary medicine vendors (PPMVs) at several locations across Kebbi state. A total of 481 participants – 13 PIC members, 48 CPs, and 420 PPMVs – attended the training, thereby expanding the PPMV model to new geographic locations and improving access to key essential medicines in remote rural areas of the country.

Uzbekistan. PQM+ conducted two training sessions on the preparation of registration standard operating procedures (SOPs) for the State Center for Expertise and Standardization of Medicines, Medical Devices and Medical Equipment in May. The purpose was to build MRA staff capacity to develop, review or revise, and use SOPs and manuals to evaluate registration applications submitted by industry. By the end of the training, participants were able to prepare SOPs, checklists, and reports for the registration activities; explain the overall quality summary and the quality information summary; conduct reviews; and identify deficiencies in the summary of product characteristics, patient information leaflet, and labeling and screen applications for marketing authorization. Advancement of this regulatory function will expedite the approval of new priority medical products and contribute to universal health coverage by expanding patient access to these products and potentially reducing their price on the local market. In addition to Uzbekistan, PQM+ is supporting 10 other countries in improving their procedures for evaluation of registration applications.

Chemistry, Manufacturing, and Control (CMC)

CMC involves the development, production, and quality control of medicines, vaccines, and medical devices that meet current GMP and international quality standards. The CMC process plays a crucial role in ensuring that these products are safe, effective, and of consistent quality. CMC processes are important because they help ensure that medical products are of consistent quality and meet required regulatory standards. This is essential for the products' safety and effectiveness.

The PQM+ CMC team's recent work has focused on technical assistance to 37 pharmaceutical manufacturers in 12 countries (Bangladesh, Ghana, India, Kenya, Liberia, Nepal, Nigeria, Pakistan, South Africa, Myanmar, Burkina Faso, and Uzbekistan) working on 61 product applications, including those for drugs, vaccines, and medical devices.

With PQM+ support, on May 2, 2023, Swiss Pharma **Nigeria** (SWIPHA) achieved WHO prequalification (PQ) for zinc sulfate DT, a medicine used to help treat diarrhea in children. SWIPHA Nigeria is the first WHO prequalified manufacturer in West Africa. (On July 12, 2023, zinc sulfate DT and syrup from PharmEvo in **Pakistan** achieved WHO PQ, thanks in part to cost- and time-saving technical discussions between PQM+ and WHO.)

Global VAX. In May, the PQM+ Global VAX portfolio supported six African regulatory authorities in visiting three vaccine manufacturing sites in India. This helped build a bridge between regulators and industry by fostering mutual support, harmonization, and a collaborative spirit in preparing for future public health emergencies of international concern.

PQM+ completed pilot testing of the risk-based inspection (RBI) GMP module with the DGDA of **Bangladesh** and Pharmacy and Poisons Board (PPB) of **Kenya** during this quarter. Currently, the test result report is in progress based on the data collected from the two countries. The data include GMP assessment reports from three manufacturers from each country (six total) and functionality test results. Pilot testing met the criteria set out by DGDA for the administrator and inspector functionalities. Ultimate adoption of the tool will help countries adopt international norms and standards for regulatory inspections, including application of risk-based approaches that ensure efficient use of inspectorate resources. The tool will greatly help NMRAs manage the inspection process effectively and efficiently.

PQM+ also developed a data collection tool and began collecting data for a landscape analysis of TB pharmaceutical products manufacturers in South Africa. Finally, PQM+ staff provided comments to the Bill and Melinda Gates Foundation on plans for an API database for Africa.

Laboratory System Strengthening (LSS)

To ensure the quality, accuracy, and reliability of medicines quality test data, laboratories must employ robust systems for medical product analysis and evaluation. Implementation of robust systems, based on proven standards of quality management and medicines testing, ensure that laboratories are operating according to good practices and procedures. This prevents errors and contamination which can compromise the validity and reliability of results. Overall, well-functioning quality management systems are essential for maintaining the integrity and quality of the work conducted in laboratories, and for ensuring that the results are reliable.

PQM+ supports 49 laboratories in 17 countries. This includes 43 national quality control laboratories (NQCLs) and six other laboratories (i.e., either private laboratories or those with a focus other than medicines quality control).

Burma. PQM+ conducted two separate five-day in-person trainings. The first, held in collaboration with the Malaria Unit from the WHO Country Office, focused on high performance liquid chromatography, dissolution, and potentiometric titration at the Department of Food and Drug Administration (DFDA) Pharmaceutical Chemistry Laboratory. The training aimed to enhance the technical expertise of DFDA analysts and standardize testing procedures across three regional laboratories. At the Burma Manufacturer 1[5] QC laboratory, the second training focused on analytical method validation and verification and laboratory safety. The training sought to enhance the skills of Burma Manufacturer 1 analysts in performing a crucial process to ensure the accuracy and reliability of quality control testing for the medicines they produce.

African Lab Network. PQM+ is helping the African Medicines Regulatory Harmonization (AMRH) program conduct the Vaccine Regulatory Reliance Laboratory Network consultancy. During Q3, PQM+ continued developing the proposed reliance network framework, progressing several key elements of the consultancy, and identifying coordination mechanisms within the various strategic, scientific, and operational elements. Staff discussed and validated an outline of the framework with a subset of stakeholders. The framework seeks to conserve resources by

[5] For public reporting, PQM+ uses aliases for manufacturers to protect the confidentiality of their data and this program's work with them.

avoiding duplication, increasing efficiency, and distributing or sharing responsibilities, among others. Other LSS highlights this quarter include the following:

- Completed an analysis of responses from NQCLs to inform mapping of laboratory capabilities for the African continental lot release network.
- Developed and shared an outline of a framework for an African continental lot release laboratory network. A subset of the African Medicines Quality Forum/African Medicines Regulatory Harmonization (AMQF/AMRH) Vaccines Subcommittee validated the outline.
- Completed a laboratory assessment for the molecular section of the Virology Laboratory at the Institute of Epidemiology Disease Control and Research (IEDCR) in Bangladesh.

Strategy and Workforce Development

Uzbekistan. Last quarter, PQM+ initiated development of a local pharmaceutical manufacturing strategy in Uzbekistan. PQM+ completed detailed plans for the activity in collaboration with the Agency on Development of the Pharmaceutical Industry ("the Agency"). This quarter PQM+ began a desk review for the strategy which included review of imported finished dosage forms, APIs, and other ingredients. The team in Tashkent continues to engage local stakeholders for more data assets for analysis, upcoming plans for the technical team, and USAID trips. The team is testing components of the Local Manufacturing of Essential Medical Products model strategy as it develops the Uzbekistan strategy.

Nepal. Nepal's pharmaceutical manufacturing strategy aims to strengthen domestic production for self-sufficiency and increase the quality of essential medicines within the country. In Q3, Nepal's Department of Drug Administration (DDA) began formulating this strategy with internal and external consultations. PQM+ developed a background paper for strategy development and engaged a PQM+ regional expert to support strategy development. In addition, staff developed a questionnaire and a list of experts for a consultative process to gather information for the manufacturing strategy.

Malawi. PQM+ staff finalized a situation analysis of the Pharmacy and Medicines Regulatory Authority. This document, aligned with findings and recommendations from the WHO-GBT self-assessment, will inform development of the next iteration and implementation of the Malawi NMRA's strategic plan.

Kenya. This quarter, PQM+ supported a five-day induction training for 25 newly recruited PPB regulatory staff members. Partnership among PQM+, the Government of Kenya, the Bill and Melinda Gates Foundation, Management Sciences for Health, Chemonics, and the World Bank made hiring, equipment, and training efforts possible. The recruits have been deployed in their respective functions and are working on backlogged regulatory tasks (e.g., dossier assessments and GMP inspections). In addition, PQM+ continued working with the Pharmaceutical Society of Kenya to validate a quality assurance and regulation course that will be linked to the previously developed PPB self-directed learning platform known as Ustadi.

Learning, Thought Leadership, and Awareness-Raising

In Q3, PQM+ continued to develop evidence around medical product quality assurance topics by providing technical contributions to help shape international guidelines from WHO, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), and other standards-setting organizations, advancing the development and

use of new tools and approaches, providing thought leadership, and raising awareness of the importance of medical products quality assurance.

Thought Leadership/Contributions to International Guidelines, and Global Collaboration. Examples of PQM+'s participation in global discussions and knowledge sharing related to medicines quality in Q3 include:

- Shared the analytical method to evaluate nitrosamine impurities in rifapentine and rifampin with WHO for consideration for inclusion in the WHO pharmacopeia.
- Conducted a workshop with technical working group members and other stakeholders in Ethiopia to identify bottlenecks hindering the Regional Bioequivalence Center from delivering BE studies for Ethiopia and the African continent.
- Provided feedback on "Quality Assurance Practices for Medical Oxygen Systems – a Technical Resource Document" developed by USAID's Medicines, Technologies, and Pharmaceutical Services (MTaPS) program.
- Submitted a poster entitled "Strengthening Nigeria's Community-Level Health System to Increase Access to Quality-Assured Medicines for Low-Income, Rural Clients" to the USAID Office of Health Systems case competition for FY2023.

Research and Analysis. This quarter, PQM+ made important progress with numerous activities to increase the evidence base related to medical product quality assurance, including:

- Conducting a survey of PQM+ countries on emergency use authorization (EUA) for medicines and an online search of published gray literature for EUA-related guidance documents.
- Refined a questionnaire on regulation and supply of MNCH medical devices and developed a questionnaire for tranexamic acid to use in data collection in five PQM+ countries (Ghana, Bangladesh, Nepal, Ethiopia, and Senegal).

New Tools and Approaches. Work developing and adapting tools and approaches to improve medical product quality this quarter included:

- Developed a model local production strategy, which will assist countries and regions with the goal of strengthening sustainable local production to improve access to safe, effective, quality-assured, and affordable medical products by providing key stages and steps that form the "how" of the strategy guide.
- Finalized a product information report (PIR) on gentamicin and job aids to support registration and inspection of gentamicin.

Advocacy and Awareness: This quarter, PQM+ posted the call-to-action paper "Expanding access to quality medicines for babies [and] children" on the PQM+ website and disseminated the paper via social media posts on Twitter and LinkedIn.

Cross-Bureau Activities and Progress

PQM+'s Cross-Bureau activities focus primarily on thought leadership and innovative and new approaches, which can then be piloted, adapted, or scaled to fit the country context. This buy-in especially aims to advance the global medical product quality assurance operational agenda and learning, with specific attention to developing or applying evidence-based approaches and tools; conducting research and analysis to support medical product quality assurance systems strengthening; and supporting advocacy on the importance of medical product quality assurance for public health.

Office of Health Systems (OHS)

These activities, funded by OHS, fall under program objectives 2, 4, and 5.

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

EUA Guidance Document for MRAs. To facilitate rapid access to safe, effective, and quality medical products, PQM+ and technical resource partner University of Washington are developing a guidance document for MRAs on Emergency Use Authorization (EUA) to expedite marketing authorization decisions and fast-track approval processes for emergency therapeutics. [6]PQM+ oriented 19 of its program country offices in Africa and Asia to the activity and disseminated a survey to collect information on countries' emergency regulatory processes and procedures for approving medicines and non-vaccine biological products. In particular, the survey was designed to capture information on pathways for emergency use authorization of these medical products. PQM+ country staff identified key regulatory informants for interviews to collect the data. An online search of published gray literature for PQM+ countries has uncovered few EUA-related guidance documents. PQM+ is collecting and analyzing survey responses while development of the draft model EUA guidance and checklist for therapeutics continues.

Key achievements include:

- Disseminated survey and began data collection; and
- Completed a desktop review of existing EUA regulatory processes and procedures for COVID-19 therapeutics in selected countries and organizations.

African Lab Network. PQM+ is helping the AMRH program conduct the Vaccine Regulatory Reliance Laboratory Network consultancy. In the previous quarter, PQM+ assessed the capacity of NQCLs in conducting quality control testing for biological products as part of that continental lot release lab network. In Q3, PQM+ continued developing the proposed reliance network framework, progressing several key elements of the consultancy and identifying

[6] PQM+ has published two additional EUA guidance documents for diagnostics and vaccines: 1) PQM+. 2021. Promoting the Quality of Medicines Plus (PQM+) A proposed model to build capacity for emergency use authorization for diagnostics: Guidance for national regulatory authorities. Submitted to the U.S. Agency for International Development by the PQM+ Program. Rockville, MD: U.S. Pharmacopeial Convention. 2) PQM+. 2021. Promoting the Quality of Medicines Plus (PQM+) A proposed model to build capacity for emergency use authorization for vaccines: Guidance for national regulatory authorities. Submitted to the U.S. Agency for International Development by the PQM+ Program. Rockville, MD: U.S. Pharmacopeial Convention.

coordination mechanisms within the various strategic, scientific, and operational elements. PQM+ gave a high-level presentation of the strategic vision for the reliance framework at the AMQF/AMRH Vaccines Subcommittee meetings in Rwanda from May 2-5. PQM+ discussed and validated an outline of the framework with a subset of stakeholders; the framework seeks to conserve resources by avoiding duplication, increasing efficiency, and distributing or sharing responsibilities.

Key accomplishments include:

- Completed an analysis of all survey responses collected (14 of 17) into the country mapping report; and
- Developed a report with gaps and recommendations based on a review of available country legislative frameworks, the African continental guidelines for vaccines and biologics, and the standards and accreditation planning document.

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

PQM+ has completed drafting Guidance for Developing a Strategy for Local Production of Essential Medicines. This guidance is intended for use by countries and regions when developing strategies for local production of essential medical products, including how to decide whether to invest in expanding local production. PQM+ incorporated several rounds of review and discussions with external stakeholders. Concurrently, the PQM+ strategy team will continue working on local manufacturing strategies in the field (e.g., in Uzbekistan, Nepal, Nigeria, Philippines, etc.); the model can then be enhanced for future iterations with findings from this work.

The latest draft will be ready for USAID review by the end of Q3/early Q4, and PQM+ plans to share the final document with WHO after approval by USAID.

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

AMR Module of PSS101 Course. PQM+ provided feedback to MTaPS on the storyboard and alpha version of the new antimicrobial resistance (AMR) Module 11 of the Pharmaceutical Systems Strengthening 101 (PSS101) course. PQM+ will deliver a training on Module 9: Medical Product Quality Assurance to the upcoming PSS101 cohort on June 30.

Social and Behavior Change Communication (SBCC). PQM+ has advanced a draft of the demand generation paper and consulted with Breakthrough ACTION to vet the approach, research, and findings as well as solicit feedback on relevant SBCC resources. The paper identifies the stakeholders at each level of the quality management system (QMS) needed to engage in key messages and interventions and identify evidence gaps for further study.

PQM+ has circulated the draft to internal reviewers for feedback prior to finalizing and sharing with USAID.

High-Performing Health Care System Tool. PQM+ is continuing to develop the expanded organization lists for national and subnational levels and across public, private, and nongovernmental organization (NGO) sectors in both Kenya and Mozambique. PQM+ has oriented the Ministry of Health (MOH) points of contact (POCs) to the activity and is continuing with Mission contacts to ensure the lists are representative. PQM+ has shared the introduction

and information letters with MOH POCs in both countries. The next step is to disseminate the letter and survey links with the MOH signatories.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Complete an analysis of all responses to the rapid assessment, develop a proposed model EUA guidance with a checklist for LMICs, and develop a one-page overview of the proposed model EUA guidance.
- Translate the full EUA guidance and the one-page overview of the proposed model EUA guidance into French and disseminate the English and French versions on PQM+ and core partner websites, Listservs, social media, and partner forums.
- Develop a webinar on proposed model EUA guidance for national MRA staff.
- Complete the reliance framework and five-year costed strategy for the African continental lot release lab network and validate all the deliverables with key African Union Development Agency-New Partnership for Africa's Development (AUDA-NEPAD) stakeholders.
- Participate in stakeholder meetings and a workshop coordinated by MTaPS and the information management system technical committee (IMS-TC) and other relevant stakeholders to develop and socialize the roadmap.
- Share the final model local production guidance with USAID and WHO following USAID's approval.
- Finalize the technical brief on social and behavior change.
- Collect and upload the data from the High-Performing Health Care (HPHC) tool and organize a half-day stakeholder meeting for each country to present the findings. PQM+ will develop a summary report to document the process of applying the tool and the key findings and recommendations from the HPHC assessment in each country.

Africa Bureau to Support the African Medicines Agency (AMA)

With funding from USAID's Africa Bureau, PQM+ is supporting AMA's transformation into a continental regulatory agency to help develop the pharmaceutical sector in Africa. This funding complements USAID's OHS investments for PY4 to support the AMA.

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

BA/BE Subcommittee. A priority area for AMRH is harmonizing requirements for registering generic[7] products, as they are the most efficient way to increase access to quality-assured, safe, and efficacious medicines. Applications for generic medicines rely heavily on the use of bioequivalence (BE) studies, a subset of bioavailability (BA) studies, to support the safety and efficacy of the generic product. PQM+ developed a concept note for a BA/BE subcommittee

[7] A generic product, as defined by the WHO, is a pharmaceutical equivalent or pharmaceutical alternative product that may or may not be therapeutically equivalent to a comparator product. Products that are therapeutically equivalent are interchangeable.

under the Evaluation of Medicinal Products technical committee (EMP-TC), discussed it at a meeting of the EMP-TC, obtained concurrence, and is now waiting on the Secretariate's meeting report. Based on the concept note and comments from EMP-TC, PQM+ drafted a TOR for a BA/BE TWG.

API Database. API regulation, including coordination of joint inspection of API manufacturing sites, is one of the AMA's critical functions. PQM+ consulted with the Bill and Melinda Gates Foundation and the IMS-TC on the design and development of an API database. PQM+ reviewed and provided technical comments on a use case, user requirements, and costing options report. Working with a local consultant, PQM+ will lead the design and development reports for the software.

The revised, approved deliverables include:

- the database design, development, and validation reports
- the consultant scope of work for cost-sharing

MedRS Training Workshop. PQM+ is supporting Africa's Intergovernmental Authority on Development (IGAD) and the East African Community (EAC) in regional RB-PMS. PQM+ consulted with both communities to understand their RB-PMS needs and to plan for a MedRS tool training workshop. Given a similar activity for MedRS training in the EAC work plan, PQM+ proposed sponsoring IGAD MRAs and Secretariate members to attend this RB-PMS workshop. PQM+ will support implementation of the workshop, participation of IGAD, and a French interpreter for Djibouti. The workshop is planned for late August. PQM+ will continue to work with colleagues in Kenya to plan the workshop, pending USAID approval.

RB-PMS Testing. PQM+ facilitated partial funding of a second round of RB-PMS testing in IGAD and proposed leveraging an EAC work plan activity for RB-PMS to sponsor IGAD's national MRAs and Secretariate to attend the training workshop.

Priority Activities for Next Quarter

Next quarter, the Africa Bureau plans to:

- Share the TOR with the EMP-TC to obtain feedback as part of Deliverable 2 of Activity 2.
- Recruit and onboard the consultant to work on a report of IGAD's 2nd round of RB-PMS
- Pending approval of the EAC work plan, begin preparations for MedRS workshop
- Provide review and input to finalization of the design, development, and validation reports of the API database

Activities and Progress by Country and Regional Buy-Ins

Africa Region

Benin

PQM+ works with the Beninois Agency for Pharmaceutical Regulation, *l'Agence Béninoise de Régulation Pharmaceutique* (ABRP), Benin's main regulatory body. 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 points of entry into the country (land, sea, and air) or at the request of any national institution. PQM+ is helping ANCQ strengthen its QMS to achieve international recognition (ISO/IEC 17025 or WHO prequalification). This would assure the reliability of testing and increase public confidence in ANCQ test results.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

Collaborative framework. Based on information gathered by PQM+ during a situational analysis in Q2 on the state of collaboration between ABRP and ANCQ, PQM+ proposed a draft collaborative framework for these two institutions. The objectives of the framework are:

1) Coordinate the roles of the two agencies related to applications for marketing authorizations, approval of other health products, and market surveillance and control, as well as for any operation intended to ensure the quality of medicines and other health products;
2) Establish the commitments and responsibilities of each partner;
3) Ensure harmony and synergy in the interventions of both agencies to ensure the quality of drugs and other health products marketed in Benin; and
4) Strengthen the fight against the illicit market and substandard and falsified medicines and other health products in Benin.

This draft framework outlines both parties' responsibilities on the medicines registration, marketing authorization, and market control and surveillance regulatory functions.

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

RB-PMS of antimalarials. In June 2023, PQM+ supervised the collection of 208 of 250 planned antimalarial samples (artemether injection, artesunate injection, quinine injection, sulfadoxine/pyrimethamine tablets, artemether/lumefantrine tablets, and quinine tablets) from five regions in Benin (Ouémé/Plateau, Mono/Cuoffo/Atlantic, Zou, Alibori, and Littoral) as part of the implementation of the 2023 RB-PMS protocol developed by the PMS-TWG in Q2. Challenges encountered in the field included low availability of quinine due to prioritization of

artesunate as a first-line treatment for malaria and storage conditions above room temperature, per the product labels. The samples are undergoing MiniLab screening.

ISO/IEC 17025 accreditation. As part of implementing its roadmap toward ISO/IEC 17025 accreditation, PQM+ trained eight analysts (five men, three women) from ANCQ on uniformity of dosage units (UDU),[8] required because ANCQ decided to include it as part of the proposed accreditation scope. To further improve the capacity and capability of analysts from ANCQ in key QC techniques and to start preparing these analysts for demonstrating these techniques during an accreditation assessment, PQM+ organized a study visit for two analysts from ANCQ to USP's ISO/IEC 17025 accredited laboratory in Ghana. The purpose of the visit was to:

- Expose the analysts to an ISO/IEC-accredited laboratory setting to observe the applied best practices; and
- Train the analysts on three techniques in the proposed accreditation scope: Fourier-transform infrared spectroscopy (FTIR), ultraviolet-visible (UV-vis) spectrophotometry, and Karl Fischer titration).

Technical assistance to ANM to expand ISO/IEC 17025 accreditation scope. As part of its support to Benin's Agency for Standardization and Metrological Service and Quality Control Management ANM to better serve NQCLs in francophone West Africa (members of the UEMOA, the French acronym for the West African Economic and Monetary Union), PQM+ trained 25 participants (18 men, seven women) on measurement uncertainty, internal auditing, and internal quality checks. The participants demonstrated appreciable knowledge improvement in the three subjects covered and will develop procedures for the topics covered to implement these processes in their laboratory.

Regulatory inspections capacity building. To strengthen the capacity of the ABRP inspectorate division for regulatory inspections, PQM+ trained 18 inspectors (14 men, four women) on GMP. In addition, PQM+ provided training on use of the RBI tool for good storage and distribution practices (GSDP) inspections.

To improve ABRP's capacity to conduct checks for medical products at importation, PQM+ worked with ABRP to draft terms of reference for a risk-based approach to importation control. In addition, PQM+ procured three pieces of a screening device using Raman spectrometry to help ABRP incorporate screening as part of its importation inspection process. These devices have been delivered.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Train inspectors of ABRP on use of the RBI tool to conduct GSDP inspections.
- Support ANCQ and ABRP to validate the collaborative framework drafted in Q2.
- Supervise the testing of antimalarials for the second (2023) RB-PMS.
- Support ABRP to finalize all waste management guidelines and SOPs.

[8] UDU is the degree of uniformity in the amount of drug substance in a dosage unit. This test is required to ensure that each dosage unit in a batch of medicine produced, has the required amount of active ingredient. This is particularly critical for products with small quantities of API within a larger dosage unit where homogeneity may be difficult to attain.

- Provide training to ABRP on use of the importation control screening devices to pilot the process PQM+ has proposed.
- Support ABRP to host the training module developed for GSDP on the Ministry of Health's online platform.

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/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), which is now *l'Agence nationale pour la sécurité sanitaire de l'environnement, de l'alimentation, du travail et des produits de santé* (ANSSEAT) to conduct sampling of medical products. In 2021, with PQM+ support, LNSP and ANRP established an official collaborative framework.

PQM+ works with the 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

Online health products sales. PQM+ analyzed responses to the questionnaire it deployed to conduct a situational analysis of online sales of health products in Burkina Faso. The analysis found no system for the regulation of online sales of medicines and a lack of understanding of what is required to regulate online sales of medicines in the country. As a result, PQM+ plans to conduct a sensitization workshop for ANRP before the authority drafts text on the regulation of online sales to provide more information on regulation of online sales of medical products. This will better prepare ANRP to contribute meaningfully to the development of the regulatory text.

Medical products QA strategic plan. In addition to the documents ANRP shared with PQM+ in Q2, PQM+ developed and deployed a key informant interview questionnaire to facilitate the completion of a situational analysis.

PQM+ has consistently followed up with ANRP to agree on a date to convene the sensitization workshop and to ensure stakeholders complete the key informant interview questionnaire, which would facilitate the completion of the situational analysis. However, delayed responses are stalling implementation—perhaps a result of a change in the agency's priorities, contrary to the needs they expressed during the PY4 work planning workshop in Ouagadougou.

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

DCM/PNA mock audit. To help DCM/PNA close the remaining gaps identified during the mock audit PQM+ conducted in Q2, the program trained eight laboratory analysts (five men, three women) on Karl Fischer titration and UDU, which they intend to include into their proposed ISO/IEC 17025 accreditation scope. DCM/PNA has had a Karl Fischer apparatus for a few

years but did not have the capacity to use it. The hands-on training showed participants how to use the device to determine the water content of reference standards and products that require it. ANCQ has decided to include this technique as part of its proposed accreditation scope and therefore required training on this advanced pharmacopeial technique.

Because DCM/PNA is new to testing using the Karl Fischer apparatus, PQM+ organized a study visit for two ANCQ analysts to USP's ISO/IEC 17025 accredited laboratory in Ghana to further train them on using the equipment and to expose them to testing in an environment that has attained international recognition per the ISO/IEC 17025 standard.

In addition, PQM+ supported certification of the equipment by a qualified vendor, also linked to DCM/PNA's accreditation scope. The certified equipment includeshigh-performance liquid chromatography tools (HPLCs), FTIR, a dissolution tester, and UV-vis spectrophotometers. This certification closes a major gap identified during the lab's mock audit, which was conducted in Q2, and helped DCM/PNA's prepare for an accreditation audit.

RB-PMS samples. In Q3, PQM+ supervised Burkina Faso's PMS-TWG to develop a 2023 RB-PMS protocol for antimalarials and antibiotics. Per the protocol, the PMS-TWG plans to collect 224 antimalarial and 192 antibiotics samples from 224 facilities. Antimalarial molecules to be sampled are artesunate for injection, artemether-lumefantrine, artesunate/pyronaridine, dihydroartemisinin/piperaquine, quinine sulfate, sulfadoxine-pyrimethamine, and sulfadoxine-pyrimethamine + amodiaquine. Antibiotic molecules to be sampled are amoxicillin, amoxicillin/clavulanic acid, ceftriaxone, cotrimoxazole, ciprofloxacin, phenoxymethylpenicillin, and erythromycin.

ANSSEAT completed confirmatory testing of the 2022 RB-PMS samples and provided the results to ANRP. Subsequently, the PMS-TWG developed a report for the 2022 RB-PMS of antimalarials. Samples came from six regions: Boucle du Mouhoun, Cascades, Centre, Centre-Nord, Hauts-Bassins, and Nord, with 285 samples collected. This number represents 81.7 percent of the number planned (349), which could not be reached due mainly to the phasing-out of quinine and artemether injectable. Of the collected samples, 283 were screened (two had inadequate quantities for testing); of those, 281 passed the MiniLab test. The other two samples, the same quinine sulfate product that failed the screening, also failed the confirmatory tests. In addition, one other sample did not meet quality specifications during confirmatory testing. Therefore, three of the 283 samples (1 percent) tested from six regions in Burkina Faso failed to meet their quality specifications. These results are not nationally representative.

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

GMP audit and ISO 9001 assessment of Burkina Faso Manufacturer 1. As follow-up to the baseline assessment by PQM+ in Q2 using WHO GMP guidelines, PQM+ worked with Burkina Faso Manufacturer 1 to develop a roadmap toward local manufacturing of antimalarials. Per the roadmap, this manufacturer is expected to submit a dossier for marketing authorization of artemether/lumefantrine by September 2024.

As part of the implementation of this roadmap, PQM+ trained technical staff of Burkina Faso Manufacturer 1 on GMP inspections, good documentation practices, and good laboratory practices. This seeks to close some gaps in the implementation of good practices that were identified during the baseline assessment.

Similar to the GMP roadmap for manufacturing of antimalarials, PQM+ worked with Burkina Faso Manufacturer 1 to develop a roadmap toward ISO 9001 certification.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Conduct a stakeholder workshop to draft ANRP's five-year medicines QA strategic plan.
- Support dissemination of the 2022 RB-PMS results.
- Supervise the sampling and testing of 2023 RB-PMS of antimalarials and antibiotics.
- Provide guidance to ANSSEAT to submit an expression of interest for ISO/IEC 17025 accreditation for its DCM/PNA.

Democratic Republic of Congo (DRC)

The widespread availability and distribution of non-quality-assured artemisinin combination therapies and non-artemisinin therapies[9] 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

RB-PMS. In Q3, ACOREP's PMS-TWG completed the sampling of 310 antimalarials (artemether injection, artesunate injection, quinine injection, sulfadoxine/pyrimethamine tablets, dihydroartemisine/piperaquine tablets, artesunate/amodiaquine tablets, artemether/lumefantrine tablets, and quinine tablets) for its 2022 RB-PMS exercise from nine USAID focus provinces: Bukavu (Sud-Kivu), Kabinda (Lomami), Kalemie (Tanganyika), Kamina (Haut-Lomami), Kananga (Kassai-Central), Kolwezi (Lualaba), Lubumbashi (Haut-Katanga), and Mbuji-Mayi (Kassai-Oriental). This was five more provinces than were sampled in 2021. Screening of these samples started at the end of June 2023.

In June, PQM+ supervised the PMS-TWG workshop to develop an RB-PMS protocol for antimalarials for 2023. With the high cost of sampling and testing from nine USAID focus provinces (mainly due to the expansiveness of DRC resulting in significant travel expenses), the PMS-TWG plans to reduce the number of provinces in 2023, in alignment with the budget approved in the PQM+ workplan. The 27 PMS-TWG members at the workshop included 15 women and 12 men).

ISO/IEC 17025 accreditation. To help LNCQ-LAPHAKI continue to follow its roadmap toward ISO/IEC 17025 accreditation, PQM+ supervised the implementation of its analytical method verification (AMV) plan for 2023, which includes verifying the compendial methods for artemether/lumefantrine tablets, artesunate injection, sulfadoxine-pyrimethamine tablets, and cotrimoxazole tablets. LNCQ-LAPHAKI submitted its raw data to PQM+ for review, at which time

[9] 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.

PQM+ noted some missing parameters. The program is assisting the laboratory to address this to finalize their report.

In November 2022, ACOREP became operational with new leadership and new offices. To help ACOREP begin to establish a quality system that meets the requirements of the ISO 9001:2015 standard, PQM+ conducted a baseline assessment to identify and determine support areas to prioritize its resources and efforts for the program year. The assessment found the following:

- The ACOREP QA team is aware of the need to establish a QMS to enhance ACOREP's progress toward WHO GBT compliance (ML 3) for regulatory functions. The existence of a zero-draft quality policy is adequate evidence of this.
- Collaborative work in this direction has started within the Southern African Development Community (SADC) TWG, which will enable access to several SOP templates.
- QMS documentation (SOPs and forms) are either non-existent / templates from SADC TWG or exist as draft documents.
- A formal QMS has not yet been developed or established.

To sensitize ACOREP's personnel on the requirements of the standard and increase their awareness of the agency's drive toward ISO 9001:2015 certification, PQM+ conducted a three-day ISO 9001:2015 virtual awareness training for all 40 ACOREP staff (32 men, eight women). The training enhanced staff knowledge and will improve buy-in from ACOREP staff on this goal the agency has set.

Objective 3: Increase financial resources for medical product QA optimization

The current testing fees at ACOREP's LNCQ-LAPHAKI needed to be re-evaluated to ensure the lab's ability to generate sufficient funding from testing medicines to sustain its QMS. To this end, PQM+ trained laboratory personnel on a new costing model that applies all the cost drivers of an accredited laboratory—such as routine maintenance, calibration and requalification of equipment, procurement of traceable standards, training and accreditation surveillance, and audit fees—to arrive at realistic testing fees. The 16 ACOREP staff trained included 13 men and three women.

In addition, PQM+ worked with ACOREP's financial administrators to design a budget template that includes key QMS-related costs.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Supervise sampling of antimalarial samples for the 2023 RB-PMS.
- Give LNCQ-LAPHAKI technical assistance on implementing measurement uncertainty.
- Guide ACOREP to develop a procedure for new testing fees for LNCQ-LAPHAKI
- Work with staff of ACOREP to develop key quality systems documents and organize training sessions for relevant Department of Pharmacy and Medicine (DPM) personnel on the approved versions of these documents.

Ethiopia

The Ethiopian Food and Drug Authority (EFDA) registers all medical products; licenses and regulates the production, import, storage, and distribution of transregional medical products; and conducts quality-control testing and post-marketing surveillance of products circulating in the local market. All other regulatory activities that are not mandated to EFDA fall under the jurisdiction of regional government and city administration regulatory bodies. The lack of clarity in mandates between EFDA and the regional regulatory bodies (RRBs), the absence of a formal reporting relationship between EFDA and those regulators, and the latter's poor capacity compromise proper regulatory oversight of medical products circulating in Ethiopia.

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

Progress by PQM+ Objective

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

Regulation of medical products is central to any functioning health system and plays a critical role in improving public health. Effective regulation of medical products promotes and protects public health by ensuring medicines quality, safety, and efficacy; promoting adequate manufacture, storage, and distribution of medicines; and strengthening the fight against SF products. Regulatory authorities are responsible for monitoring the quality of medical products circulating in the market through the application of various regulatory procedures, including marketing authorization and PMS.

Activity 2.1 Support EFDA in addressing WHO's GBT assessment findings and prepare it for WHO ML 3. PQM+ provided support for onsite benchmarking for WHO GBT ML 3, including:

- Preparing regulatory functions for an on-site audit. This included:
    - Follow-up on implementation of the quality management system;
    - Document inventory and assistance on alignment of documents; and
    - Training for medicine registration and licensing directorate staff (15 women, 20 men) on developed and revised guidelines and SOPs.
- Developing an SOP for internal communication on market surveillance and control regulatory function activities.
- Revising the SOP for handling rapid alerts arising from quality defects.
- Revising the EFDA 2023 GMP guideline for pharmaceutical products.
- Delivering an EFDA-organized training on WHO GBT tools and documents (guidelines and SOPs for medicine sector directors, team leaders, and ports of entry and exit).
- Training medical representatives from manufacturers and importers on the control of advertisement and promotion guidelines (27 men, six women).

To address gaps identified during WHO's GBT assessment, PQM+ supported EFDA in finalizing Clinical Trial Directive No. 964/2023, issued under Article 71, Sub-article 2 of the Ethiopian Food and Medicine Administration Proclamation No. 1112/2019. The directive will be an instrument for the authority to outline the legal requirements under each activity of the clinical trial process. Other key benefits include improved information sharing and increased transparency between all stakeholders involved in clinical trial activities. Making this clinical trial directive available and implementing it is part of EFDA's IDP. PQM+ also provided technical support in reviewing and updating the Clinical Trial Authorization Guideline, 2017, to harmonize requirements and processes.

This quarter, PQM+ provided technical and financial assistance to conduct familiarization workshops on directives, guidelines, and SOPs to EFDA's clinical trial and pharmacovigilance team members. The workshops' objective was to improve the quality of work on pharmacovigilance and clinical trial activities by increasing team members' awareness of guidelines and procedures they should follow while conducting activities. The workshop took place from May 2-5 in Adama with 23 participants (nine women, 14 men) in attendance.

PQM+ provided technical support to EFDA during the formal WHO GBT assessment that took place from June 12-16. Benchmarking of the regulatory functions used GBT, followed by discussions and agreement about the findings and recommendations to include in the IDP.

After the official onsite inspection of EDFA by the WHO experts, PQM+ supported EFDA in developing the IDP based on WHO's inspection findings.

Activity 2.2 Build capacity of branch EFDA laboratories toward ISO/IEC 17025:2017 accreditation and the main lab to maintain its accreditation. EFDA's main laboratory was accredited in 2011 for seven test methods with support from predecessor program PQM, and the scope of accreditation gradually expanded to 16 methods. In PY4, PQM+ sought to support EFDA's medical device laboratory and further expand its accreditation scope. One area of support was the quality assurance of medical gloves, a product that has been especially challenging since the start of the COVID-19 pandemic.

EFDA has five branch laboratories strategically positioned at geographical locations based on the level of risk that SF products will enter the country there. These laboratories are closer to the end user, and their role is to assess the quality of medical products circulating in their catchment areas. They are also actively involved in the PMS programs. These geographical locations make them ideal to fight the circulation of SF products and protect public safety in their surroundings. Currently, none of these laboratories are ISO/IEC 17025:2017 accredited or WHO prequalified, meaning their test results may not be of sufficient quality or withstand legal scrutiny. During PY4, PQM+ supported implementation of the branch-specific roadmap toward ISO/IEC 17025:2017 accreditation with EFDA's central lab experts.

Activity 2.3: Support EFDA to conduct a national RB-PMS of selected malaria and MNCH medicines. One core support area during PY4 is assisting EFDA in implementing RB-PMS. This quarter, EFDA completed testing of 133 collected samples (91 MNCH medicines and 42 antimalarials). Laboratory testing found only one substandard sample. Sample collection occurred in selected sites from Addis Ababa, Oromia, Ahmara. Somali, and Southern Nations, Nationalities, and Peoples' (SNNP) regions. This is not nationally representative; security concerns hampered efforts to collect samples in some parts of the country.

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

Ethiopia considers building capacity for local pharmaceutical production to be a critical strategy to ensure timely access to quality-assured essential medicines at an affordable price. In the past 15 years, the Growth and Transformation Plan II, the National Strategy and Plan of Action for the Development of Pharmaceutical Manufacturing in Ethiopia, and various other government policies and strategies underwent a redesign to promote the local production of pharmaceuticals. Despite the remarkable efforts and commitment from the government in creating an enabling policy environment for developing local pharmaceutical production, little progress has resulted in terms of actual capacity to cover national needs for essential medicines from local sources. Moreover, local manufacturers face formidable challenges to remain in business, let alone invest in quality improvements and capacity expansions.

Activity 4.2: Build the capacity of selected local pharmaceutical industries for achieving WHO PQ and local GMP certification. In Ethiopia, few Giemsa stain[10] manufacturers supply products to the public procurement agency. In PY4, PQM+ is seeking to identify those manufacturers, conduct a rapid gap assessment, and provide relevant technical support for some of those identified.

In Q3, PQM+ assisted local manufacturers to prepare for WHO-PQ inspection. Assessment preparations took place for two local manufacturers, with gaps identified and on-site discussions to develop corrective and preventive action (CAPA) plans. The manufacturers are audited by WHO's Local Production and Assistance (LPA) and the manufacturers are awaiting the final assessment report to develop the CAPA plans. PQM+ will support both manufacturers' development and implementation of CAPA plans.

In addition, PQM+ collaborated with EFDA and MoH on a half-day workshop to validate the "Gap Assessment Report on the Quality of Giemsa Stain" with follow-up and technical assistance toward implementation of the CAPA plans proposed for local Giemsa manufacturers.

Challenges. Ethiopia's security situation has been deteriorating because of the current conflict and may continue to affect progress toward some activities that require travel. PQM+ will put efforts toward addressing issues through virtual communication, continuous discussion, and engagement with relevant government counterparts.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Train the national PMS TWG on the revised MedRS tool and develop an RB-PMS protocol.
- Support EFDA in developing IDPs based on WHO's recent GBT inspection.
- Provide supportive supervision to branch EFDA labs.

Ghana

The Food and Drugs Authority of Ghana (FDA Ghana) is the national regulatory body responsible for the regulation of food, drugs, clinical trial protocols, and other products. FDA

[10] Giemsa stain enables diagnosis of malaria and other parasites.

Ghana 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. FDA Ghana is ISO 9001-certified and, in 2020, attained WHO ML 3. Its Center for Laboratory Services and Research (CLSR) is also ISO/IEC 17025 accredited and WHO prequalified. 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 MCH commodities such as oxytocin.

Implementation of PY4 activities for PQM+ Ghana paused for most of April and May as PQM+ waited for its PY4 funds to be obligated. The funds were obligated in late May 2023.

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

RB-PMS. PQM+ supervised the screening of antimalaria samples for the 2022 RB-PMS collected from seven regions (Central, Ashanti, Greater Accra, Volta Region, Upper West, Upper East, and Western Region). Of the 66 antimalaria samples collected, two (3 percent) were not registered. These unregistered samples failed the risk-based testing at level 1. Another 64 samples (97 percent) underwent level 2 (MiniLab) testing. All 64 samples tested (100 percent) passed level 2 testing and 20 percent of these samples and all MCH samples are undergoing confirmatory testing. These screening results are not nationally representative.

Furthermore, in June 2023, PQM+ supervised the PMS-TWG to develop its 2023 RB-PMS protocol for antimalaria and MCH medicines. 12 members (8 men and 4 women) of the PMS-TWG attended this workshop. This year, the group plans to sample artemetherinjection, artesunate injection, artemether/lumefantrine tablets, artemether/lumefantrine suspension, oxytocin injection, misoprostol tablets and ferrous sulfate tablets from 10 regions in Ghana.

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

In Q3, PQM+ trained local manufacturers on impurities testing to produce quality-assured antimalaria and MCH medicines. The 23 participants (18 men, five women) represented six manufacturers (Ghana Manufacturers 1,2, 3, 4, 5, and 6). The training involved theory and practical illustrations using appropriately selected product monographs (USP, British Pharmacopoeia, and the International Pharmacopoeia), and real data from impurities study activities. The course enabled participants to understand how impurity tests in the various compendia (including relevant associated general chapters) meet regulatory compliance requirements. Impurities testing is a critical test that each manufacturer must conduct for the antimalaria or MCH product they produce. This training will help close some gaps identified by PQM+ and improve participants' progress toward GMP compliance.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Train local manufacturers of antimalarials and MCH products on dossier compilation, per the roadmaps toward local registration or WHO PQ.
- Ensure that local manufacturers finalize the following quality documents for implementation in Q4:
    - Stability studies protocol;
    - Analytical method verification protocol; and
    - Process validation protocols.
- Supervise the sampling of antimalaria and MCH products for the 2023 RB-PMS.
- Support the dissemination of the 2022 RB-PMS results.

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

In May, PQM+ supervised the first meeting between LNCQM and DNPM to discuss the implementation of their collaborative framework, developed in PY3 with support from PQM+, which delineates agreed-on areas of the institutions' collaboration and their individual responsibilities. The meeting covered several issues and identified key challenges, including delays in payment to LNCQM for services rendered to the DNPM and non-adherence by LNCQM to timelines to submit test reports to DNPM. The pharmacy directorate also used the opportunity to update LNCQM on its drive to become an autonomous agency, and both institutions discussed ongoing and planned RB-PMS activities.

Recommendations included:

- DNPM should make prompt payment for testing services provided by LNCQM.
- DNPM should finalize the 2022 RB-PMS report by the end of May 2023.
- DNPM should sign the ministerial decree on LNCQM testing fees.
- Accelerate the process to transform DNPM to an autonomous agency.
- Resolve the issue of LNCQM reporting lines.

LNCQM committed to ensuring the timelines for submitting future reports would be respected.

Also in Q3, PQM+ facilitated a workshop to help LNCQM develop a three-year plan for capacity building that includes activities in the roadmap toward ISO/IEC 17025 accreditation related to metrology—maintenance, calibration, qualification, and proper use of equipment at LNCQM. The June workshop in Conakry included 11 staff members (10 men and one woman) from LNCQM. The group drafted the three-year plan, which is now under joint revision by LNCQM leadership and PQM+.

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

Antimalarial and MNCH samples screening: In Q3, DNPM finalized the 2021 RB-PMS report, which the PMS-TWG subsequently validated in June 2023. In addition, LNCQM completed confirmatory testing of the 2022 antimalarial and MNCH samples and submitted the results to DNPM. DNPM then drafted the 2022 RB-PMS report, which the PMS-TWG reviewed in June. Of the 167 samples (95 antimalarial and 72 MNCH) collected and tested from seven regions in Guinea, seven antimalarial samples (quinine and sulfadoxine/pyrimethamine tablets) and 30 MNCH samples (dexamethasone, amoxicillin, oxytocin injection, and iodated polyvidone) failed to meet their quality specifications. These results are not nationally representative. Key recommendations by the PMS-TWG were to take immediate regulatory actions on the failed batches, train wholesalers on GSDP, and update the list of facilities in Guinea.

Family planning RB-PMS. To facilitate the RB-PMS of family planning (FP) products, PQM+ recruited 12 university students to collect 204 FP samples of medroxyprogesterone acetate 150 mg/ml, ethynylestradiol/levonorgestrel 0.05 mg/0.25 mg, and ethinyestradiol/norethisterone 0.05 mg/1 mg from eight regions in Guinea.

Mapping wholesalers. PQM+ deployed the questionnaire it developed in Q2 to map the 10 importers/wholesalers in Guinea to the procurement and distribution of FP medicines in the country. Mapping contraceptive products importers/wholesalers in the private sector in Guinea revealed little interest for these products based on the minimal demand from community pharmacies. Also, the limited stocks available do not correspond to the list of essential medicines in terms of combinations and dosages. With regard to GSDP, all the wholesalers indicated that staff have received adequate training in this area. Contraceptives are distributed the same way as other medications, through secured distribution channels. The cold supply chain is in place if required, but for the contraceptives that are stocked, it is not necessary. The information gathered during this mapping will help PQM+ prepare for a training on GSDP in Q4.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Conduct training on good receiving, storage, and distribution practices for FP wholesalers/distributors.
- Supervise the development of the 2023 RB-PMS protocol for antimalarials and MNCH medicines.
- Support DNPM's Dossier Evaluation Committee to convene one dossier evaluation session to review dossiers submitted for registration of antimalaria/MCH medicines.
- Finalize the OpERA assessment.

Kenya

PQM+ delivers technical assistance to Kenya's Pharmacy and Poisons Board (PPB), National Quality Control Laboratory (NQCL), Ministry of Health's Division of National Malaria Program (DNMP), Department of Family Health (DFH), Division of Health Products and Technologies (DHPT), and the counties to strengthen in-country stakeholders' capacity in ensuring access to quality-assured medical products in the country.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ is supporting the DNMP and PPB to monitor the quality of malaria rapid diagnostic test kits (mRDTs). To implement this, PQM+ is supporting the development of a PMS protocol that will guide the pharmacovigilance (PV) PMS TWG to undertake the PMS activity. In Q3, PQM+ collected the relevant information and data to develop the protocol. When Kenya implements the PMS, it will be the first time a quality survey for mRDTs is implemented there.

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

The PPB sought to hire 95 regulatory officers to assist them with their work to achieve ML 3 and related workload activities, with a target of achieving ML 3 by May 2024. USAID approved hiring 25 officers. PQM+ supported recruitment and onboarding of the 25 regulatory staff, helping shortlist and interview applicants. The new officers will enable PPB to address numerous human resource recommendations arising from the June 2022 WHO GBT assessment conducted for PPB to attain ML 3. PQM+ assisted the PPB in reducing a backlog of more than 240 outstanding recommendations; as of a WHO virtual assessment in May, only 53 remain, with 23 of those related to human resources (staffing and training).

PQM+ supported a five-day training for the recruited staff. In addition, PQM+ continued working with the Pharmaceutical Society of Kenya to validate the quality assurance and regulation course that will link to the previously developed PPB self-directed learning platform (Ustadi).

PPB representatives train new staff on PMS activities (left) and dossier screening (right).

PQM+ supported county-level implementation of QA strategies of the MOHs, DHPT, and DNMP in health facilities in county of Busia. This was done through revision of 10 health product technology (HPT) quality assurance SOPs for Busia County. The SOPs are developed from national procedures that can be adopted by other counties.

The program worked with PPB to review the guidelines for licensing and inspection of pharmaceutical manufacturing facilities including for vaccine manufacturers. PQM+ also supported the development of one guideline, one SOP, and Key Performance Indicators as recommended from the WHO GBT ML 3 assessment conducted in June 2022.

PQM+ helped the NQCL develop 12 SOPs during a three-day workshop. The documents have now been validated and are awaiting approval.

In support of the NQCLs vaccine testing preparedness, PQM+ conducted a gap analysis, and generated a recommendation report in support of bridging those gaps.

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

PQM+ supported the Ministry of Health's DHPT to host a meeting of representatives of the local pharmaceutical manufacturers. The meeting discussed the challenges facing local manufacturing and proposed interventions that the government can implement to support the growth of local production of quality assured medicines, including those for malaria. Some of the difficulties identified included delays in timely registration of locally produced medicines arising from challenges at the regulatory authority and, inadequate technical competences by local manufacturers in developing dossiers and responding to queries from PPB. As an output of the meeting, the manufacturers will develop a summary of the challenges and the requested interventions to present to the government for addressing.

PQM+ supported the participation of two staff from PPB and NQCL to attend a vaccines manufacturing workshop in India.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support the PV/PMS TWG to develop a PMS protocol for malaria rapid diagnostic tests and other medical devices, using the risk-based approach.
- Collaborate with DHPT and DNMP to conduct supportive supervision activities in Busia County to monitor progress in implementing action plans and developed/revised SOPs on QA of antimalarial medicines and other essential HPTs.
- Sensitize PPB PMS staff on the revised SOP on investigation of malaria product quality complaints.
- Support completion of 10 more county SOPs related to HPT QA.
- Identify, develop, and upload new content to PPB's Self-Directed Learning Platform, Ustadi.
- Support leadership and change management workshop.
- Undertake review of NQCL laws and make recommendations including sustainability of HR.

Lesotho

With USAID funding from the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), PQM+ is helping Lesotho develop appropriate regulations and support good governance. The national medicines system in Lesotho plays a crucial role in protecting and improving public health by ensuring that essential medical products, such as antiretroviral (ARV) medicines, that are available and used in Lesotho are of good quality, efficacious, and safe for human use. Currently, the Ministry of Health (MOH) is performing some basic medical product regulatory functions through its Directorate of Pharmacy, but the country is moving toward an independent regulatory authority as recommended by WHO and the soon-to-be enacted Lesotho Medicines and Medical Devices Control Authority (LMMDCA) Bill, 2019.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ continued to support the Pharmacy Directorate of the Lesotho Ministry of Health to strengthen its regulatory functions by developing appropriate regulations and supporting good governance.

Activity 1.1: Strengthen the national regulatory system in Lesotho by supporting the establishment of the national medicines regulatory authority. PQM+ conducted a gap assessment workshop using the WHO GBT to identify strengths, areas of improvement, and priorities. The six priority regulatory functions covered during the assessment are: (i) national regulatory system, (ii) registration and marketing authorisation, (iii) pharmacovigilance, (iv) market surveillance and control, (v) licensing of establishments, and (vi) regulatory inspections.

PQM+ supported the establishment of a TWG to lead the implementation of a roadmap toward establishment of a national regulatory authority. The technical working group had a kick-off meeting in May with Lesotho's Director General of health as its chair.

PQM+ assisted with the formation of a subcommittee within the TWG to lead the drafting of regulations as guided by the draft LMMDCA bill.

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

PQM+ continued to support the Pharmacy Directorate of the Lesotho Ministry of Health to strengthen its regulatory functions by developing appropriate regulations and supporting good governance.

Activity 2.3: Strengthen the capacity of Lesotho NMRA in pharmaceutical regulatory inspections. PQM+ provided technical support to the Pharmacy Directorate of the Lesotho Ministry of Health to develop necessary guidelines and procedures for Good Manufacturing Practice/Good Storage Distribution Practice (GMP/GSDP) inspections. The developed guidelines and procedures were harmonized with WHO and Southern African Development Community (SADC) guidelines and GMP/GSDP requirements.

Activity 2.4: Strengthen licensing of establishments to support decentralized distribution of ARVs and other medicines. PQM+ facilitated a technical workshop in Berea with multi-stakeholders from the Lesotho Ministry of Health and other in-country health systems strengthening

implementing partners to support development of guidelines, SOPs, and tools for licensing of pharmaceutical establishments in Lesotho. Specific workshop activities included:

- Identifying and drafting guidelines on the procedures to apply for a license and on content and format of the license application.
- Drafting procedures for assessment of applications for licensing activities, including license issuance, renewal, modification, or revocation.
- Drafting procedure for granting or re-granting a license or approval of a substantial modification.
- Drafting guidelines on the structure with clear responsibilities to conduct establishments licensing activities.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Conduct a regulatory inspection training: With participants, PQM+ will provide three inspections targeted at solid oral dosage forms, sterile preparations, and a wholesaler in South Africa.
- Conduct a workshop for the development of a guideline and SOPs for a risk-based approach for monitoring the quality and safety of ARVs and other essential medicines and facilitate the review of medicines inspection reports.
- Provide technical support to develop regulations, guidelines, and procedures for the registration and marketing authorization function.
- Provide technical support for updates and validation of vigilance SOPs and guidelines.
- PY5 workplan finalization.

Lebohang Mazibuko of PQM+ addresses workshop attendees during the gap analysis workshop in Maseru. (PQM+ photo)

Liberia

In Liberia, PQM+ is strengthening the country's regulatory system, specifically supporting the Liberia Medicines and Health Products Regulatory Authority (LMHRA) in six of the eight regulatory functions per the WHO GBT.

PQM+ supported the LMHRA to develop appropriate regulatory tools for its efficient operations and to remove substandard antimalarial and MCH medicines from circulation. PQM+ supported the LMHRA quality control lab in developing a laboratory quality management system.

Also this quarter, PQM+ supported Liberia Manufacturer 1 toward attaining a manufacturing license and GMP certificate from the LMHRA.

Progress by PQM+ Objective

Objective 1: Improve governance for medical product quality assurance systems

This quarter, PQM+ supported the LMHRA in developing two new regulations. In May, the LMHRA board approved four previously submitted regulations—defects and quarantine of medicinal products, subcontracting testing services, registration of medical devices, and the variation of medical products. LMHRA disseminated the approved regulations on June 20 to marketing authorization holders, the Ministry of Health, Pharmacy Board, and other partners. To date, LMHRA has operationalized 11 regulations with PQM+ support.

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

This quarter, LMHRA disseminated RB-PMS results for rounds 2 and 3. Here are highlights from the presentation. Note these are results of risk-based sampling and are not nationally representative:

Round 2:

- 146 samples collected from six counties
- 34% from the public sector, 66% from the private sector.
- 69% antimalarials; 31% MNCH.
- Overall failure rate of samples collected: 16%
- 13% of antimalarials failed; 22% of MNCH medicines failed.

Round 3:

- 146 samples collected from six counties
- 37% from the public sector; 63% from the private sector
- 63% antimalarials; 37% MNCH.
- Overall failure rate of samples collected: 11%
- 13% of antimalarial samples failed; 7% of MNCH medicine samples failed.

- 6 of 15 batches that failed were unregistered.

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

PQM+ provided common technical document (CTD) dossier compilation training to 15 staff of Global Pharmaceutical Manufacturing and Laboratories (Pvt) Limited, equipping the staff with the necessary knowledge and skills to compile CTD dossiers. This training has improved the company's regulatory submission process and increased its chances of successful product registration and approval.


Left: A staff member receives a certificate of completion. Right: Training participants engage in a roundtable discussion.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Complete the development of course material for the medical product short course.
- Continue to support the lab in the development of a laboratory quality management system.

Madagascar

PQM+ collaborates with Madagascar's medicines regulatory authority, *Agence du Médicament de Madagascar* (AMM), to strengthen its capacity to assure the quality of medicines and medical product throughout the country. AMM performs all regulatory functions through four technical departments: pharmaceutical inspection, registration, pharmacovigilance, and quality control. The National Pharmaceutical Quality Control Laboratory (*Laboratoire National de Contrôle de Qualité des Médicaments*/LNCQM*)* is part of the AMM's QC department. PQM+ is helping AMM strengthen the LNCQM's capacity to prepare for ISO/IEC 17025:2017 accreditation and WHO prequalification.

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.

Activity 2.1: Strengthen post-marketing surveillance of medicines quality in Madagascar using a risk-based approach. PQM+ continued supporting AMM in implementing their first round of risk-based post-marketing surveillance (RB-PMS) protocol for reproductive health and antimalarial

medicines. AMM completed sampling of medicines in twelve (12) regions and the laboratory received the samples for confirmatory testing. With PQM+ support, the laboratory will continue to test samples and finalize the report in the next quarter.

PQM+ conducted a workshop with AMM and the PMS technical working group to validate the jointly developed guideline on reporting, investigating, recall, storage, and disposal of substandard and falsified medical products and the document on monitoring and evaluation framework for RB-PMS.

Activity 2.2: Strengthen the capacity of Madagascar's Laboratoire National de Contrôle de Qualité des Médicaments. PQM+ issued the report on the assessment of the laboratory's new premises. This report includes recommendations to upgrade the laboratory as per international standards.

PQM+ continued working with LNCQM on the laboratory procedures review. With laboratory staff, PQM+ reviewed five (5) procedures and two (2) new HPLC instructions this quarter. The procedures and instructions will be used as training materials.

Table 1: Status of Labs Accreditation in Madagascar

Laboratory	Accreditation Sought	QMS	Initial Gap Assessment	CAPA	LIF	Official Inspection/ Pre-assessment
Laboratoire Nationale de Contrôle Qualité des médicaments (LNCQM)	ISO 17025 : 2017	Review ongoing	Complete	Yes	No	Laboratory is in the process of relocating to a new location.

Activity 2.3: Strengthen the capacity of AMM in pharmaceutical regulatory inspection. PQM+ conducted a five-day training on pharmaceutical regulatory inspection using the RBI tool, developed by PQM+, based on good storage and distribution practices. The RBI methodology and tool will allow AMM to prioritize the selection and inspection of distribution facilities with the highest risks. Nineteen (19) pharmacists from across the country attended.

From left to right: Training participants, AMM staff, and PQM+ and USAID representatives attend a ceremony to hand out certificates of attendance. Photo credit: PQM+ team

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

Activity 5.1: Develop and implement a short course on RB-PMS in collaboration with FOP-UOA and AMM. PQM+ facilitated a conference on RB-PMS in collaboration with the Faculty of Pharmacy at the University of Antananarivo (FOP-UOA) and AMM in May. Eighty (80) people, mainly student pharmacists and professional pharmacists, attended. PQM+ presented on RB-PMS technical approaches and the head of the Pharmacovigilance (PV) Service at AMM presented on the importance of PV.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Train LNCQM analysts on method validation/verification, calculation of measurement uncertainty, preventive maintenance, and analytical methods using HPLC equipment.
- Finalize the RB-PMS protocol report.
- Finalize the PY5 workplan.

Malawi

PQM+ collaborates with Malawi's Pharmacy and Medicines Regulatory Authority (PMRA) to revise and update the PMRA strategic plan of 2018 – 2023 with the aim of aligning the plan with current developments in the pharmaceutical sector in Malawi, the region, and globally. Strategic plans for medicines regulatory authorities are a crucial tool for improving governance of medical product quality assurance systems. If well implemented, the new strategic plan for PMRA will guarantee sustainable access to quality-assured safe and effective medical products that address the local health needs in Malawi.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

At the close of Q2, PQM+ had finalized the implementation plan and planned travel to Malawi for an in-country kick-off meeting in early Q3. In Q3, following the onboarding of a strategic planning consultant, PQM+ through a consultative process with PMRA stakeholders started the revision and updating of PMRA's strategic plan from 2018-2023. PQM+ held an in-country project kick-off meeting with key stakeholders including PMRA, USAID, Government of Malawi (GoM), and other in-country development partners.

PQM+ worked collaboratively with PMRA to establish key contacts for workplan activities.

- PQM+ developed stakeholder engagement tools which were distributed in-country, the tools were used to gather data from various stakeholders to finalize the inception report.
- PQM+ engaged PMRA staff, customers, GoM representatives, and development partners through key informant interviews and focus group discussions. PQM+ finalized a situational analysis report based on collected feedback.
- PQM+ facilitated drafting of the strategic plan zero draft in collaboration with PMRA.

- PQM+ continued virtual stakeholders' engagements and finalized the strategic plan zero draft with PMRA senior management and further presented the zero draft to the PMRA Finance and Administration committee and Executive Board.
- PQM+, in collaboration with PMRA's strategic planning team, consolidated feedback from PMRA's board and finalized the strategic plan first draft for secondary review.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Receive and incorporate any final inputs from the Finance and Administration Committee, the Board, and other stakeholders.
- Develop the final PMRA strategic plan (2023/24-2027/28).
- Support the development plans for the launch and dissemination of the strategic plan.
- Finalize the strategic plan revision report.

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 an ML1 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. In January 2023, LNS achieved ISO/IEC 17025 accreditation for four quality control techniques, for its medicines quality control laboratory (LCQM) with direct support from PQM+, which started in 2020.

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 medicines registration.

In addition, PQM+ is providing tailored technical assistance to the Medicines Quality Control Laboratory within LNS to attain ISO/IEC 17025 accreditation to expand their accreditation scope to include pharmaceutical microbiology testing.

Note: As of the end June 2023, PQM+ had not received its PY4 funds for Mali therefore it is unlikely it will complete the implementation of its PY4 workplan. PQM+, in Q4, will determine which activities can be implemented by September 2023 once funds are obligated.

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

Microbiological testing capacity building. To further strengthen the capacity of LNS's microbiology laboratory for conducting microbiological QC tests on medicines, PQM+ provided hands-on quality control training on three techniques: microbial enumeration testing (MET), microbial tests for specified microorganisms (MTSM), and sterility tests. Participants included six microbiologists (three men and three women) who reviewed the required standard operating procedures related to these techniques.

Medical devices capacity building. PQM+ is supporting LNS to operationalize its medical devices laboratory. As part of this work, PQM+ provided a two-day virtual training to LNS's medical staff on various aspects of medical devices and in-vitro diagnostics (MD/IVD), including MD/IVD QMS, laboratory competency, and specific testing requirements for mRDTs. Five analysts (three men, two women) attended. This training was useful for the participants as they prepare to update the various SOPs related to new medical device testing methodologies being developed and implemented in LNS. The participants were engaged throughout the training, asking several questions, and participating in discussions.

Regulatory inspections capacity building. To help strengthen Mali's capacity for regulatory inspections, PQM+ conducted a baseline assessment of DPM and included Mali's *Inspection de la Santé* (IS)'s current system/processes for pharmaceutical inspections. This assessment revealed that the two institutions collaborate to execute the regulatory inspection function. DPM works with all the central structures of the various ministerial departments, non-governmental organizations, associations, and professional orders at the national level and with the national MRAs of the Economic Community of West African States (ECOWAS) countries, the Regional Economic Communities (RECs) in Africa, WHO, and the West African Health Organization (WAHO) at the sub-regional level. IS regularly works mainly with the national structures but on an ad hoc basis at the sub-regional level. The analysis also showed that inadequate human resources constitute a major gap for conducting regular inspections. DPM has only two inspectors and IS has 17 inspectors (not only for medical products). With this limited workforce, applying a risk-based approach to regulatory inspections will help the agencies optimize their resources to be able to conduct routine inspections. The findings of this assessment will help PQM+ prepare a training on using the RBI tool for GSDP inspections.

Priority Activities for Next Quarter

Next quarter, pending obligation of PY4 funding, PQM+ plans to:

- Provide training on the use of the RBI tool for GSDP inspections.
- Support DPM's Dossier Evaluation Committee to convene one evaluation session to review dossiers submitted for registration of antimalarials/MNCH medicines.
- Support the operationalization of LNS's five-year strategic plan by convening a donor round table to develop a resource mobilization plan.
- Support LNS to submit and expression of interest to the West African Accreditation System (SOAC) for ISO/IEC 17025 scope expansion.
- Supervise Mali's PMS-TWG as it develops its fourth RB-PMS protocol using the MedRS tool.
- Provide hands-on training on mRDT testing.

Mozambique

Mozambique recently established an autonomous medicines regulatory authority (MRA), ANARME-IP (*Autoridade Nacional Reguladora de Medicamentos, Instituto Publico)*, which encompasses the *Laboratório Nacional de Comprovação da Qualidade* (LNCQ) as a division within ANARME-IP. PQM+ has been providing technical assistance to ANARME-IP in its transition to an autonomous national MRA and assistance toward attaining WHO GBT ML 3 and achieving ISO 9001:2015 certification. Additionally, PQM+ has been assisting LNCQ to identify

and bridge gaps toward attaining ISO 17025:2017 accreditation, including developing the necessary QMS documents, manuals, and processes.

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

Sub-Objective: Provide technical assistance to ANARME-IP to conduct risk-based post-marketing surveillance for antiretroviral medicines and long-acting contraceptive implants. Due to the existing challenges with medicines storage and distribution infrastructure, there have been concerns on the quality of ARVs in the supply chain in Mozambique, especially at the lower levels of the system. This threatens the benefits of antiretroviral therapy to the patients and may lead to treatment failure. Additionally, poor-quality contraceptive implants risk method failure and potentially compromise the reproductive health of women in Mozambique. PQM+ is supporting ANARME-IP to assess the quality of ARVs and contraceptive implants through RB-PMS to provide the necessary evidence to support programmatic decisions. PQM+ is using a systems strengthening approach, taking the opportunity to strengthen overall PMS systems for ANARME-IP and contribute toward achievement of WHO GBT ML 3. In Q3, PQM+:

- Supported the division of pharmacovigilance and clinical trials at ANARME-IP to develop a scope of work for the activity as well as the training agenda to support capacity development for ANARME-IP personnel. Training on the use of the MedRS tool as well as protocol development is scheduled for July, with sample collection and testing expected to follow in August.
- Engaged the *Central de Medicamentos e Artigos Médicos* (CMAM, the Center for Medicines and Medical Articles) to identify the ARVs in use in the national health system. This is to facilitate the identification of appropriate testing methodology, confirmation of current laboratory capacity, and laboratory supply needs (reagents, reference standards).
- Engaged ANARME-IP and the LNCQ to determine viability and possible support for testing ARV samples collected during previous PMS activities. This involved the review of sample expiry dates, time since sample collection, and existing sample storage conditions. This will be part of the upcoming protocol development discussions with the ANARME-IP PMS TWG.

Sub-Objective: Support LNCQ to strengthen its reliability testing capacity for PMS and prepare for ISO 17025:2015 accreditation. To support PMS activities and to strengthen overall laboratory systems, PQM+ is working with the LNCQ to develop capacity to produce valid and reliable sample testing results. Additionally, ANARME-IP is pursuing WHO GBT ML 3 and ISO 17025:2017 accreditation for the LNCQ. PQM+ is providing technical assistance to LNCQ in addressing the gaps identified in the roadmap toward ISO 17025:2017 accreditation. In Q3, PQM+:

- Engaged suppliers for the procurement of a water purification system, reagents, and reference standards for the laboratory, inclusive of equipment maintenance, calibration, qualification, and performance verification. Procurement of these items and services is expected to be completed in Q4.

- Supported LNCQ to design and schedule training for laboratory personnel on compendial testing techniques. This training and certification is scheduled for August.

Additionally, PQM+ provided technical support to ANARME-IP in preparing for ISO 9001:2015 certification. ANARME-IP received this certification in Q3, a crucial milestone as an assurance that the authority will employ international best practices when implementing regulatory measures in the certified areas.

Table 2: Status of Labs Accreditation in Mozambique

Laboratory	Accreditation Sought	QMS	Initial Gap Assessment	CAPA	LIF	Official Inspection/ Pre-assessment
Laboratório Nacional de Comprovação da Qualidade (LNCQ)	ISO 17025:2017	Development and review of most QMS documentation completed; pending some requiring direct in-person PQM+ SME support	Initial gap assessment by PQM+ completed/ conducted	A mock audit to be conducted after closure of the gaps identified in the initial gap assessment. Previous CAPAs from the failed PTs have been investigated and closed	Not available	Not done

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Work with ANARME-IP to implement the planned RB-PMS activities. Training for the PMS-TWG on using the MedRS tool for product scoring and selection, as well as on development of the PMS protocols, is scheduled for July. To improve cost efficiency, the protocol development process for the two product lines will occur concurrently with the support of PQM+.
- Conduct sample collection and testing per the developed protocols and prepare the PMS report.
- Complete the procurement process and work with ANARME-IP to facilitate delivery of the equipment (water purification system), supplies (reagents and reference standards), and services (equipment calibration, qualification, and performance verification).
- Conduct training of the LNCQ team on compendial testing as part of laboratory capacity strengthening and in preparation for ISO 17025:2017 accreditation.
- Engage with ANARME-IP on key priorities for FY24 to facilitate planning for PY5 activities.

Nigeria

PQM+ is focused on helping ensure the quality of medicines and other medical products in Nigeria, with an emphasis on malaria, 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 2: Country and regional regulatory systems to assure the quality of medical products in the public and private sectors improved

During Q3, PQM+ in Nigeria delivered the following:

- Technical assistance to Nigeria's National Agency for Food and Drug Administration and Control (NAFDAC) Central Drug Control Laboratory to close CAPA items from the WHO-PQ inspection findings.
- Support to the Pharmacy Council of Nigeria (PCN) in cascading training on ISO 9001:2015 to Lagos Zonal Office.
- Internal auditing and Stepwise Assessment Tool Towards Accreditation (SATTA) training for the NAFDAC Agulu Laboratory, Agulu and Vaccine, Biologics and Medical Devices Laboratory, Yaba.
- Support in the calibration and qualification of equipment in the microbiology lab and the National Institute for Pharmaceutical Research and Development (NIPRD) central lab.
- Support to NIPRD with laboratory consumables to strengthen microbiological quality control (sterility, microbial limit, and bacterial endotoxin tests) of medical products.
- Coordination of interlaboratory comparison (ILC) participation between NIPRD and NAFDAC on microbiological testing.

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

During Q3, PQM+ support helped Nigeria achieve the following:

- WHO prequalification of Swipha's 20mg zinc sulfate dispersible tablets.
- Successful inspection of Nigeria Manufacturer 8 by UNICEF with no critical observations.
- Facilitation of the second module of quality risk management training for 53 participants (28 men, 23 women) from the industry and the Centre for Drug Discovery, Development, and Production (CDDDP), a PQM+ partner.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Conduct a capacity building workshop for industry on annual product quality review.
- Conduct a comprehensive review of the zero draft of the national strategic plan for the pharmaceutical sector.
- Support scheduled PIC/S inspections in the five supported states and the Federal Capital Territory (FCT).
- Print updated inspectors' manual and submit it to PCN.

- Print and distribute information, education, and communication (IEC) materials (posters) to community pharmacists (CPs) and patent and proprietary medicine vendors (PPMVs) in the supported states and the FCT.

Rwanda

PQM+ is building the capacity of the Government of Rwanda (GOR) to manage the country's pharmaceutical system, focusing on product quality assurance, to meet its public health needs. The primary focus is strengthening the medicines regulatory system in quality assurance areas, including those outside the mandate of other USAID programs (e.g., RB-PMS and drug quality control laboratory strengthening). This will contribute significantly to improving the Rwanda Food and Drug Authority (Rwanda FDA) regulatory system as an essential public health function and advancing implementation of the government's National Pharmaceutical Sector Strategic Plan in collaboration with other organizations such as Rwanda Medical Supply Limited, the Regional Center of Excellence for Vaccines, Immunization, and Health Supply Chain Management.

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

A functional and strong national pharmaceutical QC laboratory is imperative to implement enforcement actions for poor-quality medicines identified through PMS or inspection and to ensure that procured and donated essential medical products meet acceptable quality requirements. In Q3, PQM+ supported Rwanda FDA to:

- Train 27 NQCL staff (18 men and nine women) on equipment performance, qualification, and preventive and corrective maintenance.
- Guide Rwanda FDA's NQCL on how to perform compendial tests of sampled medicines.
- Acquire and install laboratory security enhancing equipment and devices (e.g., temperature/humidity monitoring devices).
- Acquire and install prioritized occupational health and safety equipment (e.g., emergency showers).
- Provide technical support in conducting proficiency testing.
- Procure reagents for testing MNCH and FP/reproductive health (RH) samples.

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

PQM+ provides technical assistance to University of Rwanda (UR) to strengthen the QA/QC systems of their teaching laboratories to complement the national quality control and assurance system. In Q3, PQM+ supported UR to:

- Assess gaps in its teaching laboratory and provide training to laboratory staff on advanced QMS and internal auditing.
- Review/develop a laboratory quality manual and SOPs.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Sample MNCH and FP/RH medical products, test the samples, analyze and compile the results, and publish the country's first RB-PMS report.
- Conduct the second RB-PMS TWG meeting.
- Subscribe to two to three scientific journals on medical product quality and safety.
- Train NQCL staff on measurement uncertainty and preventive and corrective maintenance, especially for dissolution, HPLCs, gas chromatography, atomic absorption spectroscopy, and liquid chromatography with tandem mass spectrometry (mainly the Agilent system).
- Conduct a mock audit and support NQCL staff to initiate the ISO 17025:2017 accreditation and WHO prequalification processes and train staff on internal auditing of the laboratory management system.
- Participate in inter-laboratory comparisons of test results of various techniques between NQCL and one of three approved providers (Sigma Aldrich, LGC-UK, or NCI-USA).
- Develop, review, and validate missing components of the current good manufacturing practices (cGMP) guidelines, including the guidelines Rwanda FDA uses for joint cGMP inspections through the East African Community Regional Medicines Regulatory Harmonization (EAC/MRH) initiative.
- Train Rwanda FDA on use of cGMP guidelines and offer technical support in adapting or adopting guidance from the EAC/MRH initiative on joint cGMP inspections.
- Provide technical assistance and expert guidance on the implementation of the signed regulatory agreement between Rwanda FDA and Ghana FDA.
- Facilitate a study visit by Rwanda FDA management (to be determined, potentially to Ghana) aimed at strengthening regulatory function and systems of the authority.
- Collaborate with Rwanda FDA to support local manufacturers of solid and liquid pharmaceutical products, medical equipment, and devices to conduct rapid quality assurance systems and cGMP capacity assessments, work with them to compile CAPA plans, and provide technical assistance to address gaps and update their QMS documents, including a quality risk management plan.
- Train Rwanda Medical Supply (RMS) Ltd. staff to build their capacity in ISO 9001:2015 QMS, internal audit, and use of its SOPs.
- Offer RMS Ltd. technical assistance in conducting an internal mock audit after the training.
- Support UR to train laboratory staff on method validation and verification, equipment calibration, design of experiments, uncertainty calculations, and more.

Senegal

PQM+ works with the new *Agence Sénégalaise de Regulation Pharmaceutique du Senegal* (ARP), a fusion of the former *Direction de la Pharmacie et du Médicament* (DPM) and

Laboratoire National de Contrôle des Médicaments (LNCM), to strengthen its market surveillance function through a PMS unit to implement RB-PMS and to improve the capacity for medicines registration. In addition, PQM+ provides support to ARP's National Medicines Control Laboratory (*Direction de Contrôle Qualité*/DICQ) to improve its capacity to test medicines.

In February 2022, following the GBT assessment of October 2021, Senegal embarked on a process to develop an action plan to attain GBT ML 3 by December 2022, based on direction from the president, Macky Sall. Both institutions, LNCM and DPM, were therefore busy with this process and started putting together the regulatory documents required. As a result, between February – April 2022, both beneficiaries were not available for implementation of PQM+ activities given ARP had prioritized development of regulatory documents (laws, guidelines, SOPs) over activities such as implementing RB-PMS (sampling and testing) and ISO 9001 support for ARP, which were in the PQM+ workplan. In April 2022, a law was passed establishing a new medicines regulatory authority in Senegal and a new Director General was nominated. This further delayed implementation as ARP also focused on the operationalization of the new agency which included the development and implementation as new organogram.

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

RB-PMS of antimalarials. In Q3, PQM+ reviewed Senegal's 2022 RB-PMS report and, in May, supported ARP's PMS Unit to disseminate the results of the PMS exercise. Of the 249 samples collected from 224 public and private sector sites, from six regions in Senegal (*Kaolack, Djourbel, Dakar, Kolda, Kedougou and Ziguinchrr*) 81 percent were registered and the other 19 percent had special importation permits. All 249 samples collected met their respective quality specifications. These results are not nationally representative.

After the dissemination workshop, the PMS unit trained the samplers designated to collect the antimalarial samples for the 2023 RB-PMS. The trainers were the president and vice president of the Senegalese PMS unit. The president emphasized the need for the samplers to comply with the minimum number of samples to collect per region, with the molecules selected for each axis, the coding of the samples, the substitution criteria, the sample expiry dates, and the need for good calibration of the thermo-hygrometers to be used. The vice president trained the samplers on the three-level approach to testing (physical and visual inspection, MiniLab™ testing, and confirmatory testing), as well as the importance of properly filling out the sampling sheets.

ISO/IEC 17025 trainings. In supporting DICQ to close its QMS gaps, PQM+ conducted a refresher training on key QMS topics (out-of-specification (OOS) and internal quality checks (IQCs)) for which the laboratory does not yet have the expertise. This training will help DICQ close its knowledge and process gaps on these topics. These two key processes ensure the validity of results generated by DICQ. The training taught 18 people about IQC and 21 people about OOS.

Due to deteriorating security conditions in Senegal toward the end of May and into June, PQM+ suspended all planned in-country activities until stability was restored. As a result, activities related to ISO 9001 were rescheduled for Q4.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Conduct a baseline assessment of ARP, per the ISO 9001 standard.
- Conduct an ISO 9001 awareness training.
- Support ARP to develop/revise QMS documents identified during the ISO 9001 baseline assessment.
- Support the PMU unit to sample and test the antimalarial samples for the 2023 RB-PMS.

Asia Region

Asia Bureau

PQM+'s technical assistance funded by USAID's Asia Bureau aims to promote regional regulatory convergence and reliance. PQM+ works 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

Toward the end of this quarter, the ASEAN PPWG provided feedback on three activities waiting on their consent: a regional workshop to disseminate findings from the PQM+-led regional quality assurance landscape analysis; active pharmaceutical ingredient training of trainers; and lot release assessment. ASEAN PPWG requested that PQM+ revise and resubmit the activities' concept notes based on their feedback. PQM+ submitted the revised concept notes and was awaiting the PPWG's final approval. Activities next quarter will depend on the final approval.

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

PQM+ developed a multi-stage selection methodology to identify priority LMICs in the Asian region for increasing domestic pharmaceutical product manufacturing capability to meet local pharmaceutical needs. The PQM+ team then developed a prioritization framework and identified several countries (i.e., Vietnam, Indonesia, Uzbekistan, Kazakhstan, and the Philippines) for evaluating eligible countries' capability to increase the local production of health products and a scoring criterion for shortlisting countries for further qualitative research.

In Q3, following discussions with USAID and based on the prioritization framework, the team selected the Philippines as the focus country to conduct a deep-dive analysis.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Onboard a consultant to kickstart the Philippines deep-dive analysis.

Bangladesh

In Bangladesh, PQM+ works with the Directorate General of Drug Administration (DGDA). DGDA oversees medical product quality in the country and develops and implements national pharmaceutical policy and regulations. The authority also registers medicines, approves licenses, inspects pharmaceutical establishments, and controls the advertisement and promotion of 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 achieve WHO ML 3 in vaccine regulation; providing technical assistance (TA) to the National Control Laboratory (NCL) to strengthen its medicines quality monitoring systems, particularly as they pertain to vaccines; and supporting manufacturers in boosting production of quality-assured first-line TB medicines and GMP.

For PY4, PQM+ expanded activities to support the Directorate General of Livestock (DLS) in strengthening regulation of animal health products in collaboration with DGDA to prevent AMR and providing technical assistance to the Institute of Epidemiology Disease Control and Research (IEDCR) for accreditation of its Public Health Laboratory.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ is supporting DGDA to finalize the regulatory framework document.

- The regulatory framework document will help DGDA to map out all activities with existing and upcoming/required legal and regulatory systems that will ensure the required level of oversight of its regulatory functions and promote good governance. PQM+ has been working with the DGDA committee to prepare the final draft of the regulatory framework. On June 25, 2023, PQM+ supported DGDA to organize the second task force committee meeting to finalize the "Regulatory Framework Document." The regulatory framework is finalized with some minimal updates in the section on definitions, good governance, and terms of references. It was decided to synchronize the Regulatory Framework Document with the proposed drug act 2023 before authorization and approval.
- PQM+ is supporting DGDA to finalize and disseminate the five-year strategic plan for the NCL.
- The Deputy Chief of the NCL and the Director of Administration at DGDA reviewed the five-year strategic plan and suggested some modifications, which PQM+ addressed. PQM+ has been working with DGDA teams to develop the document.

PQM+ supported the Ministry of Health and Family Welfare (MoHFW) of Bangladesh to develop the Fifth Health, Population, and Nutrition Sector Program (HPNSP- 2024-2029).

- In Q3, PQM+ supported DGDA in developing the Annual Operation Plan of the Administration and Management of Quality and Affordable Drugs (AMQAD). The first draft of the plan has been submitted to the MoHFW for review.

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

Sub-Objective 2.1. Support DGDA to make improvements across seven regulatory functions toward sustainable systems development for DGDA. PQM+ continued to support DGDA toward the eventual achievement of WHO ML 3 through the implementation of an effective QMS and IDP.

- In May, WHO reviewed DGDA's CAPA progress and provided recommendations. PQM+ closely supported DGDA during the review visit, and supported DGDA staff to address the recommendations.
- To comply with a QMS sub-indicator (RS05.11), DGDA requested PQM+ support of an external audit to assess the regulatory system performance toward ML 3. From May 22

to 24, the PQM+ technical team performed an external audit of the regulatory system of all nine functions: National Regulatory System (RS), Registration and Marketing Authorization (MA), Vigilance (VL), Market Surveillance and Control (MC), Licensing and Establishment (LI), Regulatory Inspection (RI), Laboratory Testing (LT), Clinical Trial Oversight (CT), and Lot Release (LR). This assessment helped DGDA better prepare for the final WHO assessment.

PQM+ is assisting DGDA to prepare the draft regulatory framework documents for medical devices.

- In Q3, PQM+ completed the "Medical Device/In-Vitro Diagnostics (MD/IVD) Regulatory Framework Gap Assessment, DGDA, Bangladesh" report and submitted it to the DGDA medical device regulatory focal point for preparing the next course of action based on the assessment's recommendations. The gap assessment report is the first guiding document for DGDA's medical device regulatory department to begin to mitigate the gaps toward establishing effective medical device regulation in Bangladesh.
- On May 9, PQM+ Chief of Party Dr. Syed Umar Khyyam met the head of the Directorate General of Family Planning (DGFP), Shahan Ara Banu, and briefed her about PQM+ activities related to the directorate. Dr. Khyyam noted that PQM+ intends to strengthen the NQCL's medical device testing laboratory to test condoms. Strengthening the RB-PMS system for condoms will guard against marketing of SF products. The DGFP Director appreciated the initiative and showed willingness to further collaborate in PQM+ Program Year 5.

PQM+ has been supporting DGDA in developing an RB-PMS system. Activities include:

- On May 8, DGDA issued a request letter to the Line Director of the National Tuberculosis Program (NTP) for providing support to DGDA's initiative to conduct RB-PMS of first-line anti-TB medicines.
- In response, on May 21, the NTP Line Director issued an official memo authorizing DGDA inspectors to collect drug samples per protocol from the NTP outlets. This is DGDA's first effort to conduct quality surveillance of programmatic anti-TB medicine in the country using the MedRS tool. Successful implementation of the first-round survey will help DGDA and NTP decide on routine/periodic RB-PMS for ensuring the quality of anti-TB medicines. This surveillance is critical to ensure effective treatment outcomes for TB patients.
- On May 25, the PQM+ Chief of Party visited the NTP program manager and shared the findings of the "Rapid Assessment of SF Anti-TB Medicine in the Private Sector" conducted in PY4, and discussed potential TB activities for the upcoming PQM+ Bangladesh PY5 work plan.
- Also that day, the USAID team visited the Cox's Bazar MiniLab site. The district inspectors demonstrated RB-PMS activities and procedures on how to test medicines using MiniLabs. The visitors emphasized expanding the RB-PMS system to monitor the quality of veterinary products to reduce the risk of AMR.
- On May 29, PQM+ conducted an online training session on protocols for field inspectors who will collect samples of first-line anti-TB medicines for RB-PMS. The 43 inspectors who attended the training session included 30 men and 13 women.
- On June 6, PQM+ supported DGDA in distributing nine cold boxes to the divisional MiniLab sites (Barisal, Rajshahi, Sylhet, Rangpur, Chattogram, Khulna, Mymensingh,

Cox's Bazar, and Dhaka) for starting RB-PMS of vaccines. These cold boxes will help the authority maintain the cold chain management of vaccines during transportation.

- On June 11, DGDA sent the final RB-PMS sampling and testing protocol of anti-TB medicines, along with the authorization letter from NTP, to the field inspectors through email. The field inspectors are collecting samples from NTP outlets for RB-PMS of anti-TB medicines using the MedRS tool.
- From January to April, 848 samples of medicine were tested through nine MiniLabs. Of these, two samples (one ciprofloxacin and one cetirizine HCL) failed initial testing, and samples were sent to NCL in April for the confirmation test.

PQM+ is providing technical support to DGDA and NCL to review and implement standard vaccine lot release guidelines.

- The Deputy Chief of NCL, Dr. Md. Harun-Or-Rashid, reviewed the draft guidelines and provided recommendations to incorporate. In Q3, PQM+ addressed the recommendations and submitted them to the PQM+ headquarters expert for technical review.

PQM+ is providing technical assistance to DGDA's regulatory inspection department to develop a RBI system to achieve ML 3 of these functions.

- On April 4, the Director General of the Drug Administration nominated three DGDA staff members to attend pilot testing of the RBI tool initiated by the PQM+ program.
- From April 11 to 14, the PQM+ headquarters team provided a virtual orientation on how the online tool operates to execute RBI to facilitate GMP inspections.
- On May 10, three DGDA inspectors attended the final testing session on RBI tool with PQM+ headquarters experts Teferi Bedane, Mohammad Asghar, and local lead Shaiful Khan. The inspectors presented all the steps and inspection elements they completed for three manufacturers to test the tool. The tool developer resolved difficulties observed during testing. Finally, the inspectors completed the overall checklist prepared for this pilot test. The tool will help inspectors conduct RBIs and perform online reporting of the findings.

PQM+ is supporting DGDA to assess the authority's current practices in providing registration for manufacturing APIs in the country.

- PQM+ supported DGDA in the assessment of DGDA's current practices of API drug master filing (DMF) and approval process of API manufacturing facilities. The report is under PQM+ internal technical review. The assessment will help DGDA to take steps and perform activities to establish an effective registration process for API.

PQM+ is supporting the rapid assessment of SF anti-TB medicines in the private sector.

- From April 9 to 13, NCL laboratory experts conducted MiniLab testing of the anti-TB medicine samples collected during rapid assessment at DGDA's Motijheel office. The representatives from the research team were present. The rapid assessment report is under review at headquarters.

Sub-Objective 2.2. Medical product NQCL capacity strengthening to support sustainable PMS program. PQM+ is providing technical assistance to enhance the capacity of NCL's vaccine laboratory to achieve and sustain WHO ML 3.

- On April 10-11, PQM+ provided technical assistance in installing enzyme-linked immunosorbent assay (ELISA) reader and washer with the help of the supplier followed by operational qualification. This machine determines the potency/efficacy of the oral cholera vaccine.
- On May 13, WHO South-East Asia Regional Office (SEARO) scientist Dr. Anil Chawla visited to the NCL vaccine wing to review the CAPA plan for lot release and laboratory testing. PQM+ supported the NCL representatives with the CAPA review meeting.
- On May 16, PQM+ met with the deputy chief of NCL and visited the NCL vaccine wing and reviewed the operationalization of new equipment. The deputy chief shared NCL's ongoing routine and development activities.
- On May 25, PQM+ organized training on the operation, cleaning, and maintenance of the endotoxin detection and analysis software WinkQCLTM (Lonza). Twenty NCL technical staff (15 men and five women) received the training and learned to operate the software and maintain the machine. The training participants will be able to apply their learning to test the endotoxin content of locally manufactured vaccines as well as imported vaccines by using the kinetic chromogenic method per the British Pharmacopeia. Later, PQM+ will provide further training on method validation or verification of the bacterial endotoxin content test for locally manufactured vaccines by the chromogenic kinetic method.

PQM+ is helping DGDA build the capacity of the Central Drug Testing Laboratory (CDTL), Chattogram to test medicine quality and continue technical assistance to the NCL physicochemical lab.

- On May 3, PQM+ conducted an online training for CDTL staff on the SOP of analyst validation as part of the quality management system. Three analysts, all men, attended.
- On May 25, PQM+ met with Md Salahuddin, Director Admin of DGDA, and shared the status of implementing the DGDA's earlier meeting decisions on functioning CDTL. The Director Admin recommended another meeting with the Director General of DGDA to review the implementation status.

PQM+ is providing technical assistance to Plasma Plus Research and Testing Laboratory (PPRTL) to address CAPA to achieve international standards on medical product testing (WHO-PQ, ISO/IEC 17025:2017).

- On May 14, PQM+ visited PPRTL to observe progress against the CAPA plan generated from the PQM+ gap assessment conducted last year. The team recommended the PPRTL management take necessary actions to close all remaining CAPAs. PQM+ supported PPRTL to review three SOPs on environmental monitoring, employee training, and the calibration program.
- On June 7, PQM+ conducted a follow-up visit to the PPRTL to review the progress against the CAPA plan and discussed it with the head of the lab and dean of the Pharmacy Department at Independent University of Bangladesh.

PQM+ is providing technical support to IEDCR toward accreditation (ISO 15189 & 15190). Achievements include:

- On April 9, the PQM+ technical team conducted a laboratory assessment in the molecular section of the virology laboratory at IEDCR. On April 11, they shared the assessment findings on equipment, room cleanliness, logbook maintenance, and room

organization with IEDCR's senior personnel and laboratory analysts. IEDCR will update the equipment database and label it with unique identification numbers and monitoring room/refrigerator/freezer temperatures, as well as prepare equipment maintenance forms and authorization forms.

- From May 8 to 11, PQM+ led a four-day training on ISO 15189 at IEDCR. The 42 participants (24 men, 18 women) included senior officials and laboratory analysts. The training focused on explaining the ISO 15189:2022 guidelines covering quality and competence in medical laboratories. During the training, participants understood the ISO 15189 standards in management, resources, process requirements, etc. This training helped them identify the necessary documents and practices to implement and plan the next steps for ISO accreditation. IEDCR Director Prof. Dr. Tahmina Shirin attended the closing session and expressed gratitude to PQM+ and hopes that participants would work toward accreditation using their newfound knowledge.
- On May 14, PQM+ assessed the virology and microbiology laboratories of IEDCR, thoroughly examining the facilities while engaging in discussions with lab analysts regarding laboratory procedures and reviewing existing documentation.
- On May 18, PQM+ met with senior management team members of IEDCR, including the director, to discuss and agree on recommended way forward activities. She suggested reviewing ISO training notes as guidance to attain the necessary standards.

Objective 3. Optimize and increase financial resources for medical product quality assurance

PQM+ is supporting DGDA and NCL management to prepare a proposal to rationalize the testing fee structure.

- On April 6, PQM+ organized a meeting for testing fee modification proposal preparation for NCL/DGDA and this proposal will be sent to Ministry for approval by DGDA. DGDA will modify the existing testing fee for CDTL, DTL, vaccines, registration, and others.
- On April 11, PQM+ facilitated a second formal meeting in the presence of DG and other Directors of DGDA, the Deputy Chief of NCL, and PQM+ Chief of Party to monitor the progress of preparing a proposal for MOHFW and Ministry of Finance for revision of testing fees.

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

PQM+ is continuing technical support to Bangladesh Manufacturer 2 toward the prequalification of first-line TB medicines.

- In April, the manufacturer completed production of two batches of 100,000 units (1’00’000 unit) of four-drug fixed-dose combination (4FDC).
- In early May, the manufacturer submitted all the relevant documents to ACDIMA BioCenter to get Jordan Food and Drug Administration approval for sending the bio-batch samples to Jordan.
- On June 3, contract research organization (CRO)-ACDIMA Biocentre in Jordan started a pivotal BE study for prequalification of first-line TB medicines of Bangladesh Manufacturer 2. The CRO completed two phases of dosing on June 7 and June 14.

PQM+ is providing technical support to Bangladesh Manufacturer 3 to conduct good practices (GxP) training for technical staff based on TNA.

- PQM+ organized an advanced training on GxP in pharmaceuticals for the technical staff of this manufacturer at its Bogura plant June 11 to 13, and its Khulna plant on June 20 to 22, to enhance knowledge and understanding of the current global regulatory requirements of basic GMP, QMS, and data integrity. In Bogura, 28 participants (27 men and one woman) attended, and in Khulna, 13 participants (all men) received training. Through this training, the technical staff learned to assess the pharmaceutical products, relevant guidelines used by the regulatory authorities for evaluation, current GMP, QMSs, and data integrity, which ultimately help them during product evaluation, licensing, and continuous monitoring.

PQM+ is providing technical assistance to build the capacity of a local CRO to support a BE study in the country.

- On May 3, PQM+ completed gap assessment reports for the three selected CROs.
- On May 7, PQM+ shared reports with the relevant CRO personnel through email. PQM+ is providing technical assistance to the CROs to develop a CAPA plan based on the assessment report's recommendation. This assessment report will help the CROs understand the gaps and lacks required to mitigate toward standardizing good clinical practices (GCP) and good laboratory practices (GLP).

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

PQM+ is providing technical assistance to DGDA for situational analysis and planning of strengthening regulation capacity, marketing surveillance, control, and quality testing of anti-microbial veterinary medicines at national and sub-national levels.

- On April 4, PQM+ had an online meeting with Siva Sai Ani Krishna and Dipankar Das on moving forward with a situation analysis of four departments of the Directorate of Livestock.
- On April 10, PQM+ met with Dr. Md. Abu Sufiun, Director, Account, Budget, and Audit, DLS. He agreed to provide information about the functions, testing scopes, equipment, and existing human resources of the labs to support preparation of the scope of work of the consultant. A four-member team was proposed to accomplish this activity.

PQM+ is providing technical support to DGDA and the Ministry of Fisheries and Livestock and DLS in developing Bangladesh National Veterinary Formulary.

- On May 30, PQM+ consultant Dr. Kazi Rafiqul Islam submitted the draft Bangladesh National Veterinary Formulary to PQM+ headquarters for review.

Table 3: Status of Labs Accreditation in Bangladesh

Laboratory	Accreditation Sought	Initial Gap Assessment	CAPA	QMS	PT/LT	LIF	Official Inspection/ Pre-Assessment
National Control Lab (Physico-chemical Lab)	ISO: IEC 17025/2017 (reaccreditation) by ANAB	Complete	Complete	Complete	Complete	Submitted and approved	Reassessment completed (August 30 to September 1). Certificate renewed in 2022. In July 2023 there will be a re-assessment.
National Control Lab (Microbiology Lab)	ISO: IEC 17025/2017 (reaccreditation) by Bangladesh Accreditation Board (BAB)	Complete	Complete	Complete	Complete	Submitted and approved	Achieved BAB accreditation in 2017

Laboratory	Accreditation Sought	QMS	Initial Gap Assessment	CAPA	LIF	Official Inspection/ Pre-assessment
National Control Lab (Physicochemical Lab)	WHO PQ	Complete	Complete	CAPA closed	Submitted and approved	Achieved WHO PQ in March 2020.
National Control Lab (Microbiology Lab)	WHO PQ	Complete	Complete	CAPA closed	Submitted and approved	Achieved WHO PQ in March 2020.
National Control Lab (Microbiology Lab +Vaccine Chemical lab)	WHO ML 3	Complete	Complete	CAPA closed	-	Reassessment by WHO is pending; ML 3 not yet been achieved

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Finalize the DGDA regulatory framework document.
- Finalize the NCL five-year strategic plan.
- Conduct a divisional workshop on National Quality Assurance Guidelines
- Prepare a proposal to rationalize the NCL testing fees.
- Complete the assessment of DGDA practices in API DMF processing and approval of API manufacturing facilities.

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+ delivered a five-day in-person training on HPLC, dissolution, and potentiometric titration at DFDA Pharmaceutical Chemistry Laboratory, Nay Pyi Taw.

- The 27 participants (two men, 25 women) from DFDA Pharmaceutical Chemistry Laboratories in Nay Pyi Taw, Yangon, and Mandalay attended the training.
- The training took place in collaboration with the Malaria Unit from the WHO Country Office, which supported the expenses (travel, lodging, per diem) for the traveling participants from Yangon and Mandalay DFDA Laboratories.
- This training strengthened the technical expertise of DFDA analysts in performing routine testing and standardizing the testing procedures across the three laboratories.

PQM+ delivered a five-day in-person training on analytical method validation and verification and laboratory safety at Burma Manufacturer 1 in Yangon.

- Participants included 14 people (one man, 13 women) from the manufacturer's QC laboratory.
- This training improved the analysts' skills in performing method validation, a critical procedure that ensures reliable and accurate QC testing on medicines they produce.
- PQM+ also revisited the analytical workflow at Burma Manufacturer 1 and assisted in reviewing and revising 12 procedures.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Conduct an on-site cGMP assessment at Burma Manufacturer 1.
- Organize an in-person training on Organizing Inter-Laboratory Comparison at DFDA.
- Organize an in-person training on measurement uncertainty and organizing intra-laboratory comparison at Burma Manufacturer 1.

Nepal

PQM+ provides technical assistance to Nepal's Department of Drug Administration (DDA) to strengthen medical product quality assurance (QA) and 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.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

Development of technical guidelines to the updated GMP code. PQM+ coordinated with DDA's inspection TWG to facilitate development of five technical guidelines to complement the updated

GMP code. In Q3, PQM+ supported DDA to finalize the fifth technical guideline in addition to the four the TWG previously approved. Further, DDA has put these guidelines in the approval process, following completion of legal review.

Guidelines on safe disposal of unwanted pharmaceuticals. DDA organized an extensive discussion on the issue of safely disposing unwanted medicines with WHO and PQM+ to examine current government guidelines and gaps. The DDA suggested adding a technical annex to the current guidelines regarding the disposal of pharmaceutical products generated through regulatory activities such as recall, testing, seizures, etc.

Assist development of the Nepal Pharmaceutical Manufacturing Strategy. The Nepal Pharmaceutical Manufacturing Strategy aims to strengthen domestic production for self-sufficiency and increase the quality of essential medicines in the country. In Q3, DDA agreed to start the strategy formulation process with internal and external consultations. PQM+ developed a background paper for strategy development and engaged a PQM+ regional expert to support it. PQM+ developed a questionnaire and list of experts for a consultative process to gather information on a manufacturing strategy.

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

Strengthen RBI of DDA. In Q2, PQM+ facilitated DDA's inspection TWG in risk ranking all the manufacturers following the RBI framework and preparation of an RBI plan. In Q3, DDA inspected 10 of 19 manufacturers categorized as high risk by the RBI framework. PQM+ is coordinating with DDA to pilot an RBI tool to inspect manufacturers and conducted an orientation session on the tool for DDA. The inspection TWG further discussed the finalization of RBI-related guidelines, SOPs, and additional steps for their approval.

Strengthen DDA's product registration and marketing authorization function. PQM+ is assisting DDA with registration and marketing authorization functionality to facilitate the medicines registration and authorization process in line with international best practices. In Q3, PQM+ supported DDA to draft five SOPs per GBT recommendations and conducted a technical review of two SOPs (labelling requirements and issuance of product and marketing license). PQM+ also coordinated with DDA and the Association of Pharmaceutical Producers of Nepal (APPON) to facilitate adoption of the CTD format. Finally, PQM+ supported DDA in drafting templates for a quality overall summary (QOS) and quality information summary (QIS) for solid oral dosage in line with the CTD format, then shared it with DDA and APPON for final review.

Strengthening the RB-PMS of DDA. During Q3, PQM+ supported DDA's nationwide RB-PMS rollout to its branch offices for sample collection. In Q3, PQM+ worked with DDA's Biratnagar branch office for sample collection in four districts, per RB-PMS protocol. With the technical and logistic support from PQM+, 38 medicines from 28 brands were sampled from both private and government-owned facilities. In addition, Birgunj and Nepalgunj branch offices continued their RB-PMS sample collection. PQM+ is assisting DDA's Management Division to prepare and finalize the report on the pilot round of RB-PMS conducted last year.

Support NML toward ISO 17025 accreditation. After a SATTA exercise in January, PQM+ and NML worked together to finalize a CAPA plan and reviewed the SATTA report for final dissemination. A PQM+ expert joined the Nepal team to facilitate two hands-on trainings on analytical method validation/verification and measurement of uncertainty to 22 lab technical personnel. PQM+ supported NML to organize a TWG meeting to follow up on the corrective

actions for nonconformances raised in the internal audit. PQM+ supported NML to organize implementation training on seven SOPs, per SATTA recommendations. PQM+ continued its assistance toward enhancing NML's warehousing capacities for storage and acquiring essential testing equipment, including a semi-micro balance, digital refractometer, F1 class weights, dissolution calibration toolkit, and file optimizer. PQM+ also facilitated the procurement of British Pharmacopoeia and Indian Pharmacopoeia for NML. The program also assisted NML with enrolling in the dissolution proficiency test program.

Assist NML in the selection of private laboratories for outsourcing testing activities. To expand quality testing of medicines in Nepal, PQM+ completed baseline assessments of another private laboratory using SATTA. The assessment report of the first private sector laboratory is finalized with a CAPA plan in place following technical reviews, while a second lab assessment report is written, along with a proposed CAPA plan.

Strengthen management information system of regulatory bodies. PQM+ is supporting DDA and NML to strengthen their information management system on the following areas:

- *Risk-based inspection tool*: PQM+ recently developed an RBI tool to assist regulatory bodies in conducting inspections using the principles of RBI. The home office chose DDA Nepal to pilot the RBI tool on GMP as a test. Presently, DDA's inspectors are participating in the pilot program, receiving direct support from experts from the PQM+ home office.
- *Making the MedRS tool interoperable with DDA's current information system*: PQM+ Nepal is coordinating with a home office expert about acquiring the source code to install MedRS on DDA's local server to allow interoperability with DDA's existing system.
- *Electronic data integrity management system at NML*: PQM+ supported NML in installing and upgrading a server to host the laboratory data and the home office assisted with finalizing the procurement of laboratory data management software. The software installation process is ongoing and user training is planned for Q4.

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

Develop a five-year laboratory optimization strategy. After approval by the Ministry of Health and Population (MoHP) to develop NML's five-year strategy, NML formed two committees: a steering committee to oversee and approve the strategy document and a working committee to provide direction in the strategy development process. In Q3, PQM+ helped with drafting the strategy through consultative meetings and interviews and facilitated three working committee meetings on the strategy to receive feedback and review the draft. PQM+ collaborated with the working committee to draft a strategy that now is under review.

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

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

Private manufacturers. In Q3, PQM+ conducted a CAPA follow-up of one manufacturer and provided support in product development. PQM+ is also helping three other manufacturers acquire innovator samples of azithromycin (Zithromax) for WHO prequalification. The other manufacturers have procured API that is WHO-prequalified or approved by a stringent

regulatory authority for product development; these manufacturers are in the process of conducting product development and stability studies.

Public manufacturer. PQM+ is working with the country's only public pharmaceutical company, Nepal Ausadhi Limited (NAL), to achieve compliance toward national GMP certification. After reassessment of NAL, in Q3, PQM+ is supporting calibration, qualification, and validation of manufacturing equipment and facilities for GMP compliance. For this, PQM+ has acquired services to assist NAL from the external service-providers. This program year, PQM+ has supported NAL with reference standards and impurities that USP has available, enabling NAL to obtain marketing authorization for new products (folic acid tablets, hemodialysis powder, and hemodialysis solution) and initiated product development for a few others.

Strengthening of local HTP manufacturers. PQM+ is assisting the health technology product (HTP) manufacturer of disposable syringes and blood collection tubes for technical assistance to attain ISO 13485. After a baseline assessment and CAPA development, the manufacturer addressed major nonconformities in Q3. PQM+ conducted a follow-up visit to the manufacturer to review the CAPA progress and assessed the feasibility of applying for ISO accreditation.

Support establishment and upgradation of bioequivalence laboratory. PQM+ Nepal supported the assessment of two potential BE laboratories (Tribhuvan University and Kathmandu University) and made recommendations to function as a CRO. In Q3, PQM+ drafted assessment reports and shared them with the BE laboratories to develop IDPs.

Improve quality assurance in the supply chain of medicines in local government units. PQM+ is working with two local government units (LGUs) in Bagmati Province to ensure quality assurance in the medicines procurement process. PQM+ assessed the quality assurance of one LGU's procurement process last year and the second is this year. In Q3, PQM+ initiated the strengthening of the procurement committee of one LGU through quantification, forecasting, and procurement training.

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

Increase awareness of SF medicines among public and health professionals. In Q3, PQM+ initiated the process of developing a training curriculum on the visual identification of SF medicines. The training curriculum aims to strengthen the capacity of health professionals such as pharmacists, physicians, nurses, and paramedics through their respective councils. Also this quarter, PQM+ partnered with Nepal's National Health Research Council to facilitate a session on "Promoting the Quality of Medicines in Nepal" at the council's annual summit for health and population scientists. PQM+ presented on the topics of quality assurance in procurement and regulatory provision. Diverse public health professionals attended and commented on the presentations, followed by an hour of panel discussions and participants' feedback.

Strengthen stakeholders' coordination through DDA to combat circulation of SF medicines. In a move to promote awareness and develop coordination between government agencies and civil society stakeholders, PQM+ supported DDA's Birgunj branch office to organize a workshop to strengthen stakeholders' coordination and collaboration to combat the circulation and proliferation of SF medicines in its customs border areas. The workshop facilitated by DDA drew representatives from customs, narcotics control, local governments, district administrations, and civil society who shared their experiences and revealed the need for better coordination and action to prevent SF medicines from proliferating in border areas. A border coordination

framework agreement to jointly combat the proliferation and circulation of SF medicines has been drafted for review by concerned authorities.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Continue to advocate with DDA for approval of the technical guidelines to the updated GMP code and prepare to disseminate the code and the guidelines.
- Support DDA to adopt the CTD format, starting with the solid oral dosage form and simultaneously supporting a manufacturer and DDA with training on dossier submission and evaluation.
- Collaborate with DDA's inspection division on piloting the RBI tool for GMP inspection of selected manufacturers.
- Collaborate with the NML to finalize the five-year strategy and share it with DDA and MoHP for approval.
- Support NML to finalize the electronic data management system installation, testing, and training to staff. At DDA, PQM+ will technically facilitate the piloting of the RBI management information system tool developed by PQM+ headquarters. The Nepal office will acquire the source code to begin integrating the MedRS tool into DDA's system.
- Continue to strengthen the QMS through development of procedures and technical training. PQM+ will support NML in drafting a training curriculum to institutionalize the training program within the organization. PQM+ will finalize the assessment and CAPA report for the second private medicines testing laboratory.
- Continue to support DDA in finalizing the SOPs and guidelines related to RB-PMS and continue to develop an RB-PMS training curriculum and materials.
- Work with two manufacturers to finalize a roadmap for WHO PQ for azithromycin tablets and further support product development of zinc sulfate and azithromycin tablets.
- Continue to support the public manufacturer to strive toward national GMP standards, focusing on the validation of its manufacturing units to meet the standards.
- Strengthen, through trainings and workshops, procurement committees and technical staff of the local government to improve quality assurance in medical products procurement at local government units.
- Organize training sessions to test and validate the training course on visual identification of SF medicines for health professionals.

Pakistan

In Pakistan, PQM+ is addressing challenges around the provision of and access to quality health services 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 AMR; 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: Develop national medicine implementation plan. Pakistan's Ministry of National Health Services, Regulation, and Coordination has assembled a TWG on development of a National Medicine Policy (NMP) comprising stakeholders and subject matter experts after thorough consultation of PQM+. This TWG will be instrumental in developing the NMP implementation roadmap. PQM+ conducted meetings with the health and pharmaceutical authorities in the provinces of Khyber Pakhtunkhwa, Punjab, Sindh, and Baluchistan to discuss the NMP implementation plan. The officials were provided with a comprehensive briefing on the NMP roadmap, outlining its strategic objectives, implementation plan, and the role of provincial governments and other stakeholders. The authorities expressed appreciation for the PQM+ initiative in strengthening the health care system of Pakistan through the NMP. The onboarding of provinces will facilitate a smooth transition and closure of this activity, ensuring implementation of the NMP across the country. Progress includes:

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

Activity 2.1: Continue to provide TA to DRAP to address gaps identified in its GBT through the implementation of an IDP. In Q3, DRAP underwent an audit by the National Regulatory System using WHO GBT indicators for nine regulatory functions. The WHO Regulatory System Strengthening (WHO-RSS) team conducted the audit from May 3 to 12.

Activity 2.2: Continue support to DRAP for its accession to PIC/S. DRAP submitted an application for PIC/S accession with technical assistance from PQM+. Before submission, the PQM+ team conducted an expert review to address gaps in the DRAP application. The PIC/S will evaluate the application at its upcoming meeting in November.

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

Activity 3.2: Continue to support NQCL to develop a lot release system for vaccines. During Q3, PQM+ provided technical support to the National Control Laboratory for Biologicals (NCLB) of DRAP to revise and implement the lot release system, per WHO guidelines. PQM+ provided guidance and support to NCLB staff during the WHO GBT inspection of the lab. PQM+ also supported the NCLB DRAP technical team in developing a QMS per WHO Guidelines and IEC/ISO 17025 standards.

Activity 3.3: Provide TA to selected labs to acquire ISO 17025 accreditation/WHO PQ for testing methods of antimicrobial and maternal and child health products. In Q3, PQM+ provided guidance and technical support to the Central Drug Testing Laboratory of DRAP in Karachi during the implementation of a CAPA plan to address major and minor observations in the laboratory's WHO PQ inspection report. The final CAPA will be submitted to WHO after completion of computer system validation, which is in process.

Mock inspection: PQM+ conducted three days of on-site mock inspection of DTL Bahawalpur following applicable WHO guidelines. PQM+ supported DTL Bahawalpur in developing and

implementing a CAPA plan to address observations in the mock inspection report and in revising the laboratory information file (LIF) per WHO PQ guidelines.

QMS for NIH Lab: PQM+ supported the NIH Lab staff in developing a QMS for the lab, including internal audit, complaint handling, document control, job descriptions, and deviation management systems. PQM+ conducted a gap assessment of the NIH-appellate lab according to the IEC/ISO 17025 standard.

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

Activity 4.1: Provide TA to four selected manufacturers to achieve WHO PQ for quality-assured manufacturing of zinc and amoxicillin dispersible tablets (key MCH priority products). Following technical justification and advocacy by PQM+, WHO's prequalification team accepted the waiver for the palatability study of zinc dispersible tablets for Pakistan Manufacturer 9. WHO will come back with suggestions for dossier modification by adding more technical information to justify a waiver of the palatability study.

Pakistan Manufacturer 2, which produces amoxicillin DT and is supported by PQM+, has drafted a CTD dossier to WHO. PQM+ reviewed the dossier and shared feedback with the manufacturer.

Activity 4.3: Continue to develop national capacity to conduct BE studies to assess the safety and efficacy of priority medical products. With assistance from PQM+, DRAP conducted a training for its staff on GCPs. After securing formal Cabinet approval to revise Biostudy Rule 2017 to remove the unnecessary requirements, DRAP issued a notification to revise the BE study application format. Both selected BE centers have submitted revised applications for a real-time BE study with PQM+ technical assistance and support.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Hold a meeting of the NMP TWG and finalize the implementation plan.
- Review the SOP on good safety surveillance practices in Punjab.
- Review guidelines and SOPs of DRAP for GBT.
- Support DRAP during the WHO final assessment on GBT.
- Implement a CAPA plan of the PIC/S DRAP gap assessment.
- Review the preparation of the WHO final audit for DRAP regarding IDPs.
- Train DTLs on the Pakistan Integrated Regulatory Information Management System interface.
- Develop a gap assessment report of NCLB.
- Train DRAP staff on GCP and GLP.
- Hold a quarterly review meeting with DRAP on PIC/S.
- Assist DRAP with submitting its application for the accession of PIC/S.
- Train BE center staff on GCP/GLP and review the draft study protocol.
- Train NCLB staff on ISO 17025 QMS standards.
- Hold a consultative workshop on the draft national medicine implementation plan.

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 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 PIC/S, as well as to support the NCEM in establishing a risk-based post-marketing surveillance (RB-PMS) system.

In PY4, 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.

WHO GBT. PQM+ is providing technical assistance to NCEM as it continues preparing for the WHO GBT assessment in February 2024 and work toward attaining ML 3. In May, WHO conducted another virtual audit for the WHO GBT. WHO and NCEM agreed on a timeline:

- Assessment of the eight regulatory functions (without lot release) in February 2024.
- An observed GMP audit of the local manufacturer has been confirmed for November 13 to 17, 2023. Since the QazVac manufacturing site will not be ready yet, NCEM will select another pharmaceutical manufacturing site for WHO inspection.
- The QazVac manufacturing site is expected to be ready next year and an observed GMP inspection of that site will happen in October or November 2024, followed by assessment of the lot release function in February 2025.

These timelines help PQM+ plan technical assistance to the NCEM for WHO GBT ML 3.

Laboratory strengthening. In Q3, PQM+ continued technical assistance to the Almaty and Karaganda MQCLs to work toward and maintain WHO PQ.

- With PQM+ technical assistance, Almaty MQCL is preparing for the WHO PQ follow-up audit and implementation of CAPA from the WHO 2022 audit; and Karaganda MQCL is preparing to maintain WHO PQ. In Q3, PQM+ provided an in-person training on nonconformity management and uncertainty measurement for 17 staff from the two labs. The nonconformity training covered establishing and maintaining an effective QMS and the ability to consistently address nonconformities related to laboratory activities and test results. Having a systematic approach to appropriately identify, document, and act on nonconformities aids in assuring the reliability and validity of laboratory results. The second training explained the concepts of measurement uncertainty and its applicability in testing laboratories. Both trainings are important for WHO PQ of the labs. These trainings will help the MQCLs meet WHO PQ requirements.

- Following the training in April, PQM+ conducted a five-day on-site mock audit of the Almaty MQCL against the requirements of WHO good practices for pharmaceutical quality control laboratories in preparation for the WHO PQ audit. The mock audit included participation from Karaganda laboratory representatives and discussion of amendments to SOPs and the lab's readiness for the WHO audit. The mock audit helps the MQCLs identify areas of strength and weakness in preparation for the WHO audit.
- In Q3, a PQM+ expert reviewed the terms of reference for the development of a feasibility study for the Astana new lab project titled "Construction of a National Center for Expertise of Medicines and Medical Devices with Laboratories." This laboratory will include premises for testing medicines, medical devices, and vaccines and will meet biosafety level 3 requirements. PQM+ sent the expert's comments and recommendations to NCEM.

GMP inspection. PQM+ is supporting Kazakhstan in strengthening the inspectorate and preparing for accession to PIC/S, which 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 toward advancing on the roadmap to PIC/S ascension. Notable achievements this quarter include:

- The PIC/s working group worked on amending the Public Health Code and other regulatory documents to bring them in line with PIC/S requirements for licensing manufacturers and handling quality defects. The PIC/S working group also focused on PIC/S indicators 1-21 to assess their status.
- A PQM+ GMP expert visited Astana for several meetings with the PIC/s working group, where they discussed several important areas for PIC/S accession. These include final review of the quality manual, key SOPs, and steps before launching the QMS system; review of the current licensing system and concrete files from 2023; and review of the current situation, clarification of PIC/S requirements, and steps to implement an effective system for handling suspected quality defects. The PQM+ expert also provided training on inspection methodology for 144 inspectors from the Committee and NCEM.

These developments help Kazakhstan prepare for PIC/S ascension. PQM+ is facilitating preparation of the NCEM's PIC/S application; the tentative timeline for application submission is January 2024.

Post-marketing surveillance. PQM+ continued technical assistance to NCEM in strengthening the PMS system by building on the work conducted in the previous quarters. NCEM faced challenges in implementing RB-PMS, as it requires changes in the national legislation and needs financial resources for conducting RB-PMS activities. PQM+ was asked to prepare a presentation for the top management of the Committee to explain the importance of RB-PMS in ensuring the quality of medicines on the market and advocate for its implementation. PQM+ prepared the presentation and provided it to the NCEM in January 2023. In Q3, NCEM and the Committee worked on introducing changes to legislative documents that will allow them to implement RB-PMS in the appropriate form. Following the virtual WHO GBT audit in May 2023, the WHO GBT team provided feedback to NCEM on PMS. NCEM has asked for technical assistance from PQM+ to address these gaps.

SEC capacity building. PQM+ continued work with the NCEM's scientific-educational center (SEC). The center is important to ensure the sustainability of PQM+'s efforts to build the capacity of the medicines regulatory workforce in Kazakhstan. PQM+ discussed with NCEM

appointing five GMP experts to the technical working group; they will work with SEC and PQM+ to draft GMP modules for manufacturers' capacity building. PQM+ received nominations from NCEM and is in the process of coordinating with the GMP experts to kickstart the module development process. But at this point, interest in the development of these modules is low due to the workload of the inspectors for this work.

Medical devices inspection. PQM+ is helping NCEM establish the medical devices inspection unit and build capacity of the group, including training inspectors with a focus on International Organization for Standardization (ISO) 13485. In Q3, PQM+ trained 57 NCEM staff on medical devices QMS auditing. PQM+ is reviewing NCEM's procedures for medical devices inspection, such as regulatory documents, SOPs, the inspections plan, and the inspection report. The review of procedures and training of staff on medical devices is important to help the NCEM align with the ISO 13485.

QMS 9001. 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 PY4 Q2, PQM+ provided technical assistance to the Committee in establishing QMS according to ISO 9001. In Q3, PQM+ identified a local QMS expert to work with the committee to establish QMS. PQM+ expert started work in close collaboration with the committee. PQM+ held several meetings with the management of the committee and conducted an audit of all departments of the Committee and relevant departments of the NCEM. PQM+ also suggested changes to the committee's structure that would help build effective collaboration. The QMS expert held a training on Implementation of a quality management system in accordance with the requirements of the international standard (ISO 9001:2015) for senior management, heads of structural divisions and for the employees of the Medical and Pharmaceutical Control Committee for a total of 167 people in two batches. This training is important to help the committee meet the ISO 9001, a requirement for the WHO GBT ML 3.

Lot release and vaccine testing. To date, PQM+ has provided TA to NCEM in implementing Institutional development plans (IDPs) on lot release and vaccine testing. PQM+ reviewed existing laboratory SOPs and provided feedback to align with the WHO GBT requirements for the laboratory testing and lot release function. PQM+ also facilitated the development of a lot of release SOP.

The timeline for the QazVac vaccine manufacturer facilities construction is delayed, their facilities will not be ready and equipped by the time of the WHO assessment in February 2024. WHO on November 13-17, 2023, will observe a GMP audit of the local manufacturer. Since the QazVac manufacturing site will not be ready by then, NCEM will select another pharmaceutical manufacturing site for WHO inspection. It is expected that QazVac manufacturing site will be ready next year and observed GMP inspection of that site will happen in October-November of 2024.

Provide TA to NCEM operationalize WHO CRP and facilitate registration of TB medicines. Since July 1, 2021, the EAEU regulation for registration of pharmaceuticals came in force in Kazakhstan and the National regulation became inactive. EAEU does not allow the use of WHO CRP for registration of WHO Prequalified medicines. In May 2024 the government of Kazakhstan approved the procedure for the national registration of strategically important medicines that also includes TB medicines. This would allow NCEM use of WHO CRP for registration of WHO prequalified medicines. PQM+ is working with NCEM staff to start WHO CRP capacity building. PQM+ experts met with employees of the Registration Department of the NCEM to familiarize them with WHO CRP requirements and process. PQM+ will continue

working with NCEM on operationalizing of WHO CRP in Kazakhstan. Operationalization of WHO CRP is important to facilitate registration of TB medicines through WHO CRP process to ensure availability of TB medicine to the public.

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

Foundations of GMP. As a cross cutting activity in PY4 Q2 in collaboration with IntraHealth International, PQM+ initiated update and repackage of the "foundation of good manufacturing practices" e-learning modules into Russian for the Central Asia region. PQM+ is in the process of translation and review of the GMP modules into Russian.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Continue technical assistance to the NCEM in preparation for the next WHO GBT assessment in February 2024
- Conduct coaching inspection of local manufacturer.
- Provide face to face trainings for Almaty and Karaganda MQCLs in August and conduct mockup audit as preparation for WHO PQ audit.
- Regular meeting with the top management of NCEM to discuss progress in joint activities.
- Continue technical assistance to the NCEM on developing approaches and procedures for RB-PMS
- Assist the Committee in establishing ISO 9001 QMS by onboarding and introducing the new technical expert.
- conduct training on medical device manufacturing audit for the medical device unit and to update and to collaboratively create inspection documents.
- Continue to translate and repackage the foundations of GMP into Russian

Tajikistan

PQM+ is supporting Tajikistan in strengthening the medicines regulatory system by providing technical assistance to the State Surveillance Service over health care and social protection of population (State service). The main objectives are to improve the medicines registration system and to support the MQCL to ensure access to quality-assured medicines in the country.

In PY4, PQM+ will help:

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

Progress by PQM+ Objective

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

Based on PQM+'s assessment findings, in PY4 Q1, PQM+ with the TWG developed two standard operating procedures (SOPs), one on screening application, and second on evaluation of assessment. The SOPs are with the State service management for review. However, despite efforts to follow up in Q3, there has been lack of engagement from the MRA to provide feedback. PQM+ will reinitiate these discussions once the electronic registration module system is completed.

In PY4, PQM+ is also providing TA to the State service in establishing registration module of the Regulatory Information Management System (RIMS), which would include a function of digitization and electronic organization with proper backups of the submitted dossiers. In PY4 Q3, PQM+ completed the adaptation of RIMs, and began internally testing the software. This is important because one of the gaps identified during the PQM+ facilitated assessment of the registration function was that the State Service only has hard copies of the product dossier submitted for registration without any back-up. These hard copies can be vulnerable for the physical damage and lost. The State Center also expressed an interest in digitization, and electronic organization with back up for these submitted dossiers. Once RIMS is tested, PQM+ will present and conduct a demonstration of the RIMS module to the MRA. In addition, PQM+ developed specifications for IT hardware for central servers' system and networking devices procurement and installation.

PQM+ is supporting registration of quality assured first and second line TB medicines in Tajikistan through existing national registration procedure to ensure that those medicines are available in the country for domestic procurement for the National TB Program (NTP). PQM+ with GDF and NTP identified and approached additional manufacturers of pediatric first line, as well as second line medicines to support registration, thus ensuring availability of those quality-assured medicines in the country. So, three additional manufacturers were engaged and in PY4 Q3, PQM+ facilitated compilation of dossiers for five additional TB medicines and submitted for registration in Tajikistan. Those medicines are Isoniazid H100, Ethambutol E100, RHZ 75/50/150, Isoniazid H300 and Linezolid 600mg. The state center formally acknowledged accepting the dossiers for these five medicines. Once registered, these quality-assured first-line pediatric medicines will be available for procurement in Tajikistan, in addition to the first set of nine quality-assured TB medicines.

PQM+ is also engaging with WHO, NTP, and GDF to advocate for procurement of WHO prequalified medicines with the Government of Tajikistan. Specifically, PQM+ contributing to the development of specifications for the procurement of TB medicines which was submitted to the MOH by the NTP in PY4 Q3.

PQM+ is providing technical assistance to the Dushanbe MQCL to strengthen its laboratory operations and QMS to comply with ISO 17025:2017. In PY3, the MQCL received ISO 17025:2017 accreditation. In PY4, Q2, PQM+ initiated the procurement of the dissolution tester which is now complete. The tester will be delivered to the Dushanbe lab soon. This procurement is important because this equipment will ensure that laboratory has appropriate support systems to comply with quality standard requirements.

In PY4 Q2, PQM+ organized a kickoff meeting with Avicenna Tajik State Medical University (ATSMU), a public university in Tajikistan and technical assistance lead Purdue University. PQM+ provided a list of courses with short descriptions for ATSMU's consideration as well as a questionnaire to identify areas of need. ATSMU completed the questionnaire. PQM+ is reviewing the response with Purdue. In Q3, Purdue University colleagues developed the schedule for the course and ATSMU has approved the schedule, and the university shared the list of course participants. This is important because this will contribute toward the development of capacity development of the future workforce in Tajikistan for the pharmaceutical sector.

In PY4 Q2, PQM+ engaged with the State Center to understand the current status and plans of developing the GMP inspection capacity. In Q3, PQM+ conducted a three-day training on PIC/S requirements for pharmaceutical inspections. Upon completion of the training, PQM+ will develop and propose a roadmap for GMP inspection development to the State Center.

As a crosscutting activity in PY4 Q2 in collaboration with IntraHealth International, PQM+ initiated update and repackage of the "foundation of good manufacturing practices" e-learning modules into Russian for the Central Asia region. PQM+ is translating and reviewing the GMP modules into Russian. This is important because the translated GMP foundations modules in Russian can be accessible by the manufacturers and regulatory authorities in TJK for free to maintain and improve their knowledge on GMP.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Implement activities with MQCL according to CAPA plan.
- Handover of dissolution tester to the MRA
- Demonstration of the RIMS
- Start of the training on identified area with the ATSMU according to approved schedule.
- Initiation of GMP inspection with the State center
- Continue repackaging of the foundations of the GMP modules.

Uzbekistan

In recent years, the Government of Uzbekistan introduced several initiatives to strengthen the local production of quality-assured medicines in the country. In support of this strategy, and generally to ensure the quality of medicines on the local market, PQM+ is assisting the Agency on Development of the Pharmaceutical Industry ("the Agency") around medicines regulatory systems strengthening. This includes improving the medicines review and registration system, supporting MQCLs to test the quality of medicines reliably and accurately, preparing the GMP inspectorate for PIC/S accession, and introducing RB-PMS to detect sub-standard and falsified medicines. The program also focuses on increasing the supply of locally manufactured, quality-assured TB medicines by providing technical assistance to pharmaceutical manufacturers.

In PY4, 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.

Following the decision of the Government of Uzbekistan to split the Development of the Pharmaceutical Industry (the Agency) and establish two organizations: the State Center for Expertise and Standardization of medicines, Medical Devices and Medical Equipment (the State Center) under the Ministry of Health and the Agency under the Ministry of Investments, Industry and Trade, in PY4 Q2, PQM+ connected with the leads for the Agency and the State Center and reinitiated most of the TA areas.

In May 2023, USP and PQM+ hosted the Minister of Health of Uzbekistan at USP's headquarters in Rockville. PQM+ discussed the areas of its TA with the state center delegation that traveled with the health minister. PQM+ in this quarter, prepared to re-start all the activities under the regulatory systems strengthening except for PIC/S because it was unclear where the GxP center responsible for GMP inspection will be housed.

In PY4 Q2, PQM+ initiated the development of the national pharmaceutical manufacturing development strategy. PQM+ completed a detailed planning for this activity in collaboration with the Agency. This quarter, PQM+ started a desk review for the strategy. PQM+ is also preparing for a TA visit from PQM+ strategy experts in July to organize a kickoff for this activity and conduct interviews with stakeholders as part of the assessment.

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

Global Benchmarking Tool (GBT). This quarter, PQM+ continued to informally advocate with the newly staffed State Center the need to prioritize and work toward WHO GBT ML 3. For example, during the delegation visit to the US in May 2023, PQM+ emphasized the importance of and the need to strategically work toward WHO GBT ML 3.

Registration system strengthening. PQM+ organized a training titled "Preparation of Registration SOPs." The training took place in two sessions for 60 staff total (30 per session) from the Uzbekistan MRA from May 18-20 (session 1) and May 22-24 (session 2). The Training built the capacity of the MRA staff to prepare and review SOPs for registration of medicines. Specifically, by the end of the training, participants were able to: prepare SOPs for the registration activities including evaluation of applications for registration by experts; SOPs and checklist for primary examination of registration documents; developing SOPs and templates for review and preparation of assessment/ evaluation reports, product information and labeling; explain Quality overall summary (QOS) and the Quality Information summary (QIS); conduct reviews and identify deficiencies in the Summary of Product Characteristics (SMPC), Patient information leaflet (PIL) and labeling.

Registration of WHO-prequalified TB medicines. To date, PQM+ has facilitated the registration of six WHO Prequalified TB medicines through WHO CRP. Application for one more medicine was submitted to the State Center for WHO CRP registration that is under review. In PY4 Q1, with no TA from PQM+, the Agency used the WHO CRP process to register three vaccines: tetanus toxoid, ROTASIL (liquid), and the BCG vaccine. This signals that the WHO CRP process is sustainable and working for products other than TB. In PY4 Q3, NTP officially asked PQM+ for support in identifying resources to facilitate the registration of the TB medicines. PQM+ is in the

process of recruiting a consultant to work with MRA, NTP, and the selected TB medicine manufacturer to facilitate registration of WHO prequalified TB medicines using CRP.

GMP inspection. Toward the end of the quarter, PQM+ learned unofficially that the GxP center will be housed within the Agency. Once official, PQM+ will work with the appointed point of contact to restart TA in this area.

Laboratory strengthening. PQM+ resumed discussions with the laboratories in April following the restructuring. Currently, only two laboratories, those which are supported by PQM+ (Tashkent and Andijan labs) are accredited and functioning. Other three regional labs were not able to go through the accreditation process and are not functioning at this point, leaving Tashkent and Andijan laboratories to provide services for the entire country. The labs and PQM+ collectively decided to continue to work on the CAPA that was developed earlier on in PQM+ following the lab assessment. In May, PQM+ facilitated two training sessions for both laboratories to strengthen their QMS specifically how to design and operationalization of processes through, the development and revision of SOPs.

QMS 9001. In PY3, PQM+ initiated TA for QMS for the ISO9001, an internationally recognized organization, and management model that will help the entire state center to improve their administrative and management processes. This activity was also on pause because of the restructuring. However, upon our recent meeting with the head of the state department, he expressed an interest in continuing this work, PQM+ with the QMS 9001 expert met with the newly assigned director of the State Center and discussed the way forward.

PMS. PMS will be within the purview of the State Center. However, it is not clear who will be responsible for PMS within the State Center. At the same time, there are issues with funding for the pilot, especially for the cost of testing of medicines. This was previously resolved, because the Agency at that time, offered to fund this. However, given the changes, it is unclear where the funding for testing will come from. During the meeting with the newly appointed Director of the State Center, he was skeptical about implementing RB-PMS in the near future, specifically referring to the absence of funding for this. PQM+ will continue to follow up with the State Center to identify the next steps.

Pharmaceutical Technology University. The university is a public private entity, and this will stay with the Agency. The main point of contact for the university also remains the same. PQM+ finalized the task order for Purdue university for PY4. In Q3, PQM+ continued trainings of the faculty, who were previously training by PQM+ on the foundations, on “regulatory” and “quality’ areas. The trainings started on May 18 for 31 faculty members at Pharmaceutical Technology University. Trainings are being delivered online with plans to finish by the end of August.

Contract research organization. PQM+ initiated desk review to understand the landscape of Uzbekistan for establishing a CRO. PQM+ CRO expert met with the Agency and State center experts to help them understand the approaches or pathways to build the base for establishing a CRO. As a next step, the Agency and State Center are going to establish a technical working group to work jointly on areas of regulatory changes needed for mandating bioequivalence studies.

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

In PY3, PQM+ continued TA to Uzbekistan Manufacturer 2 on the prequalification of their TB drug levofloxacin. PQM+ is working closely with the manufacturer to prepare the dossier for

levofloxacin for WHO PQ. PQM+ also sourced a comparator from US, a well-regulated market for comparators and provided to Uzbekistan Manufacturer 2. The comparator is needed for the product biowaiver study, a requirement for the dossier for WHO PQ. PQM+ expects the draft of the dossier to be ready in Q4.

The local Uzbekistan pharmaceutical industry should be GMP compliant before accession to PIC/S, training will assist the local industry in understanding of GMP requirements and facilitate achievement of GMP compliance. PQM+ is working with a local expert to provide GMP trainings for manufacturers. In this quarter, PQM+ continued to work with the vendor to finalize training materials for the planned GMP modules for the manufacturers.

As a crosscutting activity in PY4 Q2 in collaboration with IntraHealth International, PQM+ initiated update and repackage of the “Foundation of Good Manufacturing Practices” e-learning modules into Russian for the Central Asia region. PQM+ is in the process of translation and review of the GMP modules into Russian, so the interested regulators and pharmaceutical manufacturers can have free access to this important resource.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Continue to follow up with the state center on point of contacts for the regulatory strengthening activities.
- Conduct kick-off for the national pharmaceutical manufacturing strategy.
- Continue working with the registration department in finalizing market authorization and registration SOPs.
- Identify a consultant to facilitate dossier preparation for TB medicines registration through WHO CRP in consultation with the manufacturer.
- Restart technical assistance to the state center on compliance to QMS 90001:2015
- Organize a TA visit from the laboratory experts to work with Andijan and Tashkent on reviewing their implementation plan and planning their needs moving forward.
- Continue TA to Uzbekistan Manufacturer 2 on product development and dossier preparation.
- Initiate GMP training for local pharmaceutical manufacturers.

Latin America and the Caribbean Region

Panama

PQM+ has been tasked with strengthening Panama's laboratory and testing capacity to improve its ability to ensure medical product quality, as well as developing or revising curricula for relevant University of Panama departments to institutionalize and standardize information and requirements. This will enable them to sustainably ensure and prepare the regulatory workforce.

To achieve this, PQM+ collaborates with key stakeholders, including the National Secretariat of Science, Technology, and Innovation (SENACYT), the main stakeholder coordinating the implementation of the action plan for local pharmaceutical development and manufacturing; the scientific research body under SENACYT (*Instituto de Investigaciones Científicas y Servicios de Alta Tecnología de Panamá,* INDICASAT); Panama's national MRA (*Dirección Nacional de Farmacia y Drogas,* DNFyD); the national quality control laboratory (*Instituto Especializado de Analisis,* IEA); and the University of Panama's Faculty of Pharmacy, among others.

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

From April 19 to 21, PMQ+ conducted a training in good practices for pharmaceutical quality control laboratories and ISO 17025:2017. The training aimed to familiarize participants with WHO guidelines that provide guidance on the QMS within which the analysis of APIs, excipients, and pharmaceutical products should be performed to demonstrate reliable results. The 48 participants (34 women and 14 men) represented the IEA, DNFyD, INDICASAT, and the University of Panama-Department of Pharmacy attended the training.

From June 30 to July 9, PQM+ conducted a series of remote trainings for nine IEA teams leading the development of ten SOPs. The first capacitation laid the foundation and established the criteria for developing IEA's Quality Management System SOPs.

Priority Activities for Next Quarter

Next quarter, PQM+ Panama plans to:

- Train DNFyD staff on good regulatory practices and CTD, the format that regulatory authorities require for submitting applications to register medicines.
- Continue to support IEA in the development of five prioritized SOPs following up on the trainings provided during this quarter.

COVID-19

Bangladesh

Cold Chain and Supply Logistics

In Bangladesh, the USAID PQM+ program is working to establish and strengthen the relationship among key stakeholders monitoring the roll-out of COVID-19 vaccines. As part of this activity, PQM+ is providing technical support to the Directorate General for Drug Administration (DGDA) to implement risk-based post marketing surveillance (RB-PMS) of vaccines, including COVID-19 vaccines. On April 2, 2023, PQM+ organized a "Cold Chain Management of Vaccines" training program in collaboration with the Expanded Program on Immunization (EPI). The main objective of this training was to provide knowledge to DGDA's inspectors on how to maintain the storage, handling, and transportation of COVID-19 vaccines and other vaccine samples during risk-based post-marketing surveillance (RB-PMS) sampling. Five resource persons of EPI provided the training. A total of 23 (F-5, M-18) participants from DGDA and NCL attended the training.

Laboratory Systems

In Bangladesh, PQM+ is working with the National Control Laboratory (NCL) to build its capacity in personal protective equipment (PPE) testing at its newly established medical device testing laboratory. PQM+ procured four (4) pieces of equipment (mask and respirator breathing resistance tester, universal tensile strength tester, medical gloves hole detector for quality testing of PPE; and paramagnetic oxygen analyzer for oxygen concentration testing to ensure the regulation system of medical oxygen) to expand the NCL's testing capacities for medical devices laboratory as a whole. In the previous quarter, the lab received and installed two pieces of equipment (mask and breathing resistance tester and universal tensile strength tester) procured by PQM+. In May, the NCL received and installed the medical gloves hole detector procured by PQM+. In Q3, PQM+ supported the lab to develop standard operating procedures (SOPs) for this newly installed equipment (3). PQM+ also supported several trainings on the newly installed equipment (3). From April 16-17, 2023, PQM+ worked with the equipment supplier, Giant Technology, to conduct a two-day, hands-on training on the Respirator Breathing Resistance Tester to 10 (F-3, M-7) NCL and DGDA technical staff focused on the scope of testing parameters as well as Standard Methods of Medical Mask testing. On April 30, 2023, and from May 2-3, 2023, PQM+ worked again with Giant Technology to conduct a three-day, hands-on training on the Universal Tensile Strength Tester Machine to ten (F-3, M-7) NCL analysts. NCL analysts learned how to use the equipment by themselves and gained the ability to provide training to other new staff in the future. Moreover, they learned how to prepare samples before loading them into the machine according to the standard methods, ensuring the quality of analysis they run on PPE. Finally, from May 14 -16, 2023, PQM+ supported NCL in the installation process of the medical gloves hole detector [Installation Qualification (IQ) and Operational Qualification (OQ)] in collaboration with the supplier. Two NCL lab staff received training on the operation and maintenance of the equipment. This equipment will help NCL to check the quality of PPE items (surgical masks, respiratory masks, and medical gloves) traded in the market. The remaining equipment (i.e., the paramagnetic oxygen analyzer) will be supplied in July 2023.

Ethiopia

Cold Chain and Supply Logistics

In Ethiopia, PQM+ is supporting the Ethiopia Food and Drug Authority (EFDA) to build capacity in cold chain regulation for vaccines. Under its previous American Rescue Plan project, PQM+ Ethiopia conducted a cold chain regulatory inspection, which highlighted gaps in terms of compliance to international regulatory requirements and best practices. The findings showed non-conformities in staff technical capacity in good distribution practice (GDP), good storage practice (GSP), good documentation practice (GDocP), and quality management system (QMS) implementation. Based on these findings, from April to June, PQM+, in partnership with the Ethiopian Metrology Institute (EMI), EFDA branch offices, and Expanded Program on Immunization (EPI) regional offices, hosted an awareness raising training in various regions of Ethiopia (Adama, Gondar, Jimma, Diredawa, Dessie, and Hawassa) on cold chain equipment metrology to a total of 349 (F-173, M-176) health professionals at immunization health facilities that are responsible for storing COVID-19 vaccines and vaccinating patients. Staff at immunization facilities play a key role in maintaining the quality of these COVID-19 vaccines. This training ensured that participants are able to maintain the quality and function of cold storage equipment at their facilities, assuring the safety and efficacy of vaccines given to patients. After training the health professionals at the immunization facilities, in May and June, PQM+ also provided hands-on calibration assistance to selected facilities for their cold chain equipment in collaboration with EMI. Over the two months, EMI calibrated 40 cold chain equipment in Addis Ababa and its surrounding areas, ensuring that this equipment functioned properly. Finally, in early June, PQM+, in collaboration with the EFDA, provided training for 58 experts from all regions in Ethiopia (9-F, 49-M) working in Ethiopian Pharmaceuticals Supply Service (EPSS) hubs and Ethiopian Airlines on GDP/GSP requirements from a regulatory perspective and calibration of cold chain equipment. EPSS is the central public procurement agency that procures, stores, and distributes medical products including the COVID-19 vaccines. Without implementing the principles of GDP/GSP and ensuring properly functioning cold chain equipment (e.g., refrigerators) it is difficult to assure quality of the vaccines throughout the supply chain system. Similarly, Ethiopian Airlines' pharmaceutical cargo department is responsible for storing and distributing COVID-19 vaccines and related commodities in Ethiopia and beyond. This awareness and advocacy training will help to ensure the proper storage and distribution of COVID-19 vaccines to health services from the national to the local level.

Policy, Planning, and Coordination

In Ethiopia, PQM+ is also working to strengthen coordination and alignment in regulatory practices between federal & regional regulatory bodies so that they will be able to share experience, align their legislation/guidelines, and advocate for the quality of medical products. PQM+ is working with the EFDA to conduct annual review meetings with regional regulatory authorities to discuss areas of collaboration in quality assurance of medical products. Since EFDA alone cannot meet its mission of protecting the public from the impact of substandard and falsified (SF) products, PQM+ will work with EFDA in creating public awareness by hosting events on the impact of SF products using appropriate local media. This quarter, PQM+ provided support for the annual joint steering committee meeting from April 13-15, between the federal EFDA and regional regulatory authorities. A total of 147 (24-F, M-123) regulators from both the federal and regions met, discussed, and communicated with each other on challenges, ways forward, and areas for future collaboration. PQM+ also worked with EFDA, the Expanded

Program on Immunization (EPI), and the National Immunization Program (NIP) at the Ministry of Health to facilitated a community mobilization event during the fourth COVID-19 vaccination campaign by recruiting three local radio stations to broadcast a radio spot for 10 days on the safety of COVID-19 vaccines to enhance confidence in getting vaccination. Based on an assessment done by the broadcast media, this radio spot, disseminated using the three national radio stations, could have reached over 40 million people. Finally, as part of both its COVID-19 and field support, PQM+ provided technical assistance for development of continuing professional development (CPD) training modular materials (e.g., job aids, PowerPoint slides) on detection, identification, response, and communication of SF medical products including COVID-19 commodities and submitted it to Addis Ababa University for approval and integration into their curriculum. Once approved, PQM+ will support the university to cascade this certification training to health professionals.

Pharmacovigilance and Safety Monitoring

PQM+ is working to strengthen product quality defect reporting through adverse drug reaction (ADR) reporting. In Ethiopia, there is a passive ADR monitoring system where healthcare providers voluntarily send ADR data and product defect reports, so medicines/vaccines quality issues, often caused by cold-chain storage problems, can be captured, and reported real-time. During this quarter, PQM+ provided technical support to EFDA pharmacovigilance team in updating the national adverse events following immunization (AEFI) monitoring guideline from 2018. The guideline was updated to provide current and comprehensive information to healthcare professionals, immunization program managers, regulators, vaccine manufacturers, developing partners, and other relevant stakeholders for establishing an effective surveillance system for COVID-19 and other vaccines. As a next step, EFDA has planned to organize a validation workshop with a wider group of stakeholders and finalize the guidelines.

Laboratory Systems

PQM+ is supporting EFDA to increase the capacity of its quality control laboratories. The EFDA has a medical devices testing laboratory aimed at testing the quality of medical devices before and after marketing authorization as part of its quality assurance process. Since 2014, the laboratory has been ISO/IEC 17025:2017 accredited for its male condom testing system based on support from PQM+'s predecessor program, PQM. The laboratory is just starting to test other medical devices like gloves, syringes, and rapid diagnostic tests (RDTs), and there is a need to build the quality management system in these areas so that the medical device test results will be accurate, traceable, internationally recognized, and help to better protect the public from diseases like COVID-19 through evidence-based decision making from accurate test results generated from the laboratory. PQM+ is supporting this activity both through COVID-19 funding, as well as its field support funding. In Q2, PQM+ provided technical support to the Medical Device Testing Laboratory of EFDA on its laboratory quality management system (LQMS) and to expand its scope of medical device testing to prepare for its ISO 17025:2017 accreditation assessment. At the beginning of Q3, from April 5-8, the medical device laboratory was assessed by the ANSI National Accreditation Board (ANAB). After the assessment, ANAB confirmed that there was no non-conformance related to testing gloves and the medical device lab is now accredited for four key glove test parameters: 1) Freedom from hole, 2) Physical Properties, 3) Dimension test, and 4) Powder Residue. Now that EFDA's lab is accredited to perform quality tests of medical gloves, it can ensure that this crucial personal protective equipment is of the required quality needed to protect the Ethiopian people now and in future public health emergencies.

COVID-19 Therapeutics

Policy, Planning, and Coordination

The USAID PQM+ program is providing technical assistance across several countries to introduce and refine a COVID-19 Test to Treat service delivery model using the currently authorized antiviral medications (nirmatrelvir/ ritonavir [Paxlovid] and molnupiravir). Manufacturing constraints and a complex regulatory pathway from licensing to market authorization/prequalification result in a protracted timeframe for availability of generic medicines, including these oral antivirals. PQM+, in coordination with relevant partners such as Reaching Impact, Saturation and Epidemic Control (RISE), is working to provide support to regulatory authorities in the ten test to treat (T2T) countries to facilitate registration/market authorization of two COVID-19 antivirals, both the branded (Paxlovid and Lagevrio) as well as the World Health Organization prequalified generic version (nirmatrelvir/ritonavir co-packaged and molnupiravir capsules). PQM+ is also supporting implementing partners in obtaining the necessary authorizations for importation of these same donated products. In Q3, PQM+ has been continuing to facilitate registration/market authorization of Movfor and Nirmacom (generic versions of molnupiravir and nirmatrelvir/ritonavir co-packaged, manufactured by Hetero Labs Limited) in the ten T2T countries.[11] Movfor has been approved or received authorization in Botswana, Ghana, Lesotho, Malawi, and Senegal with approvals expected soon for Cote D'Ivoire and Rwanda. Nirmacom has been approved or received authorization in Lesotho and Malawi, with approvals expected soon in Botswana and Ghana.

In response to hesitations from regulatory authorities to approve the two anti-viral products (including specifically El Salvador and Mozambique), PQM+ prepared a scientific, technical, and regulatory information package to assist regulators in making informed regulatory decisions. The information package is also useful for manufacturers/applicants, procurement agencies (national, regional, and international), donor communities, and healthcare providers as it's a compilation of relevant data and scientific recommendations concerning the safety, efficacy, and use of the two antiviral products. In addition, PQM+ is preparing a model emergency use authorization (EUA) dossier to aid regulators during future outbreaks or health emergencies. In Q4, PQM+ will hold workshops in four T2T countries (El Salvador, Cote D'Ivoire, Mozambique, and Senegal), with regulators from other T2T countries invited, to disseminate the information package and model EUA dossier.

Finally, in Q3, PQM+ continued to work with its two identified manufacturers, Strides Pharma Science (India) and Remington Pharmaceutical Industries (Pakistan) on the development of nirmatrelvir/ritonavir. Strides conducted a bioequivalence (BE) study which failed. The root-cause of the failure was linked to ritonavir that they were developing in-house. As a result, Strides decided to proceed with procuring ritonavir from a qualified source. Since PQM+ planned to cost-share in the purchase of a hot melt extruder (HME) specifically to process ritonavir, they no longer needed the equipment. Instead, they requested cost sharing for the procurement of a roller compactor to process nirmatrelvir. Although approved for cost-sharing by T2T/USAID, Strides later decided to abandon development of nirmatrelvir/ritonavir. Their rationale is that there will be lower probability of gaining the targeted market share due to waning COVID infections and anticipated late entry on the list of suppliers. Similar to Strides, Remington decided to procure ritonavir from a qualified source due to complexities of product development. This prompted Remington to request cost-sharing of a roller compactor instead of

[11] Bangladesh, Botswana, Côte d'Ivoire, El Salvador, Ghana, Lesotho, Malawi, Mozambique, Rwanda, and Senegal

an HME. Additionally, cost sharing was offered for active pharmaceutical ingredient (API). Currently PQM+ is finalizing documentation on the roller compactor. The process for API cost-sharing will begin in Q4.

Ghana

Human Resources for Health

In Ghana, PQM+ received Global VAX funding to support the Ghana Food and Drug Authority (FDA) to build their capacity for regulatory oversight of vaccines biomanufacturing. As part of this work, PQM+ planned a second joint activity to expose national regulatory authority (NRA) delegates from the Global VAX beneficiary countries to the vaccine manufacturing ecosystem of a country with WHO-listed regulatory authority.

To this end, PQM+, in collaboration with the USP India office, organized a study visit to India, a country with a mature regulatory system, a strong vaccine manufacturing environment, and a major exporter of vaccines to the African continent. The primary objective of the study visit was to expand the African regulators' knowledge and understanding of the prerequisites that support a sustainable vaccine manufacturing ecosystem across the region and impart practical knowledge to draw from in their progress of attaining and/or maintaining WHO GBT Maturity Level 3 for vaccines.

PQM+ Ghana funded the participation of five regulatory staff (F-1, M-4) from FDA Ghana in this study visit. This study visit included site visits to the state-of-the-art facilities of USP-India and three Indian vaccine manufacturers based in the Hyderabad area - Biological E Ltd., Indian Immunologicals Ltd., and Auro Vaccines Private Ltd, each providing a unique example based on their company history and product portfolio. The site visits offered the Ghana delegates an opportunity for firsthand exposure to the physical setup and operations of commercial vaccine manufacturing facilities and quality control laboratories in a setting that was informal and neutral as the delegates participated under a learning agenda instead of their NRA roles as inspectors/auditors.

The interactive sessions and extensive Q&A opportunities during the site visits provided the FDA Ghana delegates with an in-depth view of the complexity and nuances of vaccine development, manufacturing and quality control and a better understanding of the key elements to be considered in establishing a viable vaccine product ecosystem. The primary takeaway message that emerged was the necessity for an appropriately trained and mature regulatory and biomanufacturing workforce experienced in biologics/vaccines.

Policy, Planning, and Coordination

PQM+ received Global VAX funding to support the Ghana FDA to acquire and operationalize a complete regulatory management system, such as the Integrated Regulatory Information Management System (IRIMS), which improves and streamlines regulatory processes. With an operational IRIMS, Ghana FDA can offer electronic services to its clients, increasing the consistency, transparency, and efficiency of their regulatory process and operations with which they manage client requests while also improving their quality management systems. Implementation of IRIMS will help Ghana FDA meet the GBT indicator (RS09.08 - The national regulatory authority uses computerized systems to process information, manage records, and analyze data). IRIMS will help to improve the regulatory oversight for all medical products, including COVID-19 vaccines, by increasing the standardization of regulatory processes. An

improved regulatory system will provide the necessary confidence among stakeholders that regulation of COVID-19 vaccines is done effectively. In Q3, PQM+, in collaboration with FDA Ghana, developed the SOW for the IRIMS and initiated the procurement process by soliciting quotations from a list of vendors developed with FDA Ghana. The vendors are expected to submit a costed proposal for the installation, customization, and qualification of the IRIMS at FDA Ghana by July 31, 2023.

PQM+ is also working with vaccine manufacturers to build their capacity in local production of vaccines. Ghana's prospective vaccine manufacturer, DEK, broke ground for the construction of its manufacturing facility in April 2023. The workforce recruitment process has begun and is ongoing. DEK requires technical advice and assistance to establish good manufacturing practices (GMP) for sterile manufacturing of biologics/vaccines. Atlantic Life Sciences (ALS) is a local manufacturer already supported by PQM+ for the manufacture of the oxytocin injection. Its vaccine fill and finish facility infrastructure is complete, its clean room facilities are ready, electrical installations completed, equipment installed and qualified and heating ventilation and air conditioning (HVAC) systems are also installed and functional. While ALS has not prioritized production of COVID-19 vaccines, it is currently Ghana's only biological products manufacturer and PQM+ has offered technical assistance for biomanufacturing capacity building interventions. In Q3, PQM+ conducted a hands-on training session for FDA Ghana and biologics manufacturing personnel from DEK and ALS on pharmaceutical biomanufacturing GMP based on "WHO Annex 2 Good Manufacturing Practices for biological products" - WHO Technical Report Series 999. This training provided a description of pharmaceutical biomanufacturing GMP regulations from starting materials to drug product distribution, demonstrated best practices in a GMP biomanufacturing environment, defined quality, and its importance in a GMP environment and emphasized the importance of manufacturing control and Good Documentation Practices. Ten (10) technical staff from DEK, ALS and FDA Ghana (F-3, M-7) participated in this five-day training on pharmaceutical biomanufacturing. Two days were virtual and covered pharmaceutical quality systems, quality risk management, role of personnel, the quality unit, clean rooms, containment, starting materials, seed lots and cell banks. The other three days were face-to-face and covered labelling, packaging, production campaigns, documentation, data integrity, distribution, complaints, and recalls. Case studies allowed the participants to gain practical insights into these manufacturing activities. The participants found the training beneficial and expressed the need for further training in biomanufacturing and possibly more exposure to biomanufacturing plants.

Pharmacovigilance and Safety Monitoring

PQM+ received Global VAX funding to support the Ghana FDA to advocate for improved safety reporting at the lower-level facilities – clinics, community-based health planning and services (CHPS) zones, and health centers. Ghana FDA is at WHO Maturity Level 4 for vigilance, indicating that it applies existing processes for pharmacovigilance in line with international best practices. During its active surveillance of AEFI from COVID-19 vaccination implemented in 2021/2022 with technical assistance from PQM+, most recorded AEFIs were reported through deliberate follow-up by the study team, which is costly and difficult to sustain. Improving spontaneous reporting will reduce the need for active surveillance to be implemented, thereby saving limited resources. However, this needs to be advocated for, especially at the lower levels of the public health system (i.e., clinics, CHPS zones, and health centers) where reporting continues to be low. In Q2, PQM+ worked with Ghana FDA to develop a strategy for improving reporting of adverse drug reactions (ADRs) and AEFIs. Three interventions were identified and are: 1) Incorporate pharmacovigilance (PV) indicators as part of the peer review process by the Ghana Health Service, 2) Increase consumer and patient education and engagement in

pharmacovigilance activities, and 3) Decentralize PV activities to the lower levels of the healthcare delivery system. Of the above three strategies, the FDA, with technical guidance by PQM+ experts, prioritized (2) and (3) due to higher impact expected from these interventions. Eight (8) out of the sixteen (16) (Greater Accra, Eastern, Northeast, Northern, Savannah, Upper East, Upper West and Western North regions) administrative regions were prioritized by Ghana FDA with technical guidance from PQM+ experts. In Q3, a training was co-facilitated by trainers from FDA Ghana's Safety Monitoring Department, the Expanded Program on Immunization, and PQM+ which covered AEFI and ADR reporting for health care workers to decentralize safety surveillance in Ghana. A total of 414 healthcare workers (HCWs) were trained (247 men and 167 women). This training strengthens the PV implementation agenda of the FDA, including improvement in AEFI and ADR reporting. In addition, PQM+ supported Ghana FDA to design and print advocacy materials (poster and leaflets on medical products safety, the need for reporting, and how to report) for dissemination in these regions at health care facilities, on public transport, schools, and at religious and community centers to raise public awareness.

Laboratory Systems

PQM+ received Global VAX funding to support Ghana FDA to strengthen the capacity of its lab to complete independent lot release of COVID-19 mRNA vaccines. Quality control (QC) testing laboratories that meet international requirements for best laboratory practices enable the regulatory authority to assess the quality of medical products. The regulatory authority needs this critical service to review applications for marketing authorization and variations to existing marketing authorizations, post-marketing surveillance, and lot release. Ghana's QC testing laboratory is ISO/IEC 17025 accredited for several parameters. This laboratory also has capacity to test some vaccine quality attributes, such as appearance, pH, sterility, and bacterial endotoxins. In 2021, through COVID-19 technical assistance funds, PQM+ procured laboratory equipment and supplies to enable the Ghana FDA QC laboratory to test the viral vector platform COVID-19 vaccines. However, the QC laboratory requires additional equipment, accessories, and consumables required for the QC testing of mRNA COVID-19 vaccines. In addition, additional capacity building is needed to enable the QC analysts to test the COVID-19 vaccines per the manufacturers' methods. This quarter, PQM+ issued a purchase order (PO) to two vendors for two pieces of equipment - a Capillary Gel Electrophoresis system and a Cell-based Flow Cytometry System - in alignment with the approved budget. This equipment will compliment other analytical equipment procured for Ghana FDA (by PQM+ through other USAID COVID-19 funded projects) and will enable the NQCL to perform analyses to assess the critical quality attributes of vaccines, including COVID-19 vaccines, for key regulatory functions including lot release and post-marketing surveillance.

This quarter, PQM+ also facilitated a study visit to further strengthen FDA Ghana's capacity in vaccines testing. The University of the Free State in South Africa hosts the biological products testing laboratory which South Africa's medicines regulatory authority uses for quality control testing of vaccines. The lab is part of the global WHO-NCL Network for Biologicals and is the only internationally recognized (ISO/IEC 17025 accredited) vaccines testing laboratory in Africa. Established in 1998, it falls under the university's Health Sciences Department. Given the proven track record of the South African National Control Laboratory for Biological Products (SANCLBP), PQM+ facilitated a study visit for analysts from the FDA Ghana's vaccine testing laboratory to give them a practical experience of testing biologics such as the COVID-19 vaccines in an accredited setting. In May 2023, PQM+ sent two analysts (F-1, M-1) from FDA Ghana to the SANCLBP in Bloemfontein, South Africa. The purpose of the trip was to introduce them to the principles and practices of vaccine testing for lot release and provide practical hands-on experience with testing of COVID-19 vaccine samples. Over a five-day laboratory

visit, the Ghana FDA analysts received hands on training on identity testing of mRNA vaccines by PCR analysis, and theoretical training on ELISA and cell culture practices also applicable to the assessment of the critical quality attributes of vaccines. Over the coming months, the analysts will conduct in-house training on topics covered during the SANCLBP visit for other staff of the Ghana FDA laboratory responsible for vaccine lot release testing. They will also develop SOPs and work instructions for the analytical techniques covered during the SANCLBP study visit.

Kenya

Human Resources for Health

In Kenya, PQM+ is supporting the Pharmacy and Poisons Board (PPB) and the NQCL to build their capacity for regulatory oversight of vaccines biomanufacturing. As part of this work, PQM+ planned a second joint activity to expose national regulatory authority (NRA) delegates from the Global VAX beneficiary countries to the vaccine manufacturing ecosystem of a country with WHO-listed regulatory authority.

To this end, PQM+, in collaboration with USP India office, organized a study visit to India, a country with a mature regulatory system, a strong vaccine manufacturing environment, and a major exporter of vaccines to the African continent. The primary objective of the study visit was to expand the African regulators' knowledge and understanding of the prerequisites that support a sustainable vaccine manufacturing ecosystem across the region and impart practical knowledge to draw from in their progress of attaining and/or maintaining WHO GBT Maturity Level 3 for vaccines.

PQM+ Kenya funded the participation of two regulatory staff from PPB and NQCL (F-1, M-1) in this study visit. This study visit included site visits to the state-of-the-art facilities of USP-India and three Indian vaccine manufacturers based in the Hyderabad area - Biological E Ltd., Indian Immunologicals Ltd., and Auro Vaccines Private Ltd, each providing a unique example based on their company history and product portfolio. The site visits offered the Kenya delegates an opportunity for firsthand exposure to the physical setup and operations of commercial vaccine manufacturing facilities and quality control laboratories in a setting that was informal and neutral as the delegates participated under a learning agenda instead of their NRA roles as inspectors/auditors.

The interactive sessions and extensive Q&A opportunities during the site visits provided the Kenya delegates with an in-depth view of the complexity and nuances of vaccine development, manufacturing and quality control and a better understanding of the key elements to be considered in establishing a viable vaccine product ecosystem. The primary takeaway message that emerged was the necessity for an appropriately trained and mature regulatory and biomanufacturing workforce experienced in biologics/vaccines. This visit also gave the Kenya delegates a new perspective on obstacles and challenges they may face in the regulation of biomanufacturing, and how to solve them, as a well as a deeper understanding of the effort required to fully undertake vaccine-related regulatory functions to prepare them in their progress toward regulatory maturation.

Policy, Planning, and Coordination

PQM+ is strengthening the PPB and NQCL to provide the regulatory oversight required to assure the quality, safety, and efficacy of COVID-19 vaccines and other biologics throughout

their production, storage, distribution, and use in Kenya. In addition, PQM+ interventions are supporting PPB and NQCL toward the achievement of WHO GBT Maturity Level 3 (ML3) for medicines regulatory authorities. In Q3, PQM+ conducted a two-day workshop with PPB's licensing and inspection departments, where PQM+ supported 11 (F-4, M-7) PPB staff to develop a guideline and standard operating procedure (SOP) in line with WHO GBT recommendations. The guideline developed was for licensing Health Product and Technologies (HPTs) manufacturing facilities, and it establishes a standardized framework for the licensing of HPTs, including vaccine manufacturing facilities, in Kenya. By adhering to this guideline, manufacturers can ensure compliance with regulatory requirements and contribute to the overall health and well-being of the population. The SOP was a procedure for parallel importation licenses which provides a systematic and transparent process for granting licenses to entities engaged in parallel importing of vaccines, ensuring compliance with relevant laws, regulations, and quality standards, ensuring PPB's ability to grant licenses for COVID-19 vaccines, as well as strengthening the licensing system for vaccines and other medical products as a whole. Both the guideline and the SOP have been finalized and are with PPB leadership for approval.

Continuous monitoring of the quality of medicines including vaccines is important for any medicine's regulatory authority. To support this, PQM+ worked to update the MedRS tool, a tool for RB-PMS developed under PQM, to include RB-PMS of vaccines. This quarter, to ensure effective roll-out and continued use of this updated tool, PQM+ conducted a three-day virtual training on the new MedRS tool and vaccines RB-PMS in June 2023. The training was attended by 13 (F-5, M-8) PMS department staff from PPB and NQCL. Also, as part of its RB-PMS activity, PQM+ conducted a two-day workshop with PPB's PMS staff for the review and update of the following SOPs to include vaccines: 1) Procedure for rapid alert notification, 2) Procedure for risk based sampling of medical products and health technologies, 3) Procedure for the prevention, detection, and response to substandard and falsified HTPs, and 4) Procedure for recall and withdrawal of medical products. The developed and reviewed documents were shared with PPB leadership for approval. With the updated MedRS tool and revised procedures, PPB will be able to survey the quality of vaccines in Kenya, to ensure they are safe and efficacious for patients.

Laboratory Systems

PQM+ is strengthening the PPB and NQCL to provide the regulatory oversight required to assure the quality, safety, and efficacy of COVID-19 vaccines and other biologics throughout their production, storage, distribution, and use in Kenya. As part of this project, PQM+ plans to assess the NQCL's capacity to support lot release and testing of COVID-19 vaccines. The NQCL needs to develop its capacity for testing of vaccines to support Kenya to produce quality assured vaccines. In Q3, PQM+, together with NQCL, held a one-day workshop to review the self-assessment previously conducted by PQM+ on the NQCL's capacity to support lot release and testing of COVID-19 vaccines against international standards. The aim of the meeting was to align on the results and priorities from the analysis and agree on next steps. The self-assessment report with recommendations has been finalized and shared with NQCL. As part of the findings from this assessment, in May 2023, PQM+ conducted a two-day workshop for document review with 12 participants (F-5, M-7) from the NQCL. The PQM+ team helped NQCL staff review and update 12 SOPs dealing with instruments, general lab procedures, such as waste disposal and storage, certain quality tests for biologics and medical devices, and human resources. These SOPs are now finalized and awaiting approval.

Mozambique

Policy, Planning, and Coordination

In Mozambique PQM+ received American Rescue Plan (ARP) funding to work with the Mozambique national medicines regulatory authority, *Autoridade National Reguladora de Medicamentos, Instituto Público*, (ANARME-IP) to conduct a RB-PMS for COVID-19 vaccines and therapeutics in Mozambique, as well as train ANARME staff on COVID-19 vaccine dossier review, quality control testing, and emergency use authorization. Poor storage and transportation conditions potentially influence the quality of medical products available to patients and clients, compromise outcomes of treatment, and increase the risk of long-term morbidity and mortality from COVID-19. Additionally, the inadequate institutional and laboratory capacity of ANARME limits its capacity to effectively monitor the quality of COVID-19 medical products in the health system. PQM+ will provide technical support to ANARME and its PMS TWG to develop an RB-PMS protocol for COVID-19 vaccines and therapeutic medical products, conduct samples collection, and utilize existing LNCQ capacity for quality control (QC) testing to support quality assurance of COVID-19 medical products. In Q3, PQM+ ran into the challenge of the Ministry of Health de-prioritizing COVID-19 as a public health emergency, leading ANARME to want to dedicate more of its time and human resources toward non-COVID-19 medicines. PQM+ explained to ANARME that the systems that it would help the regulatory authority to develop for COVID-19 vaccines and therapeutics would strengthen ANARME's overall system and processes for vaccines evaluation, registration, and post-marketing surveillance. With this explanation, in June, PQM+ was able to work with ANARME's Division of Evaluation of Medicines, Biologicals and Health Products to capture their expectations and needs for the RB-PMS of vaccines training during a short training needs assessment. PQM+ also began planning for this training which will be conducted in July.

Laboratory Systems

PQM+ is also working with the *Laboratório Nacional de Comprovação da Qualidade* (LNCQ) to effectively support RB-PMS activities for COVID-19 vaccines and therapeutics. LNCQ requires the necessary testing capacity that ensures generation of valid and reliable results. PQM+ has been supporting the LNCQ to strengthen its capacity for compendial testing and close the gaps identified in the roadmap towards ISO 17025:2017 accreditation as part of the laboratory systems strengthening assistance. In Q3, PQM+ identified and contracted firms to provide laboratory equipment maintenance, qualification, and calibration services for LNCQ. PQM+ also identified and contracted suppliers to provide laboratory reagents, reference standards, and proficiency testing samples for LNCQ. PQM+ obtained approval to procure a water purification system for LNCQ as well as two laboratory fridges to ensure that the lab has the necessary equipment to store and test vaccine samples. In addition to procuring needed equipment and supplies for LNCQ, PQM+ will also build the capacity of laboratory staff to perform some of the quality tests necessary for testing vaccines. In Q3, PQM+ began planning for a training scheduled to take place at the lab in August.

Nigeria

Human Resources for Health

In Nigeria, PQM+ received Global VAX funding to support the National Agency for Drug Administration and Control (NAFDAC) to update its existing guidelines for imported COVID-19

vaccine regulation, laboratory testing, vaccine manufacturing site inspections, and post-approval changes of COVID-19 vaccines. To build staff capacity in vaccine biomanufacturing regulation, PQM+ planned a joint activity to expose NMRA delegates from the Global VAX beneficiary countries to the vaccine manufacturing ecosystem of a country with WHO-listed regulatory authority. To this end, PQM+, in collaboration with the USP-India office, organized a study visit to Hyderabad, India, a country with a mature regulatory system, a strong vaccine manufacturing environment, and a major exporter of vaccines to the African continent. The study visit took place from May 22-25, 2023.

The primary objective of the study visit was to expand the African regulators' knowledge and understanding of the prerequisites that support a sustainable vaccine manufacturing ecosystem across the region and impart practical knowledge to draw from in their progress of attaining and/or maintaining WHO GBT Maturity Level 3 for vaccines.

PQM+ Nigeria funded the participation of two regulatory staff (F-1, M-1) from NAFDAC in this study visit. The study visit included site visits to the facilities of USP-India and three Indian vaccine manufacturers based in the Hyderabad area: Biological E Ltd., Indian Immunologicals Ltd., and Auro Vaccines Private Ltd, each providing a unique example based on their company history and product portfolio. The site visits offered the NAFDAC delegates an opportunity for first-hand exposure to the physical setup and operations of commercial vaccine manufacturing facilities and quality control laboratories in an informal and neutral setting. The interactive sessions and extensive Q&A opportunities that the site visits provided, contributed to the delegates getting an in-depth view of the complexity and nuances of vaccine development, manufacturing and quality control and a better understanding of the key elements be considered to establish a viable vaccine product ecosystem. The study visit also provided an opportunity for NAFDAC to improve its interactions with other NMRA delegates representing the other Global VAX portfolios in Africa.

Laboratory Systems

PQM+ is also working to strengthen NAFDAC's laboratory testing function for vaccines. PQM+ is supporting the lab to develop, review, and revise new and existing laboratory procedures focused on vaccines. This quarter, PQM+ worked with lab staff to build the capacity of NAFDAC to perform equipment preventative maintenance in the vaccine lab. In May, PQM+ collaborated with local engineers from qualified vendors to perform the preventive maintenance training for three vaccine testing lab staff (one instrument engineer and two lab technicians). The equipment included the CFX96 real-time PCR equipment, Osmometer D300, pH meter, and the UV-VIS spectrophotometer. The equipment covered COVID-19 specific testing (identity test) and general tests (pH, osmolality, bacterial endotoxin, and mycoplasma screening test). The training engineers also learned the principles of equipment lifecycle management and factors guiding equipment decommissioning when preventive maintenance becomes ineffective, allowing them to maintain the quality of the equipment in the future. This activity has been completed as per the Nigeria Global VAX approved work plan.

In addition to ensuring NAFDAC's vaccine lab has appropriately maintained equipment, PQM+ also worked to procure consumable materials the lab would need to test the quality of COVID-19 and other related vaccines. All the supplies and consumables needed for PCR testing of COVID-19 vaccines were delivered in May 2023. This material, provided by PQM+, will further capacitate the vaccine lab to conduct COVID-19 specific QC testing. It will be used to implement a second phase of hands-on training on QC testing of COVID-19 vaccines and related biological products PQM+ has planned for the next quarter. Finally, in Q3, PQM+ conducted two stages of

theoretical and hands-on training for NAFDAC staff. From May 29-30, provided a theoretical overview of the development and validation of novel analytical methods for quality control testing of COVID-19 (and other) vaccines produced using mRNA and vector-based approaches for 18 (F-6, M-12) vaccine lab staff. From June 26-30, PQM+ then facilitated hands-on training for those same 18 staff (F-6, M-12) on osmolality, bacterial endotoxin testing, viral RNA isolation, RNA and DNA quantitation by Qubit fluorometry, cDNA synthesis, reverse transcription real-time PCR detection of mRNA in Moderna and Pfizer/BioNTech vaccines, and adenovirus DNA isolation from Janssen COVID-19 vaccine samples. During this training, from June 28-29, PQM+ also trained staff on conducting a lot release exercise and supported lab staff to develop summary protocol reviews of the Pfizer vaccine during this training. From this training, NAFDAC vaccine lab staff granted lot release approvals of ten different biological products. Staff at both trainings represented all departments at the lab, including quality assurance, microbiology, chemistry, and tissue culture. These trainings will help strengthen the lab analysts' capacity to perform lot release and quality control testing responsibilities.

Rwanda

Human Resources for Health

In Rwanda, PQM+ received Global VAX funding to provide technical assistance to the Rwanda Food and Drug Authority (Rwanda FDA) to strengthen its capacity to provide regulatory oversight of COVID-19 vaccines imported into the country and expected to be manufactured locally in the near future. This will help assure the efficacy, quality, and safety of COVID-19 vaccines and biological products used in Rwanda. In Q3, to build human resource capability, PQM+ planned a joint activity to expose NMRA delegates from the Global VAX beneficiary countries to the vaccine manufacturing ecosystem of a country with WHO-listed regulatory authority. To this end, PQM+, in collaboration with the USP-India office, organized a study visit to India, a country with a mature regulatory system, a strong vaccine manufacturing environment, and a major exporter of vaccines to the African continent. The study visit took place from May 22-25, 2023, in Hyderabad. The primary objective of the study visit was to expand the African regulators' knowledge and understanding of the prerequisites that support a sustainable vaccine manufacturing ecosystem across the region and impart practical knowledge to draw from in their progress of attaining and/or maintaining WHO GBT Maturity Level 3 for vaccines.

PQM+ Rwanda supported the in-person participation of four (F-1, M-3) regulators from Rwanda FDA and the NQCL. This study visit included site visits to the facilities of USP-India and three Indian vaccine manufacturers based in the Hyderabad area: Biological E Ltd., Indian Immunologicals Ltd., and Auro Vaccines Private Ltd, each providing a unique example based on their company history and product portfolio.

Senegal

Policy, Planning, and Coordination

In Senegal, PQM+ received Global VAX funding to support the medicines regulatory authority (*l'Agence Sénégalaise de Réglementation pharmaceutique* (ARP) to reach WHO GBT Maturity Level (ML) 3. Specifically, PQM+ is working to strengthen the systems for registration and marketing authorization (MA) for biologics such as COVID-19 vaccines. In June 2023, PQM+ had to reschedule two activities (Activity A4 and B1: Pharmacovigilance training and Study visit

to FDA Ghana) in Senegal because of the political situation which led to widespread protests. PQM+ considered virtual implementation in the interim, but the internet was also cut off during the riots. Though Senegal is still considered high-risk, PQM+ has begun tentatively rescheduling activities. Throughout Q3, PQM+ worked with ARP to plan for the following three study visits intended to expose regulatory personnel of ARP to key regulatory functions as defined by WHO, such as medicines registration and MA, PV, and laboratory testing (LT). 1) Study visit to FDA Ghana for MA: PQM+ developed a concept note for the visit with input from ARP and shared this with FDA Ghana. FDA Ghana accepted the concept note and agreed to hosting Senegal ARP. ARP subsequently designated four regulatory staff to attend. Due to mounting political tensions in Senegal leading to uncertainties for travel and slow responses from ARP, FDA Ghana, ARP and PQM+ met virtually and agreed to reschedule the study visit for August 2023. 2) Study visit to the Moroccan Poison Control Center (MRPC) WHO-collaborating center for PV: PQM+ drafted a concept note for the study visit in collaboration with ARP and shared this with the MRPC. MRPC accepted to host the four ARP regulatory officers and proposed the end of July for the visit. 3) Study Visit to CHMP for LT**:** PQM+ worked with ARP to reach out to the *Centre Humanitaire des Metiers de la Pharmacie* [Committee for Medicinal Products for Human Use] (CHMP), a WHO prequalified laboratory based in France with capabilities for testing biological products. They have accepted to host three analysts from Senegal's national quality control lab, *Direction de Controle Qualite* (DICQ), but a date is yet to be determined.

Despite the delay in activities on the ground later in the quarter, PQM+ was also able to support ARP in its PMS work. In Q3, PQM+ provided ARP with an overview of RB-PMS and the MedRS tool developed under PQM and updated by PQM+ with inclusion of a vaccines module. The emphasis of this overview was on the structure of the upgraded tool with the vaccines module, the function, and the functionality of each module in the tool. Furthermore, PQM+ worked with ARP to develop a risk-based protocol for vaccines using the new version of the MedRS tool. The protocol focuses on the three most common vaccines, COVID-19 mRNA, anti-tetanus vaccines and pentavalent (for diphtheria, tetanus, polio, etc.). Members of the PMS Unit engaged in an in-depth and collaborative discussion to determine and finalize the appropriate risks associated with the three selected vaccines. This decision-making session allowed them to leverage their collective expertise and insights to allocate appropriate risk scores under each risk factor for each vaccine. After the data input of vaccines available in Senegal, regions, cities, and facilities into the MedRS tool was completed and processed, the PMS Unit decided to sample vaccines from Dakar, Diourbel, Kedougou, Matam, and Saint Louis, after discussion with the group. With the MedRS tool, the randomization was done on the facilities in the five cities, and one sample will be collected at 45 facilities. The timelines for the sampling and testing will be determined by the PMS Unit as this will be managed and funded by ARP.

Pharmacovigilance and Safety Monitoring

PQM+ received Global VAX funding to support ARP to strengthen its PV systems. While ARP has the mandate to conduct PV activities, it requires a legal framework for reliance on PV data from regional and international organizations. It also must implement the necessary procedures to conduct PV activities and to communicate and collaborate with other stakeholders, such as the expanded program on immunization, to take appropriate joint actions whenever required. Following the training PQM+ provided to ARP the previous quarter, in Q3, PQM+ worked with ARP to draft an active surveillance protocol for vaccines in Senegal, including COVID-19 vaccines. While some AEFI data has been collected through passive surveillance systems, which relies on healthcare providers to report by their own initiative, ARP is interested in collecting more specific information on AEFIs through an active surveillance program. With this active surveillance protocol, ARP will enroll vaccinated candidates and follow them post-

immunization to collect detailed information on any adverse events they experience. The protocol outlines the objectives of the surveillance, the surveillance design/method to be used, how AEFIs should be notified and any ethical considerations. Data collected from active surveillance will help the country understand the AEFI experienced by its population thereby guiding decisions of the use of these vaccines.

Human Resources for Health

PQM+ received Global VAX funding to support ARP to reach ML 3. Specifically, PQM+ is working to strengthen the systems for registration and MA for biologics such as COVID-19 vaccines. To build human resource capability, PQM+ planned a second joint activity to expose NRA delegates from the Global VAX beneficiary countries to the vaccine manufacturing ecosystem of a country with WHO-listed regulatory authority.

To this end, PQM+, in collaboration with the USP India office, organized a study visit to India, a country with a mature regulatory system, a strong vaccine manufacturing environment, and a major exporter of vaccines to the African continent. The primary objective of the study visit was to expand the African regulators' knowledge and understanding of the prerequisites that support a sustainable vaccine manufacturing ecosystem across the region and impart practical knowledge to draw from in their progress of attaining and/or maintaining WHO GBT Maturity Level 3 for vaccines.

PQM+ funded the participation of four regulatory staff [F-1, M-3] from ARP in this study visit. This study visit included site visits to the state-of-the-art facilities of USP-India and three Indian vaccine manufacturers based in the Hyderabad area - Biological E Ltd., Indian Immunologicals Ltd., and Auro Vaccines Private Ltd, each providing a unique example based on their company history and product portfolio. The site visits offered the Senegalese delegates an opportunity for firsthand exposure to the physical setup and operations of commercial vaccine manufacturing facilities and quality control laboratories in a setting that was informal and neutral as the delegates participated under a learning agenda instead of their NRA roles as inspectors/auditors.

The interactive sessions and extensive Q&A opportunities that the site visits provided, contributed to the delegates getting an in-depth view of the complexity and nuances of vaccine development, manufacturing and quality control and a better understanding of the key elements be considered to establish a viable vaccine product ecosystem. The primary takeaway message that emerged for the Senegalese participants was the necessity for an appropriately trained and mature workforce experienced in biologics/vaccines.

Laboratory Systems

PQM+ is also working to strengthen the laboratory testing function and equip and build capacity for testing of biologics. Senegal has a NQCL with some capacity to test biologics in country, specifically the yellow fever vaccines that Institut Pasteur Dakar (IPD) produces. This laboratory, however, requires new equipment, accessories, and consumables to test COVID-19 vaccines. In Q3, PQM+ issued a purchase order (PO) to four vendors for four pieces of laboratory equipment being procured for Direction de Controle Qualite (DICQ). The type of equipment includes: Osmometer, UV-Vis Spectrophotometer SoloVPE, qPCR – Real-Time PCR System, and Molecular Devices SpectraMax M5 Multi-Mode Microplate Reader. This equipment is necessary to capacitate the NQCL to perform analyses to assess the critical quality attributes of vaccines and facilitate lot release or post-marketing surveillance.

South Africa

Policy, Planning, and Coordination

In South Africa, PQM+ received Global VAX funding to strengthen the South African Health Products Regulatory Authority (SAHPRA)'s capacity to provide regulatory oversight to assure the efficacy, quality, and safety of vaccines, including COVID-19 vaccines and biologics, throughout their production, storage, distribution, and use in country. In Q2, PQM+ conducted a rapid strengths, weaknesses, opportunities, and threats (SWOT) analysis of SAHPRA's current MA processes and procedures. The results from the SWOT analysis were used to formulate key recommendations which include: building internal staff capacity and resources to, 1) address the current and expected workload, 2) limit reliance on external experts, specifically for pharmaceutical evaluation, inspectorate activities, and clinical evaluation. Based on this recommendation, during Q3, PQM+ developed a training program focused on Market Authorization and Licensing. This training is planned for mid-July and will include attendees from the licensing units of SAHPRA, Department of Health, and the South African Pharmacy Council.

Related to this activity, PQM+ is tasked with developing a biomanufacturing competency framework and database for SAHPRA. Vaccine manufacturing is an advanced industry, requiring a workforce with specialized and diverse technical knowledge, skills, and abilities (i.e., competencies) obtained through education, training, and experience. Recognizing the common need for biomanufacturing and regulatory capacity development across the African region, PQM+, in collaboration with Purdue University Biotechnology Innovation and Regulatory Science (BIRS) Center, is in the process of developing a regional competency framework with focus on vaccines and biologics-specific regulatory job functions to support the broader continental workforce development activities. As of Q3, PQM+ completed the first draft of the framework, using the WHO Global Competency Framework for Regulators of Medical Products (Draft Version 1.6.4 - June 2022) as reference for the key roles and role-specific activities required for the regulation of medical products. PQM+ technical leads reviewed the initial draft to ensure technical robustness and complementarity to the WHO framework. The final draft is being processed.

Human Resources for Health

PQM+ received Global VAX funding to strengthen SAHPRA's capacity to provide regulatory oversight to assure the efficacy, quality, and safety of vaccines, including COVID-19 vaccines and biologics, throughout their production, storage, distribution, and use in country. To build human resource capability, PQM+ planned a joint activity to expose NMRA delegates from the Global VAX beneficiary countries to the vaccine manufacturing ecosystem of a country with WHO-listed regulatory authority. To this end, PQM+, in collaboration with the USP-India office, organized a study visit to India, a country with a mature regulatory system, a strong vaccine manufacturing environment, and a major exporter of vaccines to the African continent. The study visit took place from May 22-25, 2023, in Hyderabad.

The primary objective of the study visit was to expand the African regulators' knowledge and understanding of the prerequisites that support a sustainable vaccine manufacturing ecosystem across the region and impart practical knowledge to draw from in their progress of attaining and/or maintaining WHO GBT Maturity Level 3 for vaccines.

PQM+ South Africa supported the in-person participation two regulators representing the NCL and the biologics unit at SAHPRA. This study visit included site visits to the facilities of USP-India and three Indian vaccine manufacturers based in the Hyderabad area: Biological E Ltd., Indian Immunologicals Ltd., and Auro Vaccines Private Ltd, each providing a unique example based on their company history and product portfolio. The two South African delegates indicated great interest in both the technical layout of laboratory facilities and the processes as it relates to the regulatory aspects. The NCL is planning a future expansion and is keen to apply global best practices.

Pharmacovigilance and Safety Monitoring

PQM+ received Global VAX funding to SAHPRA to develop a national guideline for RB-PMS for medicines and vaccines. In Q3, PQM+ completed updating the MedRS tool, created by the PQM program. The tool allows countries to estimate risks related to medicines, geographical areas, and facilities within the pharmaceutical supply chain and then make informed decisions, on which medicines to focus on, how many samples are statistically representative and where to sample from. Initially, the tool was designed for RB-PMS of medicines, but now includes additional modules to allow for the design of a COVID-19 and other vaccines quality surveillance protocol. With the updated tool, in Q3, PQM+ supported SAHPRA to finalize its guideline for RB-PMS in South Africa. In Q2 PQM+ conducted a workshop with SAHPRA to introduce the principles of RB-PMS and the use of the MedRS tool to develop a PMS protocol for COVID-19 therapeutics. This quarter, PQM+ hosted a second workshop for the development of a PMS protocol for vaccines using a RB-PMS approach with the updated MedRS tool in May. SAHPRA was the first NMRA to pilot the adapted version of the MedRS tool for vaccines. The workshop included seven participants (F-3, M-4) from the PMS TWG and focused on the risk-based development of a PMS protocol including the development of a sampling plan. The protocol is being finalized for sign-off and execution.

Laboratory Systems

PQM+ received Global VAX funding to strengthen SAHPRA's capacity to provide regulatory oversight to assure the efficacy, quality, and safety of vaccines, including COVID-19 vaccines and biologics, including through quality testing. At the moment, SAHPRA outsources its testing of medicines and biological products, but it is imperative that it maintain its governance and authority to receive timely testing results from its identified testing laboratories. SAHPRA currently uses two external laboratories affiliated with academic institutions for QC testing: NWU's Research Institute for Industrial Pharmacy (RIIP) incorporating the Centre for Quality Assurance of Medicines (RIIP®/CENQAM®) for small molecules and University of the Free State (UFS) - South African National Control Laboratory for Biological Products (SANCLBP) for biologics. As part of this activity, in March, PQM+ had facilitated a general TWG meeting with SAHPRA to discuss the creation of a core task force to plan activities related to the quality control laboratories, SANCLBP and RIIP®/CENQAM®. Members of the task force include representatives from each of the laboratories, the SAHPRA evaluations (market authorization) unit, biologics unit, pharmacovigilance unit, and post-marketing surveillance team. The task force would aid in developing individual tasks associated with implementing a road map to strengthen the laboratory network and assist in the identification of challenges, brainstorming proposals, decision-making, resource mobilization, and validation of best solutions for planning and deployment of tasks to support the laboratory network. In April 2023, PQM+ developed the terms of reference for the SAHPRA task force to formalize and structure their activities.

The current relationship in terms of information flow between SAHPRA and the two quality control laboratories in the network is not well defined. In order to map out requirements for a laboratory information management system (LIMS), the basic procedures for communication of information need to be documented and agreed on between the different parties. In May 2023, PQM+ initiated a process with SAHPRA, and RIIP, incorporating CENQAM® and SANCLBP, to document the SOPs for information flow within their respective workflows. PQM+ will consolidate these draft SOPs into a single document which will become the cornerstone to inform the information flow requirements within a LIMS mapping.

Uzbekistan

Policy, Planning, and Coordination

In December 2022, the Government of Uzbekistan announced the decision to split Uzbekistan's medicines regulatory authority and establish two organizations: the State Center for Expertise and Standardization of medicines, Medical Devices and Medical Equipment (the State Center) under the Ministry of Health and The Agency for Development of the Pharmaceutical Industry (the Agency) under the Ministry of Investments, Industry and Trade. The State Center will be responsible for the regulatory functions and the Agency will be responsible for development of the pharmaceutical industry. This decision is a step in the right direction as it eliminates conflict of interests which existed when the same organization (the Agency) was responsible for the industry development and regulatory work. However, the final structure and responsibilities of both newly established organizations are still being defined. PQM+ will need to continue working with both organizations as some of the PQM+ COVID-19 activities fall under the Agency's responsibility and some of them under the State Center's responsibility. Second, the government of Uzbekistan reported deaths of children in Uzbekistan due to the consumption of imported contaminated cough syrup. WHO issued a warning citing this tragic event. Following this tragic incident, the government of Uzbekistan is still investigating. Several people, including former staff of the Agency and State Center were arrested (including the senior managers) and fired. All these developments caused significant disruption to the regulatory work in Uzbekistan.

Following these events, in Q2 and Q3, PQM+ connected with the leads for the Agency and the State Center and reinitiated most of the technical assistance. In May 2023, USP and PQM+ hosted the Minister of Health of Uzbekistan at the USP office in Rockville. PQM+ discussed the areas of PQM+ technical assistance with the State Center delegation that traveled with the health minister.

While things are still settling at the State Center, the National Immunization Program (NIP) that falls within the MoH has not been impacted and therefore PQM+ is continuing to provide technical assistance to the NIP to strengthen their vaccine safety surveillance capacity. In Q3, PQM+ worked with NIP on activity implementation, including advocating for NIP to establish a working group to develop an AEFI surveillance guideline. NIP developed a draft guideline which is being reviewed by PQM+ and will be sent to NIP for revision. PQM+ also reviewed the training program NIP drafted on epidemiological surveillance of AEFI. PQM+ will provide feedback to NIP to improve the training program.

The restructuring also impacted the lot release activity, as the new structure was being developed and there were personnel changes at the State Center. However, in Q3, PQM+ continued to follow up with the State Center on this and organized an introductory meeting with the Head of the Laboratory of Vaccines, Serum Preparations and Microbiological Research and the Deputy Head of Certification Body for Medical Products. During this meeting, PQM+

discussed the status of vaccines testing and lot release, as well as WHO GBT self-benchmarking work so far. In a scheduled follow-up meeting in Q4, PQM+ will introduce WHO GBT indicators for lot release and provide recommendations for strengthening the lot release function by the State Center to achieve corresponding WHO GBT indicators.

Progress by Health Elements

Maternal and Child Health (MCH)

PQM+'s Core MCH work focuses on helping MRAs and manufacturers improve their systems. PQM+ also supports global leadership efforts in advancing USAID's, global, and country MCH agendas and increasing access to QA life-saving medicines for women and children in LMICs.

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+ finalized a Product Information Report (PIR) for gentamicin and disseminated via the program website and PQM+ country offices. PQM+ also developed two related job aides to support inspection and registration of gentamicin for national MRAs. The French translations of the PIR and job aids are complete and will be disseminated following a thorough review of the translations.

PQM+ initiated discussions with MTaPS and GHSC-PSM on opportunities for dissemination of the Call-to-Action paper including a webinar/call with USAID missions and partners to orient them to the paper. The paper was added to each partner's website, to the CHTF website, and disseminated via social media posts on Twitter and LinkedIn. Next steps include dissemination to USAID missions and partners. Webinars are scheduled for July.

PQM+ refined the questionnaire for MNCH medical devices and developed a questionnaire for tranexamic acid – both focused on regulation and supply – and defined the list of priority devices and countries for survey dissemination. Data for the MNCH devices survey is being gathered in Ghana, Bangladesh, Nepal, Ethiopia, and Senegal. PQM+ began literature searches to identify the current global situation for these commodities in terms of general availability, and regulatory issues around sourcing and quality assurance and how country level data could inform evidence gaps for further investments.

For TXA, PQM+ identified Mali, Madagascar, Ghana, and DRC for data collection and plans to add spot check testing of TXA.

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

PQM+ provided review and comments to the "Quality Assurance Practices for Medical Oxygen Systems – a Technical Resource Document" developed by MTaPS for applying quality assurance practices to health-facility medical oxygen. The technical resource aims to cover quality assurance practices as they relate to sourcing and/or producing medical oxygen on-site, and its storage and distribution so that patients receive oxygen that is safe, reliable, continuous, and of acceptable quality.

PQM+ supported the participation of three African regulatory authorities to a high-level policy discussion hosted by the World Bank from June 7 to 9, 2023, on pathways to safe medicines: protecting patients through unified global action. The event was used to reinvigorate the fight against falsified and substandard quality medicines.

Priority Activities for Next Quarter

Next quarter, PQM+ Core MCH plans to:

- Continue to advance data collection, analysis, and draft the report on the regulatory landscape of MCHN medical devices in LMICs.
- Continue to advance the data collection, analysis and draft the TXA report. Continue to draft the sampling protocol and testing plans.
- Submit an abstract for RHSC General Membership Meeting (GMM) in Accra in October under the following sub-theme: Examining our financial landscape & our future security. Topic: Kenya pilot experience with the SF burden model for oxytocin.

Neglected Tropical Diseases (NTDs)

The November 2020 WHO NTD global roadmap, Ending the Neglect to Attain the Sustainable Development Goals: A Roadmap for Neglected Tropical Diseases 2021-2030, sets goals for an integrated approach across all NTD diseases as well as targets to reduce the number of people requiring NTD treatment 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 PQM+'s NTD work is to ensure the availability of affordable, quality assured NTD medicines for patients in need.

Progress by PQM+ Objective

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

PQM+ is continuing to work with existing and newly identified manufacturers of NTD medical products to ensure that enough sources of quality-assured medicines are available on the market.

- Held biweekly meetings with India Manufacturer 1 to review the major SOPs and protocols to address the CAPA deficiencies for albendazole 400 mg tablets. The GMP CAPA response and supporting documents were finalized and submitted to WHO on June 11th. The acceptance of the CAPA and the site approval is pending WHO PQ. Discussion on further production of the company's experimental batches of mebendazole 500 mg tablet is on hold and pending more details on whether a tech transfer is possible. For Praziquantel 600mg, the BE study is complete with positive preliminary results showing the product passes the requirement for bioequivalence.
- For India Manufacturer 2, the product development is in progress for albendazole 400mg tablets. The dissolution profile study and product development report was reviewed, and the issue of the media problem has been addressed with the current revised International Pharmacopeia for Albendazole. For ivermectin 3mg tablets, the project timeline has been received. API characterization and the first pilot batch production is to be produced during Q4 of 2023.
- Completed a dossier review for Bangladesh Manufacturer 1 for azithromycin 500 mg and still awaiting product shipment to U.S. market for submission for WHO PQ.

- Kenya Manufacturer 1 agreed to provide information on the API source and PQM+ shared prequalified sources of Praziquantel 600 mg tablet API supplier. The API supplier selection is in progress.
- Bangladesh Manufacturer 2 received three API batches and the drug master files (DMF) from Hisun; pending letter of access. Drug product development is in progress.
- Held a meeting on April 13th with ESPEN to demo the NTD dashboard and progress a discussion of possible long-term hosting. The tool is now 508 compliant and PQM+ added more data on manufacturers of NTD APIs and FPPs to the dashboard. The tool was posted as lead story on the PQM+ website on 5/30, and invitations for the launch were sent mid-June.
- The task order with Purdue was approved and fully executed. PQM+ held an activity kick-off meeting with the instructional designer, IHI, and Purdue to review the roles and responsibilities, deliverables and timelines, and next steps for development of the two new eLearning courses: 1) Pharmaceutical quality management system: elements and quality review practice and 2) GMP in QC laboratory and analytical method validation.
- PQM+ is developing a 5-page executive summary of the NTD landscape analysis that will include supply landscape, risks, need for diversification to inform donors and other stakeholders with planning investments.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Conduct site visits to Kenya Manufacturer 1 and Bangladesh Manufacturer 1.
- Continue working with India Manufacturers 1 and 2 and Bangladesh Manufacturer 2.
- Complete the executive summary of the NTD landscape analysis and disseminate.
- Launch the NTD dashboard publicly and continue exploring long-term hosting options.
- Disseminate updated GMP course guideline documents.
- Develop instructional design for new eLearning modules on advanced GMP topics.

Tuberculosis (TB)

PQM+ seeks to ensure an uninterrupted supply of lifesaving quality-assured TB medicines by providing direct support to manufacturers of priority TB products. It also explores innovative manufacturing processes for priority TB medicines, develops technical documents such as product information reports, and works with partners to ensure that medicines registration processes do not create hurdles for introducing and scaling-up new TB medicines.

In PY4, PQM+'s core TB work is focusing on increasing the supply of quality-assured essential medical products of public health importance.

Progress by PQM+ Objective

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

In Q3, PQM+ continued supporting a pharmaceutical manufacturer of first-line four-drug fixed-dose combination (4FDC) TB medicines in Pakistan. To date, PQM+'s technical assistance to Pakistan Manufacturer 4 resulted in the compilation of a dossier, including reports on the stability and bioequivalence studies and successful submission of the dossier for WHO. This was an important milestone toward prequalification of the product, thereby ensuring that TB patients in Pakistan have access to locally produced quality-assured TB medicines. PQM+ continued helping the manufacturer respond to the additional data and comments requested by WHO. As part of full prequalification, WHO conducted an onsite inspection from September 19-23, 2022. Although the inspection report showed no critical observations, it outlined several deficiencies. PQM+ worked with the manufacturer to develop and submit CAPA to WHO to address those deficiencies. In Q3, PQM+ worked closely with Pakistan Manufacturer 4 to address the gaps identified in the CAPA, including training, document review, and SOP updates. For example, PQM+ visited the site and provided training on the change control SOP and template to Pakistan Manufacturer 4's technical team and provided suggestions to their technical team for successful implementation of CAPA.

PQM+ is also providing technical assistance to Pakistan Manufacturer 4 for two-drug fixed-dose combination (2FDC) TB medicines. PQM+ technical assistance focuses on compiling the dossier, conducting a BE study, and developing the product. Pakistan Manufacturer 4 completed milestone two of the agreement with PQM+. The manufacturer selected Jordan's ACDIMA Center for Bioequivalence and Pharmaceutical Studies as the CRO. ACDIMA, Pakistan Manufacturer 4, and PQM+ completed a bioequivalence protocol for the 2FDC, which was submitted to the WHO assessment team and reviewed. ACDIMA, Pakistan Manufacturer 4, and PQM+ addressed WHO's comments on the protocol. The 2FDC bioequivalence study was completed in March. The next step is data analysis and report development. The preliminary report results show the inequivalence of the 2FDC against its comparator. Further data analysis and discussion on the next action item is in progress.

Pakistan Manufacturer 1 received PQM+ technical assistance to update the dossier along with stability studies of the 4FDC product. Thae manufacturer is addressing the challenges identified by WHO during the BE and stability study to update its dossier for submission for WHO PQ.

In Q1, PQM+ completed the validation of the analytical methods to test for nitrosamine impurities in rifapentine and rifampin TB medicine, followed by development of a training slide deck that will be an important resource for the medicines regulatory authorities and interested manufacturers. In Q3, PQM+ discussed with WHO the possibility of inclusion of the analytical methods developed by USP in WHO pharmacopeia and sent the method for evaluation.

Also, in PY4 Q2, PQM+ finalized work with Virginia Commonwealth University (VCU) on phase 2 optimization, scale up, and integration of the synthesis process for developing an alternative route for producing API for a priority TB product. The teams successfully identified a synthesis route and demonstrated each step of the continuous manufacturing process. That quarter, with USAID's guidance, PQM+ identified a potential manufacturer to receive the technology transfer. PQM+ also extended VCU agreement to include the technology transfer phase. USAID facilitated a kickoff meeting with VCU and the potential technology transfer recipient. Separately, VCU also filed a global provisional patent for the new technology. In PY4 Q3, PQM+

initiated the technology transfer to Indian Manufacturer 1 by providing the technology reports for the alternate synthesis route and analytical methods.

In PY4 Q2, PQM+ also finalized the scope of work for the optimization of rifamycin-S. In Q3, PQM+ initiated a procurement to identify a vendor to conduct optimization for rifamycin-S. No vendors applied. The call for applications has been reopened and extended.

In PY3, PQM+ signed a non-disclosure agreement with South Africa Manufacturer 1, a manufacturer that currently produces two TB API. PQM+ is providing technical assistance to South Africa Manufacturer 1 for WHO PQ of isoniazid API, one of the two TB APIs that the manufacturer produces. During the visit, PQM+ conducted an onsite GMP assessment of the manufacturer's facility and helped with draft preparation of the isoniazid DMF. In Q4, PQM+ will conduct an onsite technical assistance visit to South Africa Manufacturer 1.

In Q3, PQM+ identified an expert to a conduct landscape analysis of TB pharmaceutical products manufacturers in South Africa. The data collection tool has been developed, data and information collection has started. The report will be developed in Q4.

PQM+ is providing technical assistance to the Regional Bioequivalence Centre Sh. Co. (RBEC) in Ethiopia. This public-private partnership was established in 2012 to serve as a CRO for the 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 will play a fundamental role in fulfilling Africa's unmet needs for the supply of safe, effective, and quality assured medicines for its people. As such PQM+ is working with RBEC through a TWG to identify the bottlenecks hindering RBEC from delivering BE studies for Ethiopia and the African continent. The TWG includes members from WHO, Armour Hansen Research Institute, Ministry of Health, EFDA, RBEC, and PQM+. In Q3, PQM+ conducted a stakeholders' workshop on April 24-27 with TWG members and other in-country stakeholders in Addis Ababa, Ethiopia. The TWG members continue to work on the technical report which will outline next steps for RBEC including operations and business plan to position itself to conduct its first BE study during the next program year.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Continue to work with Pakistan Manufacturer 4 to address the gaps identified in the WHO audit for 4FDC. Investigate preliminary results for BE report outcome for 2 FDC.
- Continue to provide technical assistance to the selected manufacturer for technology transfer for rifapentine API.
- Continue to work with TWG for the support of RBEC and CROs and finalize the technical report.
- Extend procurement for a vendor to conduct optimization for rifamycin-S.
- Complete data collection and preliminary analysis for landscape analysis of South African manufacturers.

Program Support

Communications

Social media: To highlight PQM+ activities and amplify our work, this quarter PQM+ shared 34 posts on Twitter and LinkedIn, earning more than 62,000 total impressions and 1,139 reactions and engagements. The top posts were:

- Nigeria SWIPA receives WHO-prequalification for zinc sulfate.
- PQM+ staff meet with Ethiopian Food and Drug Administration to strengthen partnership.
- CEO from Drug Regulatory Authority of Pakistan visits PQM+ headquarters.

Success stories: We published three success stories and a press release on the PQM+ website:

- Ethiopia expands laboratory capacity across the country.
- WHO prequalifies West Africa's first national medicines quality control laboratory.
- Pakistan builds new partnership with the private sector to improve surveillance of COVID-19 vaccination.
- Press release: Nigeria Pharmaceutical Company First to Receive WHO Prequalification in West Africa.

Newsletter: PQM+ shared its 11th newsletter, which had a strong open rate of 48 percent. The new issue spotlighted:

- Manufacturers in Nigeria and Pakistan achieved WHO prequalification to manufacture zinc sulfate, an essential medicine for newborn and child health.
- A Ghana national medicines quality control laboratory is the first in West Africa to receive WHO-prequalified status.
- Ethiopia's medical device lab achieves accreditation.
- PQM+ releases a new online dashboard for NTD medicines data.

Videos: PQM+ shared a video on ensuring quality tools to fight malaria for World Malaria Day.

Website: We are developing expanded country pages, which we plan to roll out next quarter. We continued to add new content to the PQM+ website, including the three success stories, the new NTD Medicines Information Dashboard landing page, links to press releases, and newsletters.