Promoting the
QUALITY OF MEDICINES Plus

PQM+ Quarterly Report – Program Year 4, Quarter 1

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About PQM+

The Promoting the Quality of Medicines Plus (PQM+) Program is a five-year cooperative agreement (No. AID-7200AA19CA00025) between the U.S. Agency for International Development (USAID) and the U.S. Pharmacopeial Convention (USP) to sustainably strengthen medical product quality assurance systems in low- and middle-income countries (LMICs). PQM+ works to improve medical product quality through cross-sectoral and systems strengthening approaches and the application of international quality assurance standards across the pharmaceutical system. By sharing scientific expertise and providing technical support and leadership, PQM+ helps to create resilient and sustainable local health systems that ensure access to quality-assured essential 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 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
AEFI	adverse events following immunization
ANAB	American National Standards Society National Accreditation Board
API	active pharmaceutical ingredient
CAPA	corrective and preventive action
CIP	Coalition of Interested Parties
CPD	continuing professional development
CRO	contract research organization
CRP	collaborative registration procedure
CSV	computerized systems validation
CTD, eCTD	common technical document / electronic common technical document
DT	dispersible tablets (amoxicillin)
EPI	Expanded Program on Immunization
EUA	emergency use authorization
FP	family planning
FPP	finished pharmaceutical product
GBT	WHO Global Benchmarking Tool to evaluate national regulatory systems
GMP	good manufacturing practice
HPLC	high-performance liquid chromatography
HR	human resources
IDP	institutional development plan
IQC	internal quality control
ISO/IEC	International Organization for Standardization/International Electrotechnical Commission
KPI	key performance indicator
LIF	laboratory information file
LMIC	low- and middle-income countries
MedRS	Medicines Risk-based Surveillance
MNCH	maternal, newborn, and child health
MOH	ministry of health

MQCL	medicines quality control laboratory
MRA	medicines regulatory authority
MTaPS	Medicines, Technologies, and Pharmaceutical Systems program
NCL	National Control Laboratory
NTD	neglected tropical disease
OpERA	Optimizing Efficiencies in Regulatory Agencies
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PIR	product information report
PIRIMS	Pakistan Integrated Regulatory Information Management System
PMI	U.S. President's Malaria Initiative
PMS	post-marketing surveillance
PPE	personal protective equipment
PQM+	Promoting the Quality of Medicines Plus
QA	quality assurance
QC	quality control
QMS	quality management system
RBI	risk-based inspection
RB-PMS	risk-based post-marketing surveillance
RIMS	regulatory information management system
RMNCH	reproductive, maternal, neonatal, child, and adolescent health
RSS	regulatory system strengthening
RUTF	ready-to-use therapeutic food
SATTA	Stepwise Assessment Tool Towards Accreditation
SF	substandard or falsified
SOP	standard operating procedure
TB	tuberculosis
TRIPS	Trade-Related Aspects of Intellectual Property Rights
TWG	technical working group
USAID	U.S. Agency for International Development
USP	U.S. Pharmacopeia
WHO	World Health Organization
WHO PQ	World Health Organization Prequalification

Letter from the Director

In the past four months, the world has yet again faced cases of contaminated liquid dosage formulations in multiple countries. The World Health Organization issued three medical product alerts noting the identification of substandard (contaminated) liquid dosage medicines in Gambia (N°6/2022), Indonesia (N°7/2022), and Uzbekistan (N°1/2023). Laboratory analysis confirmed that those products contained unacceptable amounts of diethylene glycol (DEG) and ethylene glycol. Multiple deaths of children from acute kidney injury cases have been associated with exposure to those products.

These painful incidents point to the undisputed necessity for systems that can control the quality of medical products in the global supply chain by generating quality data for regulatory decision-making. One of the ways that PQM+ addresses this need is by building the capacity of national drug quality control laboratories to test the quality of medicines accurately and reliably according to international standards of the World Health Organization (WHO) Good Practices for Pharmaceutical Quality Control Laboratories (GPPQCL) and the International Organization for Standardization (ISO) requirements for competence of testing and calibration laboratories. Since its inception in September 2019, PQM+ has supported 46 medical products and diagnostic labs across 23 countries; nine of these labs achieved WHO prequalification or ISO accreditation in three international standards. During Program Year 4, Quarter 1, PQM+ supported Mali's *Laboratoire National de la Sante* (LNS) and the Pakistan Drugs Testing Laboratory Punjab, Rawalpindi, to obtain ISO ISO/IEC 17025:2017 accreditation, and the Pakistan Institute of Medical Sciences (PIMS), Islamabad's diagnostic laboratory, to obtain ISO 15189:2012 accreditation. WHO's assessment of Rwanda's laboratory testing function using the Global Benchmarking Tool (GBT) yielded no negative observations and resulted in a score of Maturity Level 3 (ML3). Our FY2023 activities are positioned to support proficiency testing in 10 countries and interlaboratory testing in Burma.

Ensuring that these labs have well-defined strategic and operational plans for the provision of sustainable services is equally important. PQM+ is providing technical assistance to the national quality control laboratories (NQCLs) of Bangladesh, Burkina Faso, Democratic Republic of Congo, Madagascar, Mali, Nepal, and Tajikistan to develop strategic plans that will ensure financial and operational sustainability. For vaccine-producing countries, NQCLs responsible for testing and release of vaccines must be functional to effectively support regulatory lot release (LR) functions to expedite the availability of and access to lifesaving vaccines. According to the WHO, the goal of the regulatory function is to ensure the quality, safety, and efficacy of biological products through a regulatory release system. In FY2023, PQM+ is providing technical support in this function to nine countries: Bangladesh, Ethiopia, Ghana, Kazakhstan, Kenya, Nigeria, Pakistan, Senegal, and South Africa. PQM+ is supporting the laboratory access and testing (LT) regulatory function of the WHO's GBT in more than 15 countries.

The African Medicines Regulatory Harmonization (AMRH) initiative is supporting the Partnerships of African Vaccine Manufacturing (PAVM) initiative's regulatory workstream to establish a Reliance Vaccine Regulatory Laboratory Network on the African continent. Under the auspices of the African Union Development Agency -New Partnership for Africa's Development (AUDA-NEPAD), PQM+ will implement an expansive scope of work aimed at assessing the capacity of NQCLs for biologics/vaccines lot release and define mechanisms for the establishment of an African Continental Lot Release Laboratory Network.

PQM+ remains dedicated to its goal of strengthening quality assurance systems to sustainably ensure the quality and safety of medical products and protect public health. With each intervention, we aim to establish long-lasting collaborative working relationships with our constituents and a sustainable community at the global, regional, and local levels to share experiences, challenges, and solutions. The solutions, including health system strengthening and quality assurance interventions that you will read about in this quarterly report, will ensure that deaths associated with DEG contaminated products do not reoccur.

Jude I. Nwokike
PQM+ Director

Executive Summary

During the first quarter of Program Year 4, the USAID-funded Promoting the Quality of Medicines Plus (PQM+) program worked in 24 countries[1] and implemented 47 work plans. The breakdown of active work plans is as follows:

- 23 Mission buy-ins[2];
- 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;
- Two regional buy-ins from USAID's Africa and Asia bureaus;
- One "cross-bureau" funding stream supporting the Office of Health Systems;
- 11 COVID-19 work plans (six under no-cost extensions from FY2022 and five with funding through much of FY2023);
- Six funded by the U.S. Government's Initiative for Global Vaccine Access (Global VAX);
- 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 MNCH.

PQM+ staff visit the vaccine testing unit at the national quality control laboratory in Senegal.

This report summarizes activities conducted during the first quarter of Program Year 4 (October 1 to December 31, 2022). These 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, Mali, Mozambique, Nepal, Nigeria, Pakistan, Panama, Rwanda, Senegal, South Africa, Tajikistan, Uzbekistan

[2] The 23 countries are the list in Footnote 1 minus South Africa, which is funded under a Global VAX buy-in.

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 partners' alignment. Through PQM+ support, stakeholders 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 is to enable public servants to define their strategic goals, identify necessary interventions to reach those goals, allocate adequate resources to execute a plan, and implement a monitoring and evaluation system to measure progress of regulatory oversight that ensures timely access to essential medicines and protection from substandard and falsified (SF) products. Key highlights from PY4Q1 governance activities follow.

Nepal. PQM+ supported the Department of Drug Administration (DDA) in organizing a **policy dialogue** focusing on the domestic production of essential medicines. PQM+ Director Jude Nwokike delivered a keynote address emphasizing the importance of the local pharmaceutical industry's role in ensuring the quality of medicines to protect public health; representatives from national-level health agencies, professional bodies and councils, academia, and private sector entities participated in this event.

Pakistan. PQM+ staff helped revise the **guidelines and regulatory requirements for approval of bioequivalence (BE) studies** to be conducted by contract research organizations (CROs) or sponsors to secure early approval for conducting these studies. If implemented, the revised guidelines will not only help shorten the approval time, but also reduce costs, facilitate the National BE policy, and indirectly increase the availability of quality essential generic medicines in the country.

Tajikistan. Following the audit report on **ISO 9001** and the implementation plan for addressing gaps identified in the last quarter of PY3, in this quarter, PQM+ worked with the State Center to develop guidelines and processes for the quality management system in line with ISO 9001 requirements.

Regulatory Systems Strengthening (RSS)

A strong regulatory system helps to ensure timely access to safe, effective, and quality-assured medical products. Robust regulatory systems are needed to protect the public health of populations by preventing the distribution of substandard and falsified (SF) medical products. SF drugs can cause serious health problems, and they can also undermine trust in the health system. PQM+ provided support in various RSS areas, including:

Regulatory competency strengthening. Continuing efforts to build capacity of regulators of medical products led PQM+ staffers to adapt an assessment tool based on the World Health Organization (WHO) Global Competency Framework for Regulators of Medical Products. The tool is intended to assess the required individual competencies (capabilities) of regulatory staff to to adequately perform their respective regulatory functions.

South Africa competency needs assessment. As part of the Global Vax project, PQM+ used the assessment tool adapted from the WHO to conduct a competency needs assessment of the South African Health Products Regulatory Authority's (SAHPRA) capacity to fulfill several regulatory function toward maturity level (ML) advancement, as defined by the WHO Global Benchmarking Tool (GBT): laboratory testing, national regulatory systems, registration and marketing authorization, regulatory inspections, licensing establishments, and lot release. The assessment was conducted over 4 days from October 12–17, 2022, and evaluated SAHPRA's internal staff capacity, skills and knowledge, training needs, access to technical resources, and efficiency to fulfill its regulatory responsibility to assure the quality, safety, and efficacy of medicines and vaccines. In addition, PQM+ performed a strengths, weaknesses, opportunities, and threats (SWOT) analysis of the individual units including the Health Products Authorization Unit, Pharmaceuticals Evaluation Management Unit, Clinical Evaluations Management Unit, and SAHPRA subcontracted external laboratories. PQM+ is finalizing the technical report based on the results of the assessments while also identifying SAHPRA's competency gaps. The report and recommendations will serve as a guide to SAHPRA to address identified competency gaps, especially those related to the WHO GBT, and as such will support the progress of SAHPRA from its current status of ML3 for vaccine producing to ultimately reach ML4.

Facilitate medicines and biological products market authorization, approval, or registration. PQM+ continues expanding the scope of its support for market authorization to meet countries' needs. An example of this work is medicines regulatory authorities' (MRAs') need to strengthen their capacity to evaluate biological products including vaccines. They also need to improve their review of bioavailability (BA) and bioequivalence (BE) studies that demonstrate that generics are equivalent to originator medicines approved for market distribution.

Senegal Training on Dossier Evaluation of Biological Products, including Vaccines. PQM+ conducted this training on November 21–24, 2022, with the objective to enhance knowledge and understanding of the current global regulatory requirements to be considered during product evaluation for the registration of biologicals. Additionally, this training aims at identifying resource personnel among the trainees to serve as future trainers in biological product evaluation for junior and new recruited *Agence Sénégalaise de Réglementation Pharmaceutique* (ARP) MRA staff. Twenty-two regulatory assessors from the Senegal ARP and university researchers and professors participated in the training.

Ethiopia BA/BE training. PQM+ provided the five-day "Comprehensive Course on Bioavailability and Bioequivalence" from December 5–9, 2022, to 26 medicine registration and licensing directorate dossier assessors from the Ethiopian Food and Drug Administration (EFDA). The training focused on bioavailability, bioequivalence, and in-vitro/in-vivo correlation (IVIVC) studies as they relate to the review and approval of COVID-19 therapeutics including the basic pharmacokinetic principles, regulatory requirements, clinical study design considerations, analytical method validation requirements, study conduct requirements (clinical and analytical), statistical analysis, reporting requirements, common deficiencies, and relevant data integrity concerns. The outcome of the training will be an increase in knowledge on the requirements for review of BA/BE studies and a corresponding decrease in the time required for registration of generic medicines—including emergency medicinal products—thus facilitating their timely access.

Asia Bureau BA/BE training. PQM+ developed and finalized course materials for a training of trainers titled "Comprehensive Course on Bioavailability (BA) and Bioequivalence (BE) Studies with Focus on Bioanalytical Method Validation and BE Study of Non-Oral Solid Dosage Forms." The course will be conducted for the 10 Association of South-East Asian Nations (ASEAN) countries during Q2.

WHO GBT and PIC/S Accession Support: PQM+ continues to work with supported countries toward achieving global standards for regulatory functions as measured through the WHO GBT maturity levels. For instance, the WHO ML3 defines a stable, well-functioning and integrated regulatory system and ML4 signifies a regulatory system operating at an advanced level of performance with continuous improvement. PQM+ also supports countries regulatory inspectorates to aspire toward PIC/S membership. PQM+ is currently supporting 11 countries[3] toward progressing their regulatory authorities or specific regulatory functions to a higher WHO maturity level and working with three countries[4] to achieve PIC/S membership. Examples of this support include the following:

Kenya. PQM+ assisted the Pharmacy and Poisons Board (PPB) in reviewing its guidelines and standard operating procedures (SOPs) as means to support PPB to address recommendations from the June 2022 WHO-GBT formal assessment to attain ML3.

Pakistan. PQM+ supported Drug Regulatory Authority of Pakistan (DRAP) to participate in mandatory PIC/S Committee meetings as a pre-applicant to learn policy and procedures for PIC/s member countries. DRAP shared at the meetings progress made on corrective and preventive action (CAPA) implementation along with expected timelines. DRAP has begun the

[3] PQM+ is supporting the following countries to achieve ML3 across multiple regulatory functions: Bangladesh, Ethiopia, Kazakhstan, Kenya, Pakistan, Rwanda, Senegal, and South Africa. PQM+ also is supporting Nigeria to achieve ML3 for lot release; Mozambique to achieve ML3 for market surveillance and control and lab testing; and Ghana to implement an integrated regulatory information system to achieve ML4.

[4] Kazakhstan, Pakistan, and Uzbekistan

risk-based good manufacturing practice (GMP) inspections of pharmaceutical establishments using PIC/S guidelines and is expected to submit the PIC/S membership application by the end of Q2.

Ethiopia. PQM+ provided technical assistance to prepare the EFDA for WHO's ML3 through addressing WHO's GBT assessment findings. Specifically, PQM+ staff helped finalize six SOPs, rectified the institutional development plan, and held a week-long workshop for EFDA aiming at addressing the feedback received from the WHO GBT team.

Kazakhstan. PQM+ helped the GMP inspectorate of the National Centre for Expertise of Medicines, Medical Devices, and Medical Equipment (NCEM) in preparation for the launch of their newly developed quality management system (QMS). Specifically in November 2022, PQM+ met with the PIC/S working group and discussed preparation for a formal WHO inspection planned toward the end of 2023, as part of the WHO GBT regulatory inspection function. The team also discussed the matrix of inspectors, trainings for inspectors, and QMS.

Uzbekistan. PQM+ assisted the national MRA (Agency on Development of the Pharmaceutical Industry) in the development of a **strategy for licensing processes for manufacturers and wholesalers** in Uzbekistan to align with the WHO and PIC/S requirements. This strategy entails cooperation between the GxP center and the Agency. The strategy is currently with the Agency leadership for review and approval.

Nepal. PQM+ helped review the existing documents from the Department of Drug Administration (DDA) and the WHO GBT assessment to finalize a list of **SOPs drafted to improve the registration and market authorization** system. PQM+ has also planned to develop training curriculum on marketing authorization focusing on dossier evaluation as per the common technical document (CTD) format to DDA assessors.

Addressing MD/IVDs regulatory and technical challenges. MD/IVDs form a broad and dynamic field within life sciences with their own challenges, limitations, and appropriately their own standards. The MD/IVD division for regulatory bodies in LMICs is normally lacking fundamental understanding of the regulatory requirements associated with these products. Due to the nature of the field of devices itself, there is a need for many different specialized experts including but not limited to engineers, software designers, microbiologists, chemists, and biochemists. The majority of LMICs do not have a dedicated staff for MD/IVDs, and most observed regulatory framework documents do not mention MD/IVDs specifically. The devices division has many opportunities to build a foundation for a self-sustainable regulatory system that should start with a fundamental regulatory management system document.

PQM+ staff conducted a remote training to the **Mozambique** MRA (*Autoridade Nacional Reguladora de Medicamentos de Moçambique,* ANARME) staff on the regulatory aspects for MDs/IVDs. Training presentations were comprehensive to instruct the MRA trainees on WHO Regulatory framework for MD/IVDs, their classification rules, dossier structure, and condom and hypodermic testing requirements.

In **Bangladesh**, PQM+ conducted an in-country training workshop on MD regulations, which instructed DGDA trainees on dossier submission/review process, testing, and regulatory requirements for condoms and hypodermic needles, QMS, ISO standards, MD/IVD manufacturer audits, and post market surveillance and vigilance system requirements. Additionally, PQM+ submitted formal documented recommendations to the DGDA for next steps in improving their regulatory system for MD/IVDs. A gap assessment document for meeting the

indicators and sub-indicators of the ML1 WHO GBT for MD/IVDs has been created to aid in understanding opportunities for improvement within DGDAs current regulatory system.

Partnership and collaboration to enhance the regional and global quality assurance of medical products agenda: PQM+ participated in **WHO Regional workshop on SF** medical products held in Johannesburg November 15–18, 2022. The workshop was organized by the WHO regional office for Africa. PQM+ contributed to discussions on the MedRS tool and other tools for conducting medicine quality surveillance. Participation further strengthened collaboration with WHO and participating MRAs from the African continent.

Minimum Common Standards for Regulatory Information Management Systems (RIMS): MTaPS and PQM+ finalized the joint work and recommended a set of 32 minimum common standards for RIMS. An advocacy brief that provides a call to action to global, regional, and national stakeholders for adopting the standards to support RIMS in LMICs and a pathway document that identifies concrete steps and specific considerations for supporting national regulatory authorities to digitalize their information management systems were developed under this activity. Furthermore, the two groups collaborated on a new joint blog post titled "Finding Common Ground: Transforming Regulatory Information Systems in LMICs." The post discusses the process and benefits of adopting these standards.

Additionally, the PQM+ and MTaPS teams presented the work that the two programs developed at the first meeting of the drafting group of the WHO's guideline on RIMS. The presentation was well received by the WHO committee, who may build upon it for developing the WHO's RIMS guideline.

To **promote south-south cooperation in regulatory technical experience** and in knowledge exchange, PQM+ coordinated a visit of Uzbekistan MRA staff to the EFDA and to local manufacturers in Quarter 1. Similarly, PQM+ coordinated a knowledge exchange visit for the Uzbekistan MRA to Morocco to visit the WHO Collaborating Center for Pharmacovigilance. The MRA is now finalizing its roadmap for establishing its own pharmacovigilance center.

Chemistry, Manufacturing, and Controls (CMC)

CMC involves the development, production, and quality control of pharmaceutical products and devices. 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.

During 2022, the PQM+ CMC team provided technical assistance to 36 pharmaceutical manufacturers in 11 countries (Bangladesh, Ghana, India, Kenya, Liberia, Nepal, Nigeria, Pakistan, South Africa, Myanmar, and Uzbekistan) working on 61 product approvals.

Bangladesh. PQM+ continued to provide technical assistance to Bangladesh Manufacturer 2.[5] The dossier application for 4FDC is under assessment for pre-qualification by WHO.

Ghana. The PQM+ CMC team continued to provide technical assistance to three manufacturers (Ghana Manufacturers 1, 3, and 6) all for artemeter/lumenfantrine during this quarter. Also, assistance was given for oxytocin at Ghana Manufacturer 1. Ghana Manufacturer 3 has made

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

significant progress in product development and is in the process of completing a dossier for prequalification.

Core NTD. The PQM+ CMC team continued to provide technical assistance to two manufacturers of NTD products: albendazole (India Manufacturer 1) and praziquantel (India Manufacturer 3). Both companies successfully completed WHO site inspections for cGMP compliance.

During 2022, PQM+ advertised an EOI and received applications from manufacturers for potential technical assistance for eight NTD products. Five manufacturers successfully submitted applications for a total of six medicines (India Manufacturer 2, albendazole and ivermectin; India Manufacturer 1, mebendazole and praziquantel; Nigeria Manufacturer 1, mebendazole; Bangladesh Manufacturer 2, azithromycin and delta-azithromycin; and Kenya Manufacturer 1, azithromycin). Most notably, Bangladesh Manufacturer 2 is already preparing to submit a dossier for WHO prequalification (PQ).

In collaboration with the Local Production and Assistance (LPA) Unit of WHO, PQM+ held the NTD Advocacy Workshop October 11–13th in Mombasa, **Kenya**. The PQM+ CMC team gave presentations titled "PQM+ Technical Assistance for Manufacturers and Regulatory Authorities" and "Data Integrity" and facilitated question/answer opportunities about steps toward achieving WHO PQ status. The workshop was attended by 38 individuals representing 18 organizations from nine countries.

At the American Society of Tropical Medicine and Hygiene 2022 Annual Meeting held October 30 – November 3, 2022, in Seattle, the PQM+ team gave presentations on "Promoting Sustainable Access to Quality-Assured NTD Products in Low- and Middle-Income Countries," and the "Neglected Tropical Diseases: Medicines Information Dashboard," both.

Core TB. The PQM+ CMC team continued to provide technical assistance to two manufacturers of TB products. Pakistan Manufacturer 4 is nearing completion of the WHO PQ process for 4FDC and is awaiting a decision for an onsite inspection schedule date. PQM+ has also initiated technical assistance with Pakistan Manufacturer 4 for 2FDC.

Technical assistance was initiated with South Africa Manufacturer 1 for isoniazid. This is the only API manufacturer currently being supported.

COVID-19 Therapeutics. With funding from USAID's test-to-treat program, PQM+ is targeting LMIC based manufacturers applying for the prequalification of MPP licensed COVID-19 therapeutics. The aim is to identify the most suitable manufacturer to offer technical assistance, to speed the attainment of WHO PQ and thus promote increased access to COVID-19 therapeutics. The PQM+ CMC team identified and initiated technical assistance with India Manufacturer 3 to expedite its WHO PQ of Paxlovid product.

Burma. The PQM+ CMC team initiated technical assistance to Burma Manufacturer 1. Burma has an interest in improving the quality of local supply of chloroquine to fight malaria, and PQM+ technical assistance will be instrumental in improving the manufacturer's quality systems.

Nigeria. PQM+ continued to provide technical assistance to six manufacturers in Nigeria during 2022 (Nigeria Manufacturers 2, 3, 4, 5, 6, and 7). Three of the manufacturers, Manufacturer 4 (sulfadoxine/ pyrimethamine 500mg+25mg tablet), Manufacturer 3 (sulfadoxine/ pyrimethamine 500mg+25mg tablet), and Manufacturer 5 (lamivudine + zidovudine 150mg+300mg tablet) all

completed BE studies, a major milestone toward reaching WHO prequalification. Additionally, Nigeria Manufacturer 4 completed a palatability study for zinc sulphate 20 mg.

Uzbekistan. PQM+ continued to provide technical assistance to Uzbekistan Manufacturer 2 for WHO PQ of levofloxacin 500mg tablets. Dossier preparation has begun, and the company targets April 2023 for submission.

In November, **USAID Liberia Mission Director** Jim Wright visited Liberia Manufacturer 1 in Monrovia. Manufacturing staff provided updates and an overview of its products to Wright and Liberia Health Minister Dr. Wilhemina S. Jallah. PQM+ coordinated with the manufacturer and the USAID Mission to facilitate the director's and minister's visit.

Asia-Bureau. The strategy team finalized its analysis and prioritization of six countries as part of Activity 4.1 under the Asia Bureau workplan and developed a draft report based on the presentation given to USAID. PQM+ staff members are developing a Local Production Model Strategy, including review of an initial draft and feedback being incorporated into a revised version. With this work, PQM+ aims to support countries and regions to develop their own strategies for local production of essential medical products. Such strategies, when diligently implemented, will facilitate attaining sustainable manufacturing of quality-assured medical products and result in improvement in access to health products.

Laboratory System Strengthening (LSS)

To ensure quality, accuracy, and reliability of medicines quality test data, laboratories must employ robust systems of medicines and medical product analysis and evaluation. Implementation of robust systems, based on proven standards of quality management and medicines testing, ensure laboratories are operating under conditions and following procedures that promote good practices. This can aid in preventing 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 of this work are reliable.

To this end, PQM+ is supporting the African Union's New Partnership for Africa's Development (AUDA-NEPAD) in assessing the capacity of selected Africa-based laboratories to conduct independent testing of biologics for lot release; and in developing a reliance framework for laboratories' network. In the first quarter of PY4, PQM+ developed a survey to assess the biologics testing capacity of national medicines control laboratories in 16 countries across the African continent. The survey assesses the preparedness of these laboratories to conduct independent lot release, routine, and investigative testing of vaccines—specifically, COVID-19 vaccines—and will be deployed in the second quarter.

During Q1 PQM+ is also supporting 41 laboratories across 23 countries[6] in achieving accreditation across ISO 17025:2017; ISO 17025:2017 (for equipment calibration); ISO 17043:2010 (for conformity assessment/proficiency testing); WHO Prequalification; and ISO 15189 (for medical laboratories). Table 1 lists the laboratories that have achieved their first ISO accreditation or WHO PQ under PQM+, with three such achievements (marked with an asterisk) in Q1.

[6] PQM+ is strengthening quality control laboratories in all 24 countries with PQM+ buy-ins except Lesotho.

Table 1. Laboratories Accredited Under PQM+

Laboratory	Title of accreditation	Date of accreditation/PQ	Type of accreditation
Kazakhstan-Karaganda NQCL	WHO PQ	March 16, 2020	WHO PQ
Bangladesh NQCL- Physicochemical lab	WHO PQ	March 9, 2020	WHO PQ
Pakistan DTL Punjab, Faisalabad	WHO PQ	March 16, 2020	WHO PQ
Uzbekistan-Tashkent NQCL	National ISO 17025:2017	December 17, 2021	ISO 17025:2017
Uzbekistan-Andijan NQCL	National ISO 17025:2017	September 21, 2021	ISO 17025:2017
Pakistan IPH Diagnostic Laboratory, Lahore	ISO 15189	September 21, 2022	ISO 15189
Pakistan DTL Punjab, Rawalpindi	WHO PQ	October 22, 2022	WHO PQ
Mali LNS	Local ISO 17015:2017 accreditation	December 9, 2022	ISO 17025:2017
Pakistan PIMS Diagnostic Laboratory	ISO 15189:2012	December 16, 2022	ISO 15189

Other PQM+ LSS highlights this quarter include:

An assessment of the Agence Nationale de Normalisation et de Métrologie (ANM) Laboratoire d' Étalonnage des Masses (LEMA) in **Benin**, toward scope expansion of its ISO 17025:2017 Calibration Laboratory accreditation. The assessment evaluated the current state of the calibration facility and its quality system to determine strengths and weakness toward including three additional measurement parameters to their scope.

To assist the Ethiopian FDA in its efforts to prevent the spread of HIV and other sexually transmitted diseases, this quarter PQM+ facilitated calibration and maintenance of its condom testing equipment. Calibration of this equipment is critical to ensuring condoms distributed throughout the county are effective in preventing the spread of diseases.

Other Q1 activities in Ethiopia included the procurement of equipment for the branch laboratory in Diredawa. PQM+ purchased a (name of system) to treat laboratory water there by ensuring water used for medicines testing is of appropriate quality and reduces the number untested medicines due to poor water quality.

To increase capacity for rapid screening of medicines quality, PQM+ facilitated the procurement of Minilabs™ for **Burkina Faso, Ethiopia, Ghana, and Guinea**. MiniLabs™ allow for primary detection of substandard medicines without wasting resources and material required for full compendial testing.

In **Pakistan,** extensive PQM/PQM+ laboratory support to the Drug Testing Laboratory (DTL) of Rawalpindi resulted in the laboratory obtaining WHO PQ status. This is the third quality control laboratory in Pakistan to receive WHO PQ. Additionally, PQM+ technical assistance was instrumental for Pakistan Institute of Medical Sciences (PIMS) hospital medical diagnostic laboratory to achieve ISO 15189 accreditation. ISO 15189 is the international standard for medical diagnostic laboratory testing. PIMS is one of the largest public tertiary care hospitals in Islamabad, serving an average of more than 9,000 patients and admitting more than 70 patients a day.

Strategic planning enables a laboratory to refine its goals and objectives and develop roadmaps for achievement. In Q1 PQM+ aided **Bangladesh, Kenya, and Mali** to review their NQCL strategic planning and documentation for alignment with country goals. In **Burkina Faso**, PQM+

supported a meeting with approximately 30 participants to mobilize resources for the NQCL's finalized strategic plan.

In **Kazakhstan,** PQM+ held a vaccine lot release training workshop where participants from the medicines regulatory agency (MRA) were instructed and trained on the development and review of vaccine summary protocols templates and checklists for multiple vaccine production platforms. The audience included participants from various regional branches of the MRA.

In **Nigeria**, PQM+ performed a preassessment (mock) audit of the National Agency for Food and Drug Administration and Control (NAFDAC) Vaccines, Biologicals, and Medical Devices Laboratory in October using the SATTA tool. The audit is in preparation for the reaccreditation of 14 scopes of ISO 17025 and scope expansion to cover 26 scopes for medical devices and in-vitro devices (IVDs). The laboratory recorded 11 nonconformances, with a SATTA score of 76 percent.

Resource Mobilization and Optimization

Continued rollout of the risk-based post-marketing surveillance (RB-PMS) approach and companion MedRS tool. In FY2023, 21 PQM+ supported countries[7] are implementing RB-PMS. As of December 31, 2022, all 21 subscribed to the MedRS online tool, 19 of which were actively using the tool for RB-PMS in various stages of the process. Botswana and Brazil, two non-PQM+ countries, expressed strong interest in the MedRS tool and requested access to it, which PQM+ granted, and are active subscribers. The Botswana MRA is currently using the tool to develop its RB-PMS protocol. A consultant in Brazil is handling the MedRS tool account for the MRA there. The Government of Egypt expressed interest in using MedRS and requested training on the tool.

During November 7–11, 2022, PQM+ facilitated the first-ever RB-PMS workshop for SAHPRA, **South Africa**. The workshop covered orientation on RB-PMS principles, establishment of a technical working group (TWG), revision of guidelines, RB-PMS implementation plan and SOPs. There is a plan for a follow-up workshop to develop a pilot protocol for quality surveillance of medicines in South Africa.

PQM+ also supported a well-received RB-PMS training in **Nepal** to develop a RB-PMS protocol for selected anti-TB and MNCH medicines. Following the training, field sample collection took place with guest participation by the USAID Contracting Officer's Representative for the Medicines, Technologies, and Pharmaceutical Services (MTaPS) program and USAID PQM+ Activity Manager. PQM+ conducted remote training for sample collectors to support **Uzbekistan's** RB-PMS activity.

Vaccines such as those to mitigate health risks from COVID-19 are also susceptible to substandard and falsification issues. The principles and practices of the PQM+ RB-PMS approach are relevant for vaccine products as well. However, special attributes that are unique to vaccines are worth considering in the implementation of RB-PMS for vaccines. PQM+ is therefore developing a vaccine module in the MedRS tool, which countries may use for developing RB-PMS for vaccines.

[7] In Africa: Benin, Burkina Faso, DRC, Ethiopia, Ghana, Guinea, Kenya, Lesotho, Liberia, Madagascar, Mali, Mozambique, Nigeria, Rwanda, Senegal, South Africa. In Asia: Bangladesh, Kazakhstan, Nepal, Uzbekistan. In Latin America: Panama.

Global VAX

During this reporting period, as part of the Global VAX initiative and recognizing the common interest and need for biomanufacturing competency development across the region, PQM+ planned a joint workshop in South Africa, in collaboration with the AUDA NEPAD, the South African Health Products Regulatory Authority (SAHPRA) and Afrigen Biologics and Vaccines, and the WHO-supported COVID mRNA Technology Transfer Hub. The hybrid formatted workshop, which was held December 6–9, 2022, aimed to develop the vaccine manufacturing competency of various stakeholders, including regulators, academia, and private industry, and provide a forum for advocacy. Approximately 200 participants from national MRAs, the vaccine manufacturing industry, and academic institutions offering biotechnology and related programs attended virtually and in person. PQM+ supported the in-person participation of attendees from **Ghana, Kenya, Nigeria, Senegal,** and **South Africa**, as well as virtual participation from Rwanda, primarily representing national MRAs and academics teaching relevant biomanufacturing courses. NEPAD, the East African Community (EAC), and the German Agency for International Cooperation (GIZ), and provided additional funding to support other participants. The workshop was organized around three focus areas: (1) overview of vaccine development and manufacturing, (2) case studies, and (3) networking. Participants also visited the Biovac and Afrigen manufacturing sites in Cape Town, which allowed them an opportunity to observe the physical setup and operations of these facilities and establish working relationships with key people at these institutions.

Asia Bureau

The strategy team finalized its analysis and prioritization of six countries as part of Activity 4.1 under the Asia Bureau workplan and developed a draft report based on the presentation given to USAID.

Test-to-Treat Project

PQM + gathered essential information on the status of registration two COVID-19 antivirals—both branded (Paxlovid and Lagevrio) and WHO-prequalified generic (nirmatrelvir/ritonavir co-packaged and molnupiravir capsules) versions—and on existing market authorization mechanisms in all 10 test-to-treat countries. This has occurred through direct contact with countries' MRAs and suppliers of molnupiravir and nirmatrelvir. Data gathered will provide guidance for procurement and potential use of these products. In addition, PQM+ made several assessments of core suppliers of these products.

Learning, Advocacy, and Awareness

In Q1, PQM+ continued to develop and advance the use of evidence-based tools and approaches to improving medical product quality, as well as to raise awareness of the importance of medical products quality assurance.

New Tools and Approaches. New and adapted tools and approaches to improve medical product quality that were advanced this quarter include:

- Adapted a competency needs assessment tool based on WHO's Global Competency Framework.
- A product information report (PIR) for gentamicin injection to support registration of this product and inspection of manufacturers of this product.

Research and Analysis. This quarter, PQM+ made important progress with numerous research-related activities, including:

- In Ghana, completed interviewing nurses, midwives, doctors, pharmacists, and pharmacy technicians for a study on the storage conditions, use and management of selected maternal and child health (MCH) commodities in four regions.
- Disseminated findings from regulatory and quality assurance system assessments conducted in Benue, Kebbi and the FCT Abuja of Nigeria.
- Developed a questionnaire to assess GMP training needs of local manufacturers for a survey to be conducted of Manufacturers' Association members in Uzbekistan.
- Used a comprehensive framework to evaluate countries' capability to increase local production of health products to assess local pharmaceutical market needs, the enabling environment, and the local manufacturing and potential export capability of five countries (Vietnam, Indonesia, Uzbekistan, Kazakhstan, and the Philippines) in Asia.

Advocacy and Awareness. PQM+ supported diverse efforts to raise awareness of the importance of medical product quality assurance, including:

- Drafting an outline for a "Raising Visibility of the LMHRA" Campaign. The campaign includes adding information on successes to the LMHRA website, distributing a newsletter, and generation of social media posts.
- Supported the DDA of Nepal in organizing a policy dialogue on the domestic production of essential medicines. Representatives from national-level health agencies, professional bodies, academia, and the private sector participated and committed to implementing policies to improve access to essential medicines for the public.

Thought Leadership/Global Collaboration. Examples of PQM+'s participation in global discussions related to medicines quality in Q1 include:

- Reviewed and provided feedback on the LSHTM Implementation Toolkit for Small and Sick Newborn Care and presented on MCH commodities in a learning seminar on the toolkit.
- **Joint UNICEF-UNFPA-WHO Meeting** with manufacturers and suppliers: PQM+ staff attended this event in Copenhagen from November 28 to December 2, 2022. PQM+ was able to meet with manufacturers, UNICEF representatives, and WHO representatives to discuss ongoing joint activities, including laboratory support, market surveillance and control, regulatory networks (including the Coalition of Interested Parties, CIP), inspections, prequalification of medicines and provision of technical assistance to manufacturers of medicines listed in the expressions of interest (EOIs). The objective was to provide a forum for scientific and technical exchanges on prequalification and related regulatory systems strengthening initiatives to streamline technical assistance provided to manufacturers and regulators.
- **NTD Advocacy Workshop**: PQM+, WHO's local production and assistance unit (WHO LPA), and the WHO PQ (WHO PQ) team held this event on October 11-13, 2022, in Mombasa, Kenya. Staff from 12 African manufacturers producing medicines for the treatment of NTD, MRAs, CROs, and WHO attended the meeting. Topics covered the WHO PQ process and its benefits and challenges for manufacturers in sub–Saharan Africa; increasing demand for high-quality NTD generic products; and technical assistance support opportunities available from WHO's LPA unit and PQM+. USAID, WHO, and PQM+ also improved their understanding of the gaps and needs of manufacturers in Africa as a result of the meeting.

Cross-Bureau Activities and Progress

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

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

Progress This Quarter

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

PQM+ is developing a model guidance for national regulatory authorities to build capacity for emergency use authorization (EUA) for lifesaving medicines.

- During Q1, PQM+ consulted with University of Washington on development of the EUA model guidance and to define the scope of collaboration and deliverables.

Next steps are to conduct a background review of findings and summary of recommendations to help MRAs in LMICs develop procedures and guidelines for industry on data packages and review processes for EUAs of medicines through adoption, implementation, and management to expedite authorization for medicines of high public importance and lifesaving benefits. PQM+ is supporting AUDA-NEPAD to develop the Africa Continental Vaccine Lot Release Laboratory Network, to assess the capacity for biologics and national quality control laboratory (NQCL) lot release among select existing Africa-based laboratories and to develop a reliance framework.

- During Q1, PQM+ developed and disseminated a survey that built on data available from the predecessor PQM program and from data available to USP/Ghana through its participation in the African Medicines Quality Forum (AMQF). PQM+ built upon the mapping of national quality control laboratories (NQCLs) in the continent that USP/Ghana had previously conducted.

PQM+ is working to improve the technical capacity of MRAs in the Intergovernmental Authority on Development in Eastern Africa (IGAD) region and/or other regional economic communities (RECs) to adopt minimum common standards for a regulatory information management system for its four main functions (registration, inspection, licensing, and market control).

- PQM+ shared approach/minimum common standards (MCS) to RIMS and advised on ways to coordinate RIMS support for the African Medicines Regulatory Harmonization (AMRH) program.

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

PQM+ is finalizing a model strategy for local and regional production of essential medical products.

- Building on the desk review in PY3, developed a working draft. The model local production strategy developed by PQM+ will guide countries and regions on critical items to address in their pharmaceutical manufacturing strategies.

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

PQM+ is working to expand and deliver USAID's Pharmaceutical Systems Strengthening (PSS 101) in-person course in collaboration with USAID's MTaPS program, and during Q1

- Confirmed delivery dates for virtual training in February.

PQM+ is helping identify social and behavior change communication strategies and approaches to reduce demand for poor-quality medical products, particularly at the consumer/community level.

- PQM+ identified resources, held a preliminary consultation with Breakthrough Action, and discussed the approach for building key messages and interventions for community-level stakeholders in the quality assurance ecosystem.

PQM+ is working to implement USAID's High-Performing Health Care (HPHC)tool in two countries.

- Held orientation call with USAID on implementation timeline and potential PQM+ countries.
- Identified PQM+ staff for Mozambique and Kenya; awaiting Mission concurrences.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Execute Task Order 4 with University of Washington for development of the EUA model guidance.
- Continue mapping exercise of NQCL laboratories.
- Contribute technical expertise to draft a roadmap with SMART (specific, measurable, achievable, relevant, and time-bound) objectives for digitalization of a RIMS for the African Medicines Agency, RECs, and national regulatory authorities.
- Finalize training for PQM+ resources/staff on the HPHC tool; identify organizations and geographic lists for survey, engage Missions, and disseminate survey.
- Deliver quality assurance/regulatory module under PSS 101 training.
- Conduct background review of grey literature on appropriate use and quality assurance considerations for communities/individuals/providers and service delivery points.

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 quality management system (QMS) to achieve international recognition (ISO/IEC 17025 or WHO prequalification). This would assure the reliability of testing and increase public confidence in ANCQ test results.

In Q1, PQM+ supervised development of the 2022 RB-PMS antimalarial testing report, which the national quality control laboratory submitted to the national regulatory agency in November 2022.

In November, PQM+ kicked off the PY4 workplan by meeting with the three project beneficiaries—ANCQ, ABRP, and the *Agence Nationale de Normalisation et de Métrologie* (ANM)—and USAID Benin. PQM+ conducted a rapid assessment of ANM's *Laboratoire d' Étalonnage des Masses* (LEMA) to understand their needs for scope expansion and get a better understanding of their QMS and human resource capacity for scope expansion. The assessment report has been completed, translated and shared with ANM. PQM+ and ANM have developed an action plan towards scope expansion in pressure, humidity, and volume.

Also, in Q1, as part of preparing ANCQ for an accreditation assessment in Q1 of PY5 and to implement the remaining activities in their roadmap toward ISO/IEC 17025 accreditation, PQM+ provided QMS training on out-of-specification (OOS) and internal quality check (IQC). Sixteen participants (10 male: 6 female) were trained. Performing IQC is a requirement of the ISO/IEC 17025 standard, but ANCQ had not started implementing it. The training was theoretical, with hands-on sessions to demonstrate how to perform IQC checks in the laboratory. Laboratories safeguarding and ensuring the integrity of the data they generate is of paramount importance. Thus, the training on OOS provided technical staff with the requisite knowledge on best practices in managing laboratory-generated results that are OOS or indicate a failure in product quality. This will equip the trainees with the skills to ensure that the results they disseminate and reports they generate are of utmost integrity and reliably inform the needed regulatory actions.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support dissemination of the 2022 RB-PMS for antimalarials results.
- Support the post-marketing surveillance technical working group (PMS-TWG) to develop the second RB-PMS protocol.
- Conduct desk review for state of collaboration between ANCQ and ABRP.

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 quality assurance (QA) and quality control (QC). ANRP collaborated with the Directorate for the Control of Drugs and Non-Food Products (DCM/PNA) within the *Laboratoire National de Santé Publique* (LNSP), 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

In Q1, PQM+ collaborated with the USAID Burkina Faso Mission to support LNSP (now called ANSSEAT) to convene a donors roundtable to encourage development partners to provide financial and/or technical support to implement the new agency's strategic plan, which PQM+ helped develop in PY3. Various development partners participated in the workshop and expressed interest in components of the strategic plan. ANSSEAT developed a roadmap for resource mobilization and mapped the development partners to key strategic plan activities.

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

Select members of the Burkina Faso national PMS-TWG trained nine samplers (7 women, 2 men) who were deployed to collect the antimalarial samples for the 2022 RB-PMS. The PMS-TWG developed all training materials and delivered the training; PQM+ observed only. The samplers received orientation on the approved 2022 RB-PMS protocol for antimalarials and training on the use of the sample collection tools.

In Q1, the samplers completed the sampling successfully, with 349 antimalarial samples collected from six regions in Burkina Faso (Centre-Nord Centre, Nord Centre, Boucle de Mouhoun, Cascades Haut Bassin, Hauts Bassin and Haut Bassin Centre). These samples have been recorded and dispatched to the national quality control laboratory for screening. Minilabs were delivered in November and ANSSEAT began screening the samples.

As ANSSEAT prepares for an accreditation audit, PQM+ in Q1 supervised an internal audit of the agency's Directorate for the Control of Drugs (DCM) by PQM+-trained quality auditors. The internal audit used the Stepwise Assessment Tool Toward Accreditation (SATTA), which ANSSEAT institutionalized with support from PQM+ in PY2. While improvements in the QMS were noted, key milestones such as equipment qualification, implementation of measurement uncertainty and internal quality checks were not completed.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support development and dissemination of the 2022 RB-PMS report and results.
- Provide technical assistance to ANSSEAT to prepare for an ISO 17025 accreditation audit, including training on Karl Fischer titration, uniformity of dosage units and coaching on some of the gaps identified during the internal audit conducted of the DCM in Q1 (Measurement uncertainty and internal quality checks)

Democratic Republic of Congo (DRC)

The widespread availability and distribution of non-quality-assured artemisinin combination therapies and non-artemisinin therapies[8] 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

General supply chain disruptions have led to delays in shipment by the sole-source vendor of the Global Pharma Health Fund (GPHF) Minilabs, Technologie Transfer Marburg (TTM), resulting in Minilabs shipment to DRC still pending. These Minilabs are required to screen samples and screening is recommended immediately after collection to ensure correct evaluation at the point of sampling; therefore, the work was put on hold. The sampling will be scheduled when PQM+ is notified that the Minilabs have been shipped to DRC.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Supervise sampling and testing of samples for the 2022 RB-PMS.
- Provide technical assistance to ANSSEAT to prepare for an ISO 17025 accreditation audit, including training on Karl Fischer titration, uniformity of dosage units and coaching on some of the gaps identified during the internal audit conducted of the DCM in Q1 (Measurement uncertainty and internal quality checks)

[8] 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.

Ethiopia

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

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

Progress by PQM+ Objective

Objective 1. Improve governance for medical product QA system

Activity 1.1 Support streamlining/mitigation of regulatory barriers to import pharmaceutical APIs: The persistent challenges of securing medical product supply chains require proactive actions by national health and regulatory authorities to predict and mitigate the impact of shortages. Ethiopia is particularly vulnerable to this challenge. Multiple bottlenecks, including the shortage of hard currency, could restrict the public's access to needed medicines. Therefore, the country needs to address challenges that local importers face in importing active pharmaceutical ingredients (APIs), since the current regulation permits importing APIs.

In Q1, PQM+ provided both technical and financial support to develop a guideline on importing APIs and raw materials aimed at medicine importers, medicines manufacturers, researchers, education institutions, etc. Development of the guideline included engagement with relevant stakeholders, including EFDA, the pharmaceutical manufacturing association, the medicine import association, and others. This guideline contains requirements for premises and facilities, personnel, and documentation for importation of APIs and raw materials. The guideline details the requirements for issuing certificates of competence, requirements at ports of entry, and requirements for pre-import permit authorization.

EFDA's implementation of this guideline will ease challenges that local manufacturers face in the availability of pharmaceutical inputs, increasing production capacity and access to essential medicines. It will also enable the regulator to ensure the safety and quality of imported APIs and raw materials which will assure the safety, efficacy, and quality of locally manufactured pharmaceutical products.

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

substandard and falsified (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 market authorization and PMS.

Activity 2.1 Support EFDA in addressing WHO's GBT assessment findings and prepare it for WHO Maturity Level (ML) 3: In Q1, PQM+ provided technical assistance to prepare the regulatory authority for WHO's ML3 through addressing WHO's Global Benchmarking Tool (GBT) assessment findings. PQM+'s technical assistance helped EFDA fulfill the GBT tool requirements including sending the completed tools for WHO's regulatory team to evaluate and verify. PQM+ also assisted with drafting and finalizing six SOPs and implementing the proposed institutional development plan (IDP) to attain WHO ML3. WHO reviewed and provided feedback on the submitted IDP, and PQM+ supported a one-week workshop for EFDA to address the feedback.

In Q1, technical and financial support also helped with development and finalization of a clinical trial directive. PQM+ finalized the directive and submitted it to EFDA for endorsement.

Activity 2.2 Build capacity of branch EFDA laboratories toward ISO/IEC 17025:2017 accreditation and of the main lab to maintain its accreditation: EFDA has five branch laboratories in strategic locations based on levels of risk of SF products infiltrating the country. 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 to protect public safety. Currently, none of these laboratories is ISO/ IEC 17025:2017 accredited or WHO prequalified, meaning that their test results may not be fully reliable, particularly for confirming quality attributes that are not easily recognized through screening, and may not withstand legal scrutiny. During PY3, PQM+ supported implementation of the branch-specific roadmap toward ISO/IEC 17025:2017 accreditation, along with EFDA's central lab experts.

In Q1, PQM+ assistance included the following:

- Support to perform preventive/corrective maintenance and calibration of EFDA's condom testing machines. This is critical to maintain the condom testing lab's accreditation.
- Working closely with the Diredawa Branch of EFDA in addressing the ISO/IEC 17025:2017 accreditation roadmap. PQM+ assisted the branch to adapt, print, sign off on, and distribute 27 SOPs, one quality manual, and two policies (one on impartiality and one on confidentiality and conflicts of interest).
- Refresher training of two branch staff members to increase skills in preparing operational and process SOPs.
- Initiating procurement of water treatment equipment for the Diredawa Branch Laboratory. This equipment will solve one of the lab's main bottlenecks related to testing capacity of medicine samples.
- Communication and follow up with the Ethiopian Metrology Institute on the topic of Diredawa Branch Laboratory equipment calibration.
- Collaboration with EFDA to conduct another round of supportive supervision on EFDA's Diredawa Branch Lab (Diredawa Medicine Quality Control Desk) from December 26 to 30 to evaluate the implementation of QMS, status of equipment, and lab premises. The supervision aimed to provide technical support for the lab staff and address deficiencies that impede the lab's readiness for ISO/IEC 17025:2017 accreditation.

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 affordable quality-assured essential medicines. 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 redesigns to promote local production of pharmaceuticals. Despite remarkable efforts and commitment from the government to create 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, available evidence indicates that existing local manufacturers are facing formidable challenges to remain in business, let alone invest in quality improvements and capacity expansions.

Activity 4.2: Build capacity of selected local pharmaceutical industries for achieving WHO PQ and local GMP certification: In Ethiopia, few Giemsa stain solution manufacturers supply their products to the public procurement agency. In PY4, PQM+ plans to identify local Giemsa manufacturers, conduct rapid assessments, and provide relevant technical support to some of them to be able to manufacture quality-assured stains for testing malaria.

In Q1, PQM+ worked with relevant stakeholders in the area and identified a list of local Giemsa stain manufacturers. The next step will be conducting a rapid assessment of these manufacturers and developing an action plan to build their capability.

Priorities Activities for Next Quarter

- Conduct gap assessment of selected local pharmaceutical manufacturers for WHO PQ.
- Support the EFDA labs in annual proficiency testing (PT).
- Support EFDA in addressing GBT findings toward WHO ML3.
- Finalize testing of PMS samples.[9]
- Procure relevant lab equipment and supplies for the Diredawa Branch EFDA Lab.
- Conduct gap assessment for local Giemsa stain manufacturers and develop an action plan to address the gaps.

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.
- The newly started pooled procurement of lab supplies experienced delays, as PQM+ still has not received all needed lab supplies to start testing the PMS samples.

[9] The RB-PMS used the MedRS for randomization of facilities and sample size calculation. But because of some security-related issues, the samples could not be collected from all regions of the country and hence it is not nationally representative.

Ghana

The Food and Drugs Authority of Ghana (GFDA) is the national regulatory body responsible for the regulation of food, drugs, clinical trial protocols, and other products. GFDA carries out key regulatory functions through its divisions: Drug Registration and Inspections; Safety Monitoring and Clinical Trials; Medical Devices and Cosmetics; Monitoring and Evaluation (M&E); and Household Chemicals Substances. GFDA is ISO 9001-certified and, in 2020, attained WHO ML3. 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 maternal and child health (MCH) commodities such as oxytocin.

Progress by PQM+ Objective

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

Minilabs for Ghana cleared Customs in November, but FDA Ghana was not available to start the sampling this quarter due to conflicts with other activities.

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

In Q1, PQM+ completed the data collection for the zone of influence (ZOI) study. The study covered four regions in the Nothern Ghana: Upper West, Upper East, North East, and Northern Region. Eight hundred respondents (nurses, midwives, doctors, pharmacists, pharmacy technicians) from 298 facilities completed the questionnaire that PQM+ developed with approval from the Ghana Health Services Ethics Review Committee.

In Q1, PQM+ followed up with Ghana Manufacturers 1, 3, and 6 — the three supported manufacturers of antimalarials – to evaluate their progress in implementing their roadmaps toward WHO prequalification of the 20/120mg formulations of artemether-lumefantrine.

In addition, PQM+ worked with Ghana Manufacturer 2 to finalize its roadmap toward production and local registration of amoxicillin dispersible tablets (DT) and iron folic acid (IFA). PQM+ also followed up with Ghana Manufacturer 4 on its progress in installation of the equipment required to produce oxytocin injection.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support the national PMS-TWG to conduct sampling of antimalarial and MCH medicines for the 2022 RB-PMS.[10]
- Finalize the ZOI report and disseminate the findings to key MCH stakeholders in the country, including the Ghana Health Services and interested MCH partners.

[10] The results of this surveillance are not nationally representative.

- Conduct training for local manufacturers of both antimalarials and MCH products on analytical method validation and process development.

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

In Q1, LNCQM submitted the 2021 RB-PMS test results to DNPM. To prepare for the sampling of the 2022 RB-PMS, the Guinea national PMS-TWG trained twenty-three samplers (10 women, 13 men) to collect the antimalarial and MNCH samples for the 2022 RB-PMS. The PMS-TWG developed and delivered all training materials; PQM+ observed this training. The samplers were refreshed on the guidelines on RB-PMS, oriented on the approved 2022 RB-PMS protocol for antimalarials and trained on the use of the sample collection tools and sampling techniques.

Minilabs were delivered in Guinea in November, and PQM+ equipped the trained samplers with the necessary logistics to conduct the sampling per the 2022 RB-PMS protocol. In December, the samplers collected 166 antimalarial and MCH samples from seven regions in the country.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support the PMS-TWG to finalize the 2021 RB-PMS report and disseminate the results.[11]
- Provide training to LNCQM on measurement uncertainty and quality risk management.
- Develop the RB-PMS protocol for family planning medicines and recruit samplers from the universities in Conakry.

[11] These results are not nationally representative.

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.

In PY4, PQM+ is working to:

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

In Q1, PQM+ focused on improving governance for medical product QA systems, strengthening regulatory systems to assure the quality of medical products in Kenya, and advancing the global medical product QA learning and operational agenda.

Quarter 1 Highlights

During Q1, PQM+ in Kenya achieved the following:

1. Supported NQCL to develop a strategic plan for 2023-2027.
2. Worked with PPB to review guidelines and SOPs to support PPB in addressing recommendations from the WHO GBT ML3 assessment conducted in June 2022.
3. Worked with the Pharmaceutical Society of Kenya (PSK) to develop a curriculum and content for a competency-based course on pharmaceutical regulation and QA for pharmacists practicing in Kenya. The course will be hosted by PSK who will administer it to the practicing pharmacists in the country as part of their annual continuous professional development program to build their QA capacity at their different areas of practice.
4. Completed analysis and synthesis of local data from eight rounds of previous (2010 – 2021) antimalarial PMS activities and disseminated it to counties. The purpose of the exercise was to analyze the trends of the quality of antimalarial medicines in Kenya using the results of PMS conducted in the period. The 2021 round used the RB-PMS methodology.
5. Helped build local manufacturers' capacity on reproductive, maternal, neonatal, child, and adolescent health (RMNCAH) and malaria products on technical compliance and PPB's capacity on regulatory support.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ worked with PPB, DNMP, two county governments, and NQCL to play key roles in the QA of medical products in the country. The program:

- Supported PPB to complete a PMS strategy and a three-year costed workplan with a monitoring and evaluation framework for the pharmacovigilance/post-marketing surveillance technical working group (PV/PMS TWG).
- Supported completion of NQCL's strategic plan that will run from 2023 to 2027.
- Worked with PPB to strengthen its regulatory oversight for COVID-19 vaccine production through revision and development of guidelines and SOPs. This will also support PPB toward achievement of WHO GBT ML3.
- Participated as an observer in the ML3 meeting with PPB to assess progress in addressing recommendations from the June 2022 assessment.

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

PQM+ worked with PPB to set up a PV/PMS TWG to support its quality monitoring of health products and technologies (HPTs) in Kenya. The TWG is now functional and participates in PV and PMS activities. PQM+:

- Worked with the PV/PMS TWG team to finish writing the report on RB-PMS for malaria and RMNCH medical products.
- Disseminated results of the RB-PMS of antimalarial and RMNCAH medical products to key stakeholders involved in QA of health commodities. The RB-PMS samples were collected from areas considered to be most-at-risk of having SF medicines through the use of the Medicines Risk-based Surveillance (MedRS) tool to stratify risk. The results of the survey, therefore, represent the likelihood of finding an SF medicine from the surveyed areas and not from the whole of Kenya and as such, are not nationally representative.
- With the PV/PMS TWG, completed piloting a model to estimate the health and economic burden of SF medical products. In Kenya, the model was deployed to understand the health and economic impact of using SF oxytocin.
- Helped PPB develop a reliance guideline for collaboration with its regional and international partners on regulation of HPTs.

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

PQM+ collaborated with PSK to enhance the technical capacity of pharmacists in QA and regulation of pharmaceuticals in the country. The program:

- Continued working with PSK to develop a competency-based curriculum and content on pharmaceutical regulation and QA. The course will improve knowledge and skills of pharmaceutical personnel in the country on QA and regulation of HPTs in Kenya.
- Supported training for three regulatory staff (one female, two male) from Kenya to attend the Global VAX Vaccine Manufacturing Workshop in Cape Town, South Africa, in December. Two other participants from Kenya (one from PPB and one from Kenya Biovax Institute) also attended the workshop with support from Rwanda Regional Centre of Excellence for Vaccines, Immunization, and Health Supply Chain Management.

Priority Activities for Next Quarter

Next quarter, PQM+ in Kenya plans to:

- Work with PPB to revise and/or develop guidelines, procedures, and checklists to meet WHO GBT ML3 requirements.
- 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 exercises in Busia and Kisumu counties to monitor progress in implementing action plans and developed/revised SOPs on QA of antimalarial medicines and other essential HPTs.
- Continue supporting the PV/PMS TWG quarterly meetings and activities.

Lesotho

PQM+ is assisting Lesotho to strengthen its national medical product regulatory system. Currently, some basic medical product regulatory functions are being performed under the Ministry of Health by the Directorate of Pharmacy, but the country is moving towards establishing an independent regulatory authority as recommended by the WHO.

Quarter 1 Highlights

Toward the end of Q1 in December 2022, PQM+ received concurrence from the USAID Mission and subsequently, AOR approval of the PQM+/Lesotho workplan, allowing for activities to commence. Immediately following the workplan approval and obligation of funds, PQM+ hired and onboarded the Senior Program Manager for Lesotho and Southern Africa, to help drive and coordinate implementation of PQM+ Lesotho workplan activities. At the close of Q1, PQM+ had finalised travel arrangements to Lesotho for an in-country kick-off meeting in early Q2.

Priority Activities for Next Quarter

Next quarter (Q2), PQM+ in Lesotho plans to implement the following activities:

1. Hold an in-country project kick-off meeting with key stakeholders including the Ministry of Health, Pharmacy Directorate, USAID/PEPFAR, National University of Lesotho, Ministry of Health Programs responsible for HIV, Maternal & Child Health, and Family Planning and Reproductive Health.
2. Work collaboratively with the Pharmacy Directorate of the MOH to establish key contacts for workplan activities.
3. Provide technical assistance (TA) in developing a roadmap with human resource needs for all regulatory functions.
4. Provide TA in developing regulations, guidelines and procedures required to support implementation of the LMMDCA Act, 2019 and creation of the Lesotho national MRA.
5. Provide TA in drafting a memorandum of understanding (MoU) for reliance with other national MRAs and for quality testing of ARVs and other medical products at in-country health training institutions such as National University of Lesotho.
6. Provide TA in adapting the SADC regional regulatory harmonization strategy and protocols for Lesotho country context.

Liberia

PQM+ is working to improve the regulatory system in Liberia, with an emphasis on supporting the Liberia Medicines and Health Products Regulatory Authority (LMHRA), as well as its QC lab, and the School of Pharmacy.

This quarter, PQM+ supported the LMHRA to complete an assessment to determine the feasibility of LMHRA adopting an integrated regulatory information management system (IRIMS). PQM+ also supported the LMHRA QC lab to conduct an internal audit. PQM+ supported the LMHRA communication campaign on medicines quality. PQM+ also coordinated with Liberia Manufacturer 1 and USAID to facilitate the USAID Mission director's visit to that manufacturer.

Progress by PQM+ Objective

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

For good regulatory practice, an IRIMS is essential. It enables national MRAs to streamline regulatory processes, boost productivity and transparency, and guarantee that patients have access to high-quality, safe, and effective medical supplies.

This quarter, PQM+ coordinated with the LMHRA to complete an assessment to determine the feasibility of LMHRA adopting an IRIMS. The assessment report identifies gaps and challenges, and details recommendations to implement an IRIMS at the LMHRA. An IRIMS will ensure the smooth flow of information and data exchanges between LMHRA regulatory divisions and/or outside partners, as well as help the LMHRA keep improving performance to adhere to all applicable rules and regulations regarding the quality, safety, and effectiveness of medications and other medical supplies.

PQM+ also supported the LMHRA to complete an internal audit of its QC laboratory. Before the audit, PQM+ reviewed the audit plan and trained members of the audit team on how to perform an internal audit. This audit is part of the LMHRA roadmap toward ISO/IEC17025 accreditation.

PQM+ also supported the LMHRA communication campaign on medicines quality by:

- Drafting an outline for a campaign to raise LMHRA's visibility, which includes working with IT personnel to update the authority's website with stories, disseminating a newsletter comprising eight success stories, and developing one month's worth of social media posts.
- Drafting a list of social media tips for the team to use moving forward.
- Developing a contact directory for the LMHRA to use when disseminating newsletters, announcements, updates, etc. This list includes ministries and agencies of the Government of Liberia, local and international media, partners in the public health sector, people who have subscribed to the mailing list via the LMHRA website, etc.
- Designing a social media content calendar to use when promoting the campaign to raise LMHRA's visibility. The calendar will be used to inform the LMHRA LinkedIn, Facebook, Instagram, and Twitter audiences.
- Developing a key messages document that LMHRA can use when developing talking points and other public-facing materials.

- Drafting a personal image and video release agreement form.
- Drafting an international awareness days calendar for the LMHRA communications team to create relevant posts and disseminate them across social media platforms.
- Designing a newsletter via Mailchimp.

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

In November, USAID Liberia Mission Director Jim Wright visited Liberia Manufacturer 1 in Monrovia. PQM+ coordinated with the manufacturer and the USAID Mission to facilitate the director's visit. Minister of Health, Dr. Wihelimina Jallah, and LMHRA Managing Director, Keturah Smith Chineh, also attended. The three guests toured the manufacturer's facility.

This quarter, PQMI+ also supported the LMHRA to review Liberia Manufacturer 1's CAPA plan.

Left: Director Jim Wright (center) listens as Prof. C. Nelson Oniyama provides an update on Liberia Manufacturer 1. Right: Minister Jallah and Director Wright view some of the manufacturer's products

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

During Q1, PQM+ supported the School of Pharmacy to validate a curriculum for medical product quality assurance. Staff from the USAID Mission, the LMHRA, the Ministry of Education, PQM+, and School of Pharmacy attended the validation meeting, where a USAID representative lauded the collaborative effort between the School of Pharmacy and PQM+. The School of Pharmacy thanked the USAID Mission for the funding support.

Participants at the medical product QA validation meeting

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support improvements to the product evaluation and registration system at the LMHRA.
- Strengthen the LMHRA's capacity to perform QC screening of medical products and conduct PMS.
- Strengthen the capacity of the LMHRA QCL.

Madagascar

PQM+ collaborates with Madagascar's medicines regulatory authority ("AMM," or *Agence du Médicament de Madagascar*) to strengthen its capacity to assure medicines and medical product quality 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 (LNCQM*, Laboratoire National de Contrôle de Qualité des Médicaments)* 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

PQM+ continued offering technical assistance to AMM in implementing their RB-PMS protocol for reproductive health (RH) and antimalarial medicines.

- PQM+ and AMM had a kickoff meeting to discuss implementation of FY2022/23 activities and timelines.
- In accordance with the RB-PMS protocol, collection of reproductive health and antimalarial medicines samples commenced in seven of Madagascar's 11 regions.

PQM+ commenced support to LNCQM in the implementation of activities per its master plan and roadmap toward ISO/IEC 17025/2017 accreditation. PQM+:

- Provided LNCQM with U.S. Pharmacopeia (USP) substance reference standards for laboratory testing and a new dissolution tester.
- Presented a preliminary assessment report of LNCQM's new premises to the AMM director and head of LNCQM. The report includes recommendations for upgrading the new space to meet international laboratory standards.
- Commenced reviewing LNCQM's database of medical product batches that have previously undergone quality testing to provide recommendations for improvement.

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

PQM+ initiated discussions with the Faculty of Pharmacy, University of Antananarivo (FOP, UOA) and AMM to develop a short course on RB-PMS building on existing PQM+ training resources.

- An online kickoff meeting included PQM+ and representatives from FOP, UOA, and AMM. Participants discussed the objectives, activities, and deliverables of the tripartite collaboration.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Facilitate experiential learning to orient the director of AMM and the head of LNCQM to the best practices, opportunities, and challenges of the Ethiopian Food and Drug Authority in Addis Ababa regarding regulation and QA of medical products.
- Conduct a workshop with AMM and the PMS Technical Working Group to:
  - Define the governance structure, including an organogram and job descriptions for staff conducting market surveillance and control activities.
  - Develop a guideline on reporting, investigating, recall, storage, and disposal of SF medical products.
  - Develop a monitoring and evaluation framework for RB-PMS.
- Conduct an on-site assessment of LNCQM's new premises to update recommendations included in the preliminary assessment report.
- Train AMM staff on risk-based pharmaceutical inspection.
- Official launch of the new dissolution tester donated by USAID.

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, but it lacks both ISO/IEC 17025 accreditation and WHO prequalification.

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

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

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

In Q1, PQM+ collaborated with LNS on a two-day workshop to validate the new five-year strategic plan, which PQM+ helped develop in Q4 of PY3. The 26 LNS participants (19 men and five women) participated in the interactive workshop. The strategic plan was reviewed in plenary and participants defined the activities for the distinct strategic objectives and related initiatives. During this workshop, PQM+ and the finance team discussed how the activities would be funded and what tools LNS might need to expand its testing revenues.

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

LNS received official communication in Q1 from the West African Accreditation System (SOAC) that it would receive ISO/IEC 17025 accreditation for four physico-chemical quality control techniques: pH, loss on drying, Fourier transform infrared spectrometry (FTIR), and Karl Fischer titration. This attests to the strong quality management system that the Mali LNS has built with PQM+ support since the program launch in 2020 and is a significant step toward ensuring that LNS operations are sustainable.

Also in Q1, the PMS-TWG completed the screening and confirmatory testing of all 341 antimalaria and MCH samples collected as part of the 2022 RB-PMS.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Supervise the screening and confirmatory testing of the 2022 RB-PMS samples.
- Support Mali's PMS-TWG to disseminate the 2022 RB-PMS results.[12]

Mozambique

Mozambique recently established an autonomous medicines regulatory authority, ANARME, IP (*Autoridade Nacional Reguladora de Medicamentos, Instituto Publico)*, which encompasses the *Laboratório Nacional de Comprovação da Qualidade* (LNCQ) as a division of ANARME, IP. PQM+ has been providing technical assistance in the transition to an autonomous national MRA and assistance moving ANARME, IP toward attaining WHO GBT ML3 and achieving ISO 9001:2015 certification. Additionally, PQM+ has been assisting LNCQ to identify and bridge

[12] These results are not nationally representative.

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

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ continued offering technical assistance to ANARME, IP in strengthening key regulatory functions to support progress toward ISO 9001:2015 certification and achieving WHO ML3. This is expected to strengthen systems to ensure access to and availability of safe, effective, and quality-assured medical products in the country.

In Q1, PQM+:

- Conducted a four-day training for technical personnel from ANARME, IP's Division of Medicines, Health, and Biological Products Evaluation. During the training on medical devices regulation and dossier review, PQM+ trained 11 participants (seven female, four male) and focused mainly on condoms.
- Facilitated the first ISO 9001:2015 audit of ANARME, IP in collaboration with Bureau Veritas®.
- Initiated discussions with ANARME, IP leadership on PQM+ support for FY 2022/23 with a view of facilitating planning and consolidation of related activities. These activities include RB-PMS for antiretroviral medicines, long-acting contraceptive implants, and COVID-19 vaccines and therapeutics.
- Designed and shared with ANARME, IP a questionnaire to collect information on medicines evaluation and registration procedures. This was in preparation for the introduction of new COVID-19 therapeutics in Mozambique and to determine the level of support PQM+ will offer.

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

LNCQ is pursuing ISO 17025:2017 accreditation with PQM+ technical support. During PY3, PQM+ supported the development and review of key QMS documents and procedures, procurement of equipment and reagents, maintenance of existing laboratory equipment and strengthening laboratory testing capacity through proficiency testing. In PY4, PQM+ is focusing the laboratory systems strengthening work with LNCQ on addressing gaps and finalizing preparation for ISO 17025:2017 accreditation.

During Q1, PQM+:

- Initiated discussions with LNCQ on existing gaps and on modalities of providing the planned technical support to the laboratory and progress toward ISO 17025:2017 accreditation. This is expected to allow planning of the available and necessary support from the PQM+ technical resources.
- Engaged LNCQ leadership and technical personnel to review plans for completing training related to ISO 17025:2017 accreditation, including hands-on practical sessions with PQM+ laboratory specialists.

- With the LNCQ, reviewed planned procurements for equipment, reagents, and services required for ISO 17025:2017 accreditation and to support the planned RB-PMS.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Complete training on ISO 17025:2017 and conduct a mock audit to determine LNCQ's progress toward achieving accreditation.
- Work with ANARME, IP and the PMS-TWG to initiate RB-PMS activities targeting antiretroviral medicines, COVID-19 vaccines, and long-acting contraceptive implants, per approved workplans. The samples for RB-PMS will be collected from areas considered to be most at risk of having SF medicines based on risk stratification using the MedRS tool. Therefore, the survey results will represent the likelihood of finding an SF medicine from the most at-risk areas and will not be nationally representative.
- Initiate procurements for equipment, reagents (including proficiency testing samples), and services (equipment maintenance and calibration).

Nigeria

PQM+ is focused on helping ensure the quality of medicines and other medical products in Nigeria, with an emphasis on malaria and MNCH medicines and family planning commodities. PQM+ collaborates with stakeholders in the public and private sectors to increase local pharmaceutical manufacturing capacity and sustainably strengthen regulatory systems at the national and state levels. PQM+ also strengthens QMS and builds laboratory capacity in QC testing in compliance with international standards.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ collaborated with the Food and Drug Services (FDS) Department of the Federal Ministry of Health (FMoH) to organize a three-day workshop of the TWG from November 9 to 11, 2022, to develop the National Strategy for the Pharmaceutical Manufacturing Sector.

- The workshop included plenary and breakout sessions of the TWG's six committees to develop key points under the various thematic areas of the strategy.
- The consultant in charge of the TWG will consolidate the various key points from the TWG into a first draft of the strategy for deliberation by the TWG at the next meeting.

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

PQM+ accomplished the following under Objective 2 during Q1.

Strengthening of Quality Control Laboratories (QCLs)

- Performed a preassessment (mock) audit of the National Agency for Food and Drug Administration and Control (NAFDAC) Vaccines, Biologicals, and Medical Devices

Laboratory in October 18-21, 2023, using the SATTA tool. The audit is in preparation for the **reaccreditation of 14 scopes of ISO 17025** and scope expansion to cover **26 scopes for medical devices and in-vitro devices** (IVDs). The laboratory recorded **11 nonconformances,** with a SATTA score of **76 percent.** The assessment indicated major nonconformances in the **lab's conduct of proficiency testing,** with a score of **zero percent (0%) and** other minor findings in the **documentation processes of the proposed scopes of accreditation.**

- Conducted a mock audit of NAFDAC's Agulu Laboratory in October25-28, 2022 using the SATTA tool, as a last step of preparation toward **reaccreditation of 16 existing scopes of ISO 17025** and **scope expansion for 25 scopes of medical devices and food**. The laboratory recorded **15 nonconformances,** with a SATTA score of **68 percent**. The assessment recorded major non conformances in the **lab's conduct of proficiency tests** with a score of **zero percent (0%)** with other minor findings in the **documentation processes of the proposed scopes of accreditation**.
- Supported the development and review of SOPs for QA of water and food during the mock audit. This is the first time that PQM+ has supported the development and review of food and water analysis SOPs at NAFDAC.
- Conducted a gap assessment of the NIPRD Microbiology and Biotechnology Department in November as part of technical assistance toward the extension of scope to microbiological quality control of medicines. The audit team **observed and recorded 26 audit findings (nonconformances)**, PQM+ is supporting the effective closure of all the findings.
- Participated virtually in the ANSI National Accreditation Board (ANAB) final assessments of the NAFDAC laboratories in November and December. The findings from the assessment are as follows:
    - Central Drug Control Laboratory – no findings, 100 percent conformance, 17 reaccreditation scopes.
    - Kaduna Laboratory Service – no findings, 100 percent conformance, 16 reaccreditation scopes.
    - Vaccine, Biologicals and Medical Devices Laboratory Service – no findings, 100 percent conformance, 14 reaccreditation scopes, and **26 new scopes in medical devices and IVDs.**
    - Agulu Laboratory Service – no findings, 100 percent conformance, 16 reaccreditation scopes, and **25 new scopes in medical devices, food, and water**.

Regulatory and Quality Assurance System Strengthening (RQAS)

- Finalized the reports of RQAS assessment surveys in three new states: Benue, Kebbi, and the Federal Capital Territory (FCT).
- Conducted dissemination meetings in October for findings of the regulatory and QA system assessments in Benue, Kebbi, and the FCT Abuja.
    - The meetings included about 30 representatives from the three states in attendance and the participants developed action plans to address the findings from the survey for each state.
- Conducted quality assurance training in December 2022 for **883** participants (376 females, 507 males) comprising **336** (153 females and 183 males) operators of

community pharmacies and **547** (233 females, 324 males) operators of patent medicine shops in the FCT.

- Inaugurated a pharmaceutical inspection committee (PIC) and a quality assurance committee (QAC) for the FCT.

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

PQM+ continued to provide support to manufacturers to produce quality-assured priority medical products (MNCH, antimalarial, and nutrition).

MNCH and Malaria Products

- **Nigeria Manufacturer 3:** Submitted their sulfadoxine/pyrimethamine SP product dossier to the WHO PQ team for evaluation; WHO has confirmed the acceptance of the dossier.
- **Nigeria Manufacturer 3:** PQM+ is providing technical assistance on equipment installation and calibration for the oral solid dosage (OSD) form line extension.
- **Nigeria Manufacturer 4:** Feedback from the WHO PQ inspection team about the PQ inspection at the manufacturing facility for sulfadoxine/pyrimethamine (SP) in Q4 of PY3 is encouraging.
  - The team noted only five major observations, none of which were critical.
  - PQM+ supported the Nigeria Manufacturer 4 team to develop and review a CAPA plan in response to the WHO PQ team's observations.
- **Nigeria Manufacturer 4:** Supported the technical team in developing a CAPA plan responding to feedback from the WHO PQ team on its inspection of the palatability and acceptability study sites for zinc sulfate dispersible tablets.
- **Nigeria Manufacturer 6:** Supported the installation and qualification of manufacturing equipment for the new oral solid dosage forms facility.

Ready-to-Use Therapeutic Foods (RUTF)

PQM+ conducted a walkthrough of Nigeria Manufacturer 8, which produces peanut butter and had expressed interest in the supply of peanut butter to manufacturers of RUTF in Nigeria. The inspection team informed the management of the company about the need for upgrades in their processes, expansion of their capacity and institutionalization of QMS towards food safety certification as conditions that will enable such an arrangement.

Capacity Building

CDDDP: Trained **14** representatives (nine female, five male) from the Center for Drug Discovery, Development, and Production (CDDDP) at the University of Ibadan on pharmaceutical quality systems (PQS) as part of institutionalizing QMS in their operations.

Priority Activities for Next Quarter

In Q2, PQM+ in Nigeria plans to:

- Convene a meeting of the TWG for the NSPP to review the first draft of the strategy.

- Conduct medical product quality assurance trainings for members of PICs and operators of community pharmacies in the other states, especially Kebbi and Benue.
- Strengthen NIPRD capacity on microbiology testing toward ISO 17025 accreditation scope extension and reaccreditation for physicochemical tests:
    - Support calibration and qualification of equipment in the Microbiology and NIPRD Central laboratories.
    - Support proficiency testing/interlaboratory comparisons (PT/ILC) for the identified microbiological testing parameters/scopes for accreditation.
    - Review microbiology SOPs for microbial limit, sterility, and bacterial endotoxin tests.
    - Conduct mock audit and follow-up on closure of the 26 nonconformances observed during the earlier reported assessment.
    - Provide supervisory support to the NIPRD QCL during the official assessment of the lab for the ISO 17025 reaccreditation and scope expansion into microbiology testing.
- Support PCN QMS champions to cascade training received for ISO 9001 to zonal offices.
    - Conduct workshop at two zonal offices, Lagos and Kano, to cascade training on ISO 9001:2015.
    - Support institutional development of a quality management system.
    - Supervise internal audit of the two zonal offices.
- Continue to provide support on progress with CAPA response to WHO PQ as well as feedback from WHO on dossier evaluation.
- Prepare Nigeria Manufacturers 4 and 6 (which both have products at advanced stages of WHO PQ) for WHO PQ inspection of their facilities.
- Continue to work with Nigeria Manufacturer 2 in building their capacity towards dossier compilation.
- Conduct a training workshop with CDDDP and industry on current trends in key areas of GMP.
- In collaboration with PCN and other stakeholders, conduct sensitization and capacity building workshops for CPs and PPMVs on various quality assurance topics on the state supply chain.
- Conclude the zero draft of the national strategic plan for the Nigeria pharmaceutical manufacturing sector and conduct a review of the zero draft by the TWGs.

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 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 and Regional Center of Excellence for Vaccines, Immunization, and Health Supply Chain Management.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ commenced offering technical assistance to Rwanda FDA to strengthen its capacity to conduct RB-PMS of COVID-19 vaccines. The assistance from PQM+ included:

- Review of RB-PMS documents (protocol, guidelines, and procedures) and incorporating information on COVID-19 vaccines and vaccines in general.
- Review of the PMS-TWG terms of reference.
- Initiation of procuring security enhancing, and occupational health and safety equipment for the quality control laboratory.
- Expanding the RB-PMS TWG (established in PY3) to include multi-sectoral vaccines experts who are responsible for vaccines-related RB-PMS activities.

Priority Activities for Next Quarter

Next quarter, Rwanda PQM+ plans to:

- Review, update, and validate RB-PMS protocol, guidelines, and procedures.
- Train RB-PMS TWG on use of validated RB-PMS protocol, guidelines, and procedures.
- Facilitate one RB-PMS TWG meeting.
- Train RB-PMS TWG on:
    - Sample collection of pharmaceutical products, including those of maternal and child health (MCH) and family planning/reproductive health (FP/RH) medicines; and
    - Testing, analyzing results, compiling, and publishing RB-PMS report.
- Support Rwanda FDA to subscribe to select scientific journals on quality and safety of medical products.
- Train Rwanda FDA staff on detecting, preventing, and responding to SF medical products, including use of Minilabs.
- Train Rwanda FDA inspectors to plan and execute risk-based inspection of establishments.
- Train QCL staff on methods and equipment suitability verification, equipment performance and preventive maintenance, equipment calibration, and measurement uncertainty.
- Conduct a mock audit and support QCL staff to initiate ISO 17025:2017 accreditation and WHO PQ process.
- Provide technical support in proficiency testing (PT) of 10 samples.
- Guide Rwanda FDA QCL on how to perform compendial tests of sampled medicines and facilitate testing of samples which QCL cannot test outside Rwanda.

- Assist Rwanda FDA to develop, review, and validate missing current GMP (cGMP) guidelines.
- Train Rwanda FDA on use of cGMP guidelines and offer technical support in adapting or adopting guidance from the Regional Medicines Regulatory Harmonization (EAC/MRH) initiative on joint cGMP inspection.
- Collaborate with Rwanda FDA to support local manufacturers (solid and liquid pharmaceutical products, medical equipment, and devices) to conduct rapid QA systems and cGMP capacity assessments and work with them to compile CAPA plans and provide technical assistance to address gaps and update their QMS documents, including quality risk management plans.

Senegal

PQM+ works with the new *Agence Sénégalaise de Regulation Pharmaceutique du Senegal* (ARP), a fusion of the former DPM and LNCM, to strengthen its market surveillance function through a PMS Unit to implement RB-PMS and to improve the capacity for medicine 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 ML3 by December 2022, based on direction from President Macky Sall. Both LNCM and DPM were busy with this process and started putting together the regulatory documents required. As a result, between February and April 2022, neither beneficiary was available to implement 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 focused on the operationalization of the new agency.

Progress by PQM+ Objective

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

In Q1, PQM+ supervised the screening of 247 antimalaria samples collected from Dakar, Zigunchor, Diourbel, Kaolack, Kolda, and Kedougou, which has been completed. The national quality control laboratory is now conducting confirmatory testing of these samples.

In addition, PQM+ completed a working session/training of management of risks and opportunities. The 15 participants from the national quality control laboratory of ARP, Direction de Contrôle Qualité (DICQ), included nine men and six women. The session enabled the laboratory personnel to appreciate the need to identify risks associated with the tasks performed and establish control measures to prevent or reduce risk and optimize opportunities. Managing risks to quality systems is a key advance requirement of the ISO/IEC 17025 standard.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Conduct a baseline assessment of ARP, per the ISO 9001 standard.
- Supervise the confirmatory testing of the 2022 RB-PMS samples.

Asia Region

Asia Bureau

PQM+'s technical assistance funded by USAID's Asia Bureau promotes regional regulatory convergence and reliance. PQM+ works with regional health networks such as 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

From December 5 to 9, PQM+ and MTaPS conducted a five-day virtual training of trainers (TOT) course on product evaluation for registration of biologicals in collaboration with the ASEAN Secretariat. The objective of the training was to:

- Enhance knowledge and understanding of current global regulatory requirements that must be considered during product registration and evaluation of biological products, including vaccines, and
- Sustainably strengthen medical products quality assurance systems in LMICs.

During the TOT, roughly 22 assessors/reviewers from 9 ASEAN member states evaluated medicines' dossiers for registration.

PQM+ is developing course materials and arranging logistics for a second TOT on bioavailability/bioequivalence. The training will take place next quarter and target the 10 ASEAN member states.

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

In PY3, PQM+ designed and used a comprehensive, multi-stage selection framework and methodology to identify priority LMICs in the Asian region whose pharmaceutical product manufacturing capability can be increased to meet local pharmaceutical needs. The methodology included a scoring criterion for shortlisting countries for further qualitative research.

In Q1, PQM+ used the framework to assess local pharmaceutical market needs, the enabling environment (business, policy, and regulatory), and the local manufacturing and potential export capability of five shortlisted countries (Vietnam, Indonesia, Uzbekistan, Kazakhstan, and the Philippines). The team organized a virtual meeting with USAID's Asia Bureau, Missions in the five shortlisted countries, and the PQM+ AOR team to share the approach, selection methodology, and initial findings. Taking into consideration feedback received during the meeting, PQM+ drafted a report capturing the preliminary observations.

Priority Activities for Next Quarter

Next quarter, PQM+ Asia Bureau plans to:

- Conduct the TOT on bioavailability/bioequivalence.
- Finalize the preliminary analysis report once USAID gives its feedback.
- Conduct interviews with subject matter experts and stakeholders in shortlisted countries to select one or two countries for an in-depth market feasibility study.

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 ML3 in vaccine regulation; providing 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.

Progress by PQM+ Objective

Objective 1: Governance for medical product quality assurance systems improved

PQM+ is helping DGDA improve its governance of medical product QA systems. During the quarter, it helped finalize the regulatory framework document. After the task force committee meeting on September 28, PQM+ updated the regulatory framework draft and sent it to USP HQ for technical review. Also, during the quarter, PQM+ finalized – with the DGDA director and NCL deputy chief – a five-year strategic plan for the NCL 2022-2026. USP HQ is now reviewing the plan. PQM+ is also helping Bangladesh's Ministry of Health and Family Welfare (MoHFW) to develop the Fifth Health, Population, and Nutrition Sector Program (HPNSP) 2024-2029. MoHFW formed a team to prepare reports on specific thematic areas in connection with preparations for the Strategic Investment Plan (SIP) for the HPNSP. PQM+ is supporting the section of the SIP that deals with quality and affordable drugs and submitted an inception report to prepare the SIP for the 5th HPNSP to the SIP team lead.

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+ is helping DGDA achieve WHO ML3 by strengthening the QMS and addressing recommendations in the country's IDP. On October 3, DGDA, PQM+, and WHO organized a meeting of the Coalition of Interested Parties (CIP). During the meeting, PQM+ presented key support areas and outcomes of the CIP. PQM+ also assisted in the revision of an SOP for competency assessment, performance evaluation, and staff appraisal, as well as preparation of a new SOP on compiling and disseminating the DGDA annual report.

In mid-October, PQM+ provided technical support to the DGDA to draft regulatory framework documents for medical devices. On October 10, PQM+ helped assess DGDA's medical devices regulation. Senior officials of the directorate, including the director general, attended the assessment meeting. The key findings of the assessment were the lack of a standardized process for device registration submission, review, and response; and the lack of a standardized regulatory inspection process for device manufacturers. Dr. Melody Scott, PQM+ technical advisor for RSS-Medical Devices, assisted in the preparation of regulatory framework documents for medical devices.

DGDA also organized a training program on medical devices regulation. DGDA's director general inaugurated the training program, while PQM+'s Chief of Party presented the training overview and objectives. Nine men and four women from the DGDA and NCL participated in the training. The participants learned the WHO Regulatory Framework for MD/IVDs, MD/IVD Classification rules, QMS ISO Standards 9001 & 13485 which helped them improve their basic knowledge of regulation and strengthen regulatory activities of medical devices. On October 13, as a part of the assessment and training, DGDA organized a practical dossier review session for DGDA and PQM+ officials. Dr. Scott facilitated the assessment, training, and dossier review session.

PQM+ continues to assist DGDA's Market Surveillance and Control Department in implementing RB-PMS of priority medicines (TB, MCH, and family planning) and vaccines. On November 8, USAID, DGDA's Director of Market Surveillance and Control, and PQM+ observed the operation of the Mymensingh Minilab and the day-to-day activities of four field inspectors. Following the visit, PQM+ conducted a refresher training on RB-PMS for existing and newly recruited inspectors. Later in the month, DGDA formed a 12-member TWG, which then supervised staff training on the MedRS tool. Following the training, the TWG met to finalize the RB-PMS protocol considering anti-TB medicines. Once the RB-PMS committee completes its review of the protocol, DGDA will begin surveilling programmatic medicines in priority health areas (e.g., anti-TB medicines).

In December, PQM+ recruited a consultant to conduct a rapid assessment of SF anti-TB medicines in the private sector.

Sub-Objective 2.2. Medical product QCL capacity strengthening to support sustainable PMS programs

PQM+ is building the capacity of the Central Drug Testing Laboratory (CDTL) in Chattogram to test the quality of medicines and is continuing technical assistance to the NCL physicochemical laboratory. During the quarter, PQM+ helped develop and approve two SOPs for medical devices equipment (medical gas mask exchange pressure difference tester and particle filtration efficiency tester); delivered theoretical training on impurity tests with high-performance liquid chromatography (HPLC) to 22 technical staff from the NCL; and, with the deputy director of the CDTL, reviewed the CDTL roadmap 2021-2025 and helped CDTL prepare a plan for international accreditation.

PQM+ is also helping the Plasma Plus Research and Testing Laboratory (PPRTL) of the Independency University Bangladesh to address CAPAs to achieve ISO/IEC 17025:2017. In December, PQM+ met with the dean of the School of Pharmacy and Public Health at Independent University, Bangladesh, to discuss increasing the demand for medicines testing at PPRTL.

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

PQM+ continues to provide technical support to Bangladesh Manufacturer 2 to achieve prequalification of first-line TB medicines. In October, the manufacturer sent a pilot bio-batch sample to the contract research organization (CRO); the result was expected by December. Earlier, PQM+ conducted a GMP inspection of the manufacturer to review the manufacturing process for 4FDC. The CRO, ACDIMA Bio-Center in Jordan, will conduct the bioequivalence (BE) study.

PQM+ is also helping a local CRO build its capacity to support BE studies in country. On July 25, 2022, PQM+ published an expression of interest (EOI) for CROs interested in receiving such technical assistance. In October, PQM+ completed its evaluation of a document submitted under the EOI.

Finally, PQM+ is providing support to the Bangladesh Association of Pharmaceutical Industries (BAPI) to develop a pool of trainers who can provide pharmaceutical training to technical staff working on manufacturing projects of APIs. As part of the planned ToT, PQM+ prepared and reviewed with DGDA and BAPI a concept note for an API industry visit to India. The purpose of the visit is to contribute to developing the competency of selected trainers so that they can deliver proper training to the technical staff of API plants which ultimately will build the country's capacity to face the challenges that evolved after Trade-Related Aspects of Intellectual Property Rights (TRIPS) exemption. PQM+ also shared the list of participants, concept note, and budget for the India visit with the WTO cell of the Ministry of Commerce for funding. In November, PQM+ reviewed the concept note, agenda, and visit plan with officials from USP India and the PQM+ regional office, and prepared a local API industry visit plan so the trainers' pool could understand the compliance standards for local versus Indian API manufacturers.

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

PQM+ is providing support to DGDA to analyze the state of anti-microbial veterinary medicines at the national and sub-national levels and is helping plan corresponding regulation capacity, market surveillance and control, and quality testing of those medicines. To that end, PQM+ organized a consultative meeting with representatives from the Department of Livestock (DLS), Ministry of Fisheries and Livestock, to discuss strengthening the quality of animal health medical products, especially the use, availability, access, and regulation of antimicrobials. DLS and PQM+ agreed to visit DLS's three testing laboratories. PQM+ will conduct an inception meeting with senior DGDA officials, and DLS will share work plan activities under PQM+.

PQM+ also provides technical support to DGDA and the Ministry of Fisheries and Livestock to develop and finalize national formularies for animal health. Furthermore, PQM+ will oversee development of the Bangladesh Veterinary Formulary (BDVF).

Other Activities

- From November 6–9, in cooperation with WHO, DGDA organized a capacity strengthening workshop on GMP guidelines to ensure compliance with DGDA's regulatory inspection department's CAPA. PQM+ facilitated two sessions on advanced GMP per WHO TRS 986 Annex 2 and WHO's Good Pharmaceuticals Practices of Microbiology Laboratories.

Table 2: Status of Labs Accreditation in Bangladesh

Laboratory	Accreditation Sought	Initial Gap Assessment	CAPA	QMS	PT/LT	LIF	Official Inspection/ Pre-assessment
National Control Lab (Physicochemical Lab)	ISO: IEC 17025/2017 (Reaccreditation) By ANAB	Completed	Completed	Completed	Completed	Submitted and approved	Re-assessment completed (August 30 to September 1). Certificate renewed
National Control Lab (Microbiology Lab)	ISO: IEC 17025/2017 (reaccreditation) by Bangladesh Accreditation Board (BAB)	Completed	Completed	Completed	Completed	Submitted and approved	Re-assessment completed 2020. Certificate renewed

Laboratory	Accreditation Sought	QMS	Initial Gap Assessment	CAPA	LIF	Official Inspection/ Pre-assessment
National Control Lab (Physicochemical Lab)	WHO PQ	Completed	Completed	CAPA closed	Submitted and approved	Achieved WHO PQ in March 2020.
National Control Lab (Microbiology Lab)	WHO PQ	Completed	Completed	CAPA closed	Submitted and approved	Achieved WHO PQ in March 2020.
National Control Lab (Microbiology Lab +Vaccine Chemical lab)	WHO ML3	Completed	Completed	CAPA closed	-	Reassessment by WHO is pending; ML3 not yet achieved

Priority Activities for Next Quarter

- Hold consultative meeting with DGDA, NCL, and PQM+ on the draft of NCL's five-year strategic plan.
- Provide training on preparing SOPs for CDTL staff.
- Finalize the DGDA regulatory framework document.
- Organize a visit for the trainers' pool to the API industrial park and to an API manufacturing company in Bangladesh.
- Organize a consultative meeting to gather input from relevant stakeholders on the draft regulatory framework document for medical devices.
- Conduct surveillance of TB medicines using the RB-PMS protocol.
- Support Bangladesh Manufacturer 2 in completing the pilot and pivotal BE study of 4FDC and address the GMP gaps identified during the September 2022 assessment.
- Conduct a gap assessment of selected CROs, focusing on good clinical practice (GCP), good laboratory practice (GLP), and other good practices (GxP) requirements.
- Review the existing vaccine lot release guidelines involving the stakeholders.
- Support Essential Drugs Company Limited (EDCL) in conducting GxP training for technical staff at EDCL regional manufacturing plants.

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+ assisted DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory to achieve reaccreditation of Fournier-transformed infrared spectroscopy (FTIR).

- DFDA Nay Pyi Taw laboratory underwent ISO 17025:2017 reaccreditation assessment by ANAB in September 2022. Of 10 scopes of testing originally accredited, DFDA achieved reaccreditation in nine scopes; FTIR was left out due to an equipment breakdown prior to the assessment.
- DFDA replaced the faulty parts of the FTIR equipment, requalified and calibrated the equipment, and reintroduced the equipment for routine testing.
- DFDA submitted all data on maintenance, qualification, and testing to ANAB in November 2022. ANAB accepted the data and added FTIR to scopes of ISO 17025:2017 accreditation for DFDA, bringing the total back to 10 scopes.

PQM+ supported DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory to participate in the PT program organized by NSI Lab Solutions, USA.

- PQM+ supported DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory to participate in proficiency testing study PH-0922 organized by NSI Lab Solutions.
- DFDA participated in two scopes: USP <621> chromatography assay via HPLC and USP <711> Dissolution assay via UV/Vis spectroscopy
- DFDA passed both scopes with satisfactory scores

PQM+ organized a technical webinar on Proficiency Testing/ Inter-Laboratory Comparison (ILC) in November 2022.

- 34 participants (31 women, three men) from the DFDA laboratories in Nay Pyi Taw, Yangon, and Mandalay, Burma Manufacturer 1 quality control laboratory, and Burma Manufacturer 2 attended the webinar
- Participants learned how to plan an ILC study, including quality assurance activities to perform prior to the study and the statistics needed to evaluate results
- The knowledge gained from this webinar will help the DFDA to organize ILC study among Burma's medicines testing laboratories.

Table 3: Status of Labs Accreditation in Burma

Laboratory	Accreditation Sought	Initial Gap Assessment	CAPA	QMS	PT/LT	Official Inspection/ Pre-assessment
DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory	ISO 17025	Completed	Completed	Completed	Completed	Completed Re-accreditation assessment.
DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory	ISO 17025	Planned	Not completed	Developed, under implementation .	Not completed	Not completed
YSI Pharmaceuticals Quality Control Laboratory	ISO 17025	Completed	On-going	Developed, under implementation .	Not completed	Not completed

Priority Activities for Next Quarter

Next quarter, PQM+ Burma plans to:

- Organize the Data Integrity Training at DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory and Burma Manufacturer 1's quality control laboratory.
- Conduct an on-site cGMP assessment at Burma Manufacturer 1's manufacturing plant.
- Administer a webinar on Medical Devices Manufacturing QMS ISO 13485to DFDA and private manufacturers.

Nepal

PQM+ provides technical assistance to Nepal's Department of Drug Administration (DDA) to strengthen medical product 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

Approval of revised GMP code: PQM+ is collaborating with DDA and the Ministry of Health and Population (MoHP) to improve medicine-related legislation, policies, and regulations and promote collaboration among stakeholders. Previously, PQM+ coordinated with DDA's TWG to support revision of the current GMP code. In Q1, MoHP approved the revised GMP code for implementation. The revised code includes manufacturing-related quality assurance components in line with WHO's main principles and clearly articulates provisions for manufacturing hazardous substances and biologicals. With the enhanced provisions, the GMP certificate validity is extended from two years to three and supports efficient management of manufacturer audits with limited resources from DDA.

PQM+ Director Jude Nwokike delivers the keynote speech at a policy dialog forum organized by DDA.

Drug Advisory Group meeting: In Q1, PQM+ supported DDA in organizing a policy dialogue focusing on the domestic production of essential medicines. The meeting hosted representatives of national-level health agencies, professional bodies and councils, academia, and private sector entities who discussed strong implementation of existing policies and government directives to strengthen domestic production. PQM+ Director Jude Nwokike gave a keynote speech on the importance of quality of medicines to improve public health and presented on PQM+'s work globally. He further emphasized the protection of pharmaceutical manufacturers and ensuring timely access of quality medicines to the public. DDA and MoHP leadership committed to implementing those policies to improve access to essential medicines for the public.

Other national guidelines and regulations: PQM+ is supporting the drafting of national guidelines on safe disposal of unwanted pharmaceutical products, PMS regulations, a national pharmaceutical manufacturing strategy, and five supplemental technical guidance documents on the revised GMP code. PQM+ participated in the WHO GBT IDP follow-up visit to review DDA and NML's progress toward meeting the IDP recommendations.

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

Strengthen risk-based inspection (RBI) of DDA: Working with DDA's inspection TWG, PQM+ facilitated development of the RBI framework and plan. In Q1, PQM+ worked with DDA to set up and analyze data of 56 manufacturers and rank them based on risk criteria to add to the previously conducted analyses of 24 manufacturers. Based on the risk analysis, PQM+ and DDA will finalize a comprehensive RBI plan for all local allopathic manufacturers and hence will guide the inspection of high-risk manufacturers. PQM+ has finalized a list of topics to develop an RBI training curriculum that includes topics on RBI guideline and framework, RBI plan, relevant SOPs, tools etc.

Strengthen product registration and market authorization function of DDA: The registration and marketing authorization function of DDA is constrained due to resource availability and an increasing number of applications from manufacturers for product registration and market authorization. PQM+ advocated for the adoption of the globally accepted WHO CTD format for dossier submission. In Q1, PQM+ reviewed the existing documents at DDA and GBT assessment to finalize a list of SOPs needed to be drafted to improve the registration and market authorization system. Drafting of SOPs[13] in consultation with the division is in progress. PQM+ has also planned to develop a training curriculum on marketing authorization focusing on dossier evaluation per the CTD format.

Activities included an RB-PMS workshop (left) and RB-PMS field sampling (right).

Strengthen RB-PMS of DDA: PQM+ is working with DDA's Management Division and branch offices to scale up RB-PMS at a national level. The program supported the PMS unit of DDA in selection of 10 tracer molecules, risk scoring in relation to the prevalence of health problems, supply chain issues, dosage forms with complex formulations, and stability concerns, among others. In Q1, to facilitate the scaling-up of RB-PMS, PQM+ conducted RB-PMS planning workshops with DDA and NML officials along with officials from the Logistic Management, Epidemiology and Disease Control, and Curative Disease divisions of MoHP. PQM+ facilitated training on the MedRS tool application, protocol design, logistics, and sampling to prepare DDA for RB-PMS fieldwork. DDA endorsed a national sampling protocol, based on which the RB-PMS sample collection has been initiated. With PQM+ support, DDA's branch office in Birgunj conducted the first phase of the scaled-up RB-PMS under its areas, where 37 samples of five medicines were collected from 12 government, public, and private pharmacy outlets.

Support NML toward ISO 17025 accreditation: PQM+ facilitated NML's organization of a TWG meeting that focused on review and planning of PQM+-supported activities, based on the IDP for ISO 17025 accreditation.

- The program assisted NML in finalizing, training, and implementing six previously drafted QMS-related SOPs. Additionally, PQM+ has facilitated development of five SOPs that are in the process of review and implementation.
- PQM+ further supported NML in finalizing and approving an internal audit plan for the current fiscal year, as well as conducting the first-ever internal audit at NML.

[13] SOP topics include: assessment of labeling requirements; obtaining manufacturing and marketing licenses; content of patient information leaflets; content on summary of product; and dossier evaluation.

- PQM+ facilitated NML in the development and finalization of an annual calibration plan of their equipment of testing and analytical sections.
- PQM+ supported NML in acquiring a central computer server and networking all critical laboratory equipment as part of strengthening the data integrity system and enabling an audit trail of their test results.

PQM+ assistance to NML included a workshop on SOPs.

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: PQM+ and four private manufacturers are working on CAPA plans to build a roadmap to obtain WHO prequalification for selected medicines. PQM+ and one manufacturer signed a roadmap agreement last quarter, while another is in the pipeline with a different manufacturer. The manufacturers initiated the process of sourcing WHO-prequalified API for product manufacturing, to be followed by stability studies and continual testing.

Public manufacturer: PQM+ is working with the country's only public pharmaceutical company, Nepal Manufacturer 6, to achieve compliance toward national GMP certification. PQM+ has suggested reassessment of this manufacturer for GMP compliance with revisiting the CAPA plan to cover entire GMP areas, including calibration, qualification, and validation of the equipment and system. Similarly, PQM+, the Ministry of Industry and Commerce, and representatives of the manufacturer discussed PQM+ support and plans for the partnership.


PQM+ meets with the Ministry of Industry & Commerce and Nepal Aushadhi Limited.

Strengthening local HTP manufacturers: Previously, PQM+ coordinated with DDA to advertise an expression of interest targeting local HTP manufacturers in Nepal for technical assistance to meet ISO standards. Of three applicants, PQM+ assessed a potential manufacturer of disposable syringes for technical assistance to attain ISO 13485.

Support establishment and upgradation of bioequivalence laboratory: Since the area of BA/BE studies is relatively nascent in Nepal, PQM+ is trying to bring all stakeholders in place so the

country has the capacity to conduct BA/BE studies to fulfill its basic needs. PQM+ is planning a series of consultative meetings to create coordination among stakeholders and assign responsibilities across agencies for initiating BA/BE studies.

Improve quality assurance in the supply chain of medicines in local government units: With evolving responsibilities under the federal structure, PQM+ is supporting quality assurance of medicines in the local government supply chain. For this, PQM+ held discussions with the leadership at MoHP and logistics management division leadership, as well as participated in a supply chain-related meeting.

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

Increasing public awareness on SF medicines: PQM+ worked with DDA to develop public service announcements on SF medicines and supported DDA to broadcast the messages in the first two months of the quarter. PQM+ will investigate the effectiveness of those messages to decide on their continuation.

Training to health professionals on visual identification of SF medicines: PQM+ designed a research study for pre- and post-training assessments of community pharmacists' awareness and behaviors on the identification of SF medicines. PQM+ is conducting the study in conjunction with the training to community pharmacists on the visual identification of SF medicines. DDA's Biratnagar branch office facilitated the second phase of the training and post-assessment of the study. Further, PQM+ is planning to scale training on the topic to other health professionals such as ancillary health workers, nurses, and medical doctors.

The DDA branch office facilitates a training on visual identification of SF medicines.

Support the Nepal Pharmacy Council on establishing a continuing professional development (CPD) course: Health professional councils, including the Nepal Pharmacy Council, are considering a mandatory CPD course for renewal of professional licenses. PQM+ held a formal discussion with the council to develop a CPD course on SF medicines. The meeting concluded with the Pharmacy Council endorsing initiation of the CPD program and forming a TWG to start preparations. Similarly, PQM+ held discussions with Nepal Medical Council, Nepal Health Professional Council, Nepal Pharmacy Council, and academia representatives on the viability of a CPD program and linkages with the academic curriculum.

PQM+ meets with the Nepal Pharmacy Council on initiation of the CPD program.

Priority Activities for Next Quarter

In Q2, PQM+ plans to:

- Work with DDA on disseminating the revised GMP code and finalizing technical guidelines.
- Work with DDA and MoHP to begin to draft PMS, disposal of unwanted pharmaceutical GMP code, and development of Nepal Pharmaceutical Manufacturing Strategy.
- Continue to strengthen the RB-PMS, inspection, and registration functions of DDA by enhancing the information system and developing procedures and training curriculum.
- Continue to strengthen the QMS through development of procedures and technical training. PQM+ will facilitate a mid-term SATTA review of NML after completion of the internal audit report. PQM+ will work with NML to begin drafting a five-year laboratory strategy.
- Work with another manufacturer to finalize a roadmap for WHO PQ for selected medicines. PQM+ will continue to support the public manufacturer to strive toward national GMP standards focusing on the validation of its manufacturing units.
- Visit selected local government units to form a technical group to review QA procedures in the supply chain of medicines at their health facilities.
- Collaborate with professional councils to train their members and hold workshops on developing training curricula for visual identification of SF medicines. Similarly, PQM+ will agree with Nepal Pharmacy Council on activities to develop a CPD course.

Pakistan

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

PQM+ Pakistan is addressing these challenges through four areas: improving governance of medical product QA systems; strengthening medical product regulations; enhancing private sector engagement; and reducing the availability of SF medical products. PQM+ works closely with the Drug Regulatory Authority of Pakistan (DRAP).

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

Objective 1: Governance for medical product quality assurance systems improved

Activity: Capacity building and strengthening of the national medicine safety surveillance system with special emphasis on antimicrobial medicines

PQM+ continues its technical assistance and collaboration with DRAP and Provincial Health Authorities by providing guidance and support for global harmonized regulatory interventions to strengthen Pakistan's medicine safety and quality surveillance system. Medication errors are common in Pakistan, leading to treatment failure or increased mortality due to infectious diseases. Proper reporting and documentation can minimize medication errors. Safety surveillance is considered a key public health and medical practice instrument to reduce risks involved with medicines, including quality issues. During PY3, PQM+ supported DRAP in establishing an online medicine surveillance system and training DRAP staff on safety surveillance activities to fill gaps identified during the GBT self-assessment.

Safety surveillance is a cross-cutting regulatory function with provincial health departments that need a harmonized safety surveillance approach in all provinces to establish a robust national medicine safety surveillance system in the country.

During Q1, PQM+ conducted a planning meeting with the leadership of the provincial health department of Punjab to identify key areas of collaboration and activities to improve the safety surveillance system on the provincial level as well as help the provincial authorities to prepare for the WHO upcoming observed audit for the medicines safety surveillance activities planned in February 2023. PQM+ has shared the list of indicators related to medicines safety surveillance based on WHO GBT fact sheets with Punjab’s Department of Health for self-assessment of Punjab’s system. PQM+ is supporting the health department in developing an institutional development plan against gaps identified during the self-assessment. PQM+ will organize a training program for dedicated medicines safety surveillance officers on collecting, analyzing, and reporting adverse drug reactions (ADRs), which will help monitor the safety and quality issues of medical products used for infectious diseases.

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

TA to DRAP to address the gaps identified in its GBT IDP: PQM+ is providing technical assistance to DRAP to achieve a higher maturity level on the WHO GBT with a focus on strengthening and improving the overall regulatory system’s compliance on all nine GBT regulatory functions to ensure sustainable improvement and global harmonization of standards.

In PY3, PQM+ continued its TA to DRAP on implementing activities identified in the IDP developed following the self-assessment and WHO pre-assessment audit in late 2019, part of

the long-term effort to achieve a higher maturity level rating. PQM+ supported DRAP for the implementation of 44 institutional development plans that involved diversified activities related to all nine regulatory functions of GBT. Major IDPs of support were the revision of guidelines and procedures, training on risk-based regulatory approaches, assessment of CTD Dossier (Marketing Authorization Application), evaluation of stability data, decision-making on medicine resistance, development of a procedure for lot release, development of an online system for safety surveillance. Moreover, in PY3, PQM+ built the capacity of DRAP staff on data standards and developed new guidelines for DRAP after consultations.

During Q1, PQM+ conducted the training of DRAP staff on the evaluation of biosimilars. At least 16 technical officers from the National Control Laboratory for Biologicals, Biological Evaluation and Registration, Pharmaceutical Evaluation and Registration, and Quality Control Division of DRAP participated in this training session. PQM+ Pakistan, through its innovative private sector engagement strategy, partnered with Roche to conduct the training for the DRAP team on the fundamentals of biotherapeutics approvals. Mr. Kowid Ho, head of international technical regulatory policy at Roche in Basel, Switzerland, conducted the training.

PQM+ has drafted a roadmap in consultation with DRAP for conducting a series of trainings from the basic competency level to the advanced level to share knowledge and build the capacity of DRAP staff on biological drugs including mRNA Vaccines, through a partnership with the international forum by the private sector. It is expected that this will help DRAP to achieve better harmonization with international standards and obtain a higher maturity level in the GBT lot release function.

Continue support to DRAP for its accession to PIC/S. As part of DRAP's efforts to harmonize the quality standards by strengthening its inspection system, DRAP is gearing up its efforts to attain PIC/S membership. A non-binding, informal cooperative arrangement among regulatory authorities in the field of GMP of medical products, PIC/S aims to harmonize inspection procedures worldwide by developing common GMP standards and by providing training opportunities to inspectors. DRAP’s compliance with PIC/S will not only ensure the adoption of international best practices for inspections (to ensure quality, efficacy, and safety) of pharmaceutical establishments and manufacturing practices to ensure the availability of quality-assured medical products for infectious and non-infectious diseases. This will improve public health outcomes and will open new opportunities for the Pakistani pharmaceutical industry. Moreover, the harmonized inspection practices are expected to quell the proliferation of SF products on the market and increase sales by licensed and compliant manufacturers, while exporters may benefit from expedited registration of their products in lucrative export markets.

Left: The WHO PQ team conducts a final audit of DTL Multan.
Right: PQM+ delivers a training to DRAP staff on the fundamentals of biotherapeutics.

During PY3, PQM+ supported DRAP in revising procedures and guidelines to harmonize them with PIC/S standards. PQM+ reviewed the DRAP gap assessment report by the PIC/S secretariat and developed a CAPA and internal audit system to review the progress continuously. PQM+ has completed review of the system and processes of DRAP, including a mock audit per the PIC/S inspection system requirements.

During Q1, PQM+ supported DRAP to participate in mandatory PIC/S Committee meetings as a pre-applicant to learn policy and procedures for member countries and share DRAP progress regarding PIC/s membership. The PIC/S committee meeting took place October 5 through 7, 2022, in Dublin, Ireland. The DRAP team attended the sessions on inspecting pharmaceutical quality systems. DRAP also presented the progress over the PIC/S CAPA implementation along with expected timelines. DRAP has started the risk-based GMP inspections of pharmaceutical establishments using PIC/S guidelines and is expected to submit the PIC/S membership application by the end of Q2.

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

Activity: Continue support for NQCLs in streamlining information sharing and reporting mechanisms for substandard and falsified medical products.

Harmonization of regulatory procedures throughout the country is necessary to create a strong national regulatory system. PQM+ is supporting DRAP and provincial health departments to establish a good, efficient collaboration mechanism for regulatory information sharing between DRAP and Provincial health departments.

In PY3, PQM+ supported DRAP to develop a coordination mechanism among NQCLs by forming a NQCL coordination forum. PQM+ provided technical support to design the web-based interface to integrate medical product testing results into PIRIMS from all five DTLs in Punjab and the CDL in Karachi. To address data confidentiality concerns and encourage the use of the system, PQM+ supported DRAP and provincial DTLs to sign memoranda of understanding regarding the regulatory information data exchange.

During Q1, PQM+ met with the IT department of the primary and secondary health care department, Government of Punjab, to share an overview of the prototype interface and demonstrate that the DTLs of Punjab can access regulatory information on registration and licensing available in PIRIMS. The IT department team is creating an interface to grant access to DTMS[14] through PIRIMS. With this interface, provincial regulatory authorities can access regulatory information to verify the compliance status of the manufacturer during post-market surveillance activities and identify suspected medical products from the market. This interface aims to facilitate coordination and communication between DRAP and provincial regulatory bodies on cross-cutting regulatory functions including RB-PMS, quality control testing, ADR reporting, etc. The development of fast-track coordination and a communication mechanism between regulatory arms will help make regulatory decisions more transparent and efficient for better health care outcomes with quality medicines.

PQM+ supported CDL-DRAP during the WHO team's final audit for prequalification and for developing a CAPA plan on the audit observations.

[14] A stand-alone system used by DTLs in Punjab for medical product sample receiving and reporting results.

PQM+ provided support to the Drug Testing Laboratory, Multan, during the final inspection conducted by the WHO PQ team from December 7 to 9, 2022, and DTL Lahore from December 12 to 14 for prequalification of the laboratory. The WHO inspection team completed the audit and will share the audit report in the next 30 days. PQM+ will continue supporting the DTL Multan lab to address the WHO audit team's observations. Prequalification of this lab will provide reliable testing services for surveillance of medicines quality, especially for infectious diseases, to two divisions of Punjab (Multan and Dera Ghazi Khan), benefiting a population of 15.7 million people who are vulnerable to SF medicines.

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

Continue TA to four selected manufacturers to achieve WHO PQ for quality-assured manufacturing of zinc and amoxicillin dispersible tablets (key MCH priority products): In Pakistan, acute respiratory infection (ARI) and diarrhea are the leading causes of childhood mortality, with 74 of every 1,000 children dying of these causes every year in the country. Amoxicillin to treat ARI and oral rehydration salts (ORS) and zinc for diarrhea remain the most prescribed medicines in public health care facilities. PQM+ selected potential manufacturers of amoxicillin and zinc through EOIs to provide technical assistance to improve the quality of products and GMP compliance of manufacturing facilities through the WHO prequalification process.

In PY3, PQM+ continued TA to manufacturers for WHO PQ, two each for zinc and amoxicillin DT. PQM+ staff conducted gap assessments of manufacturing facilities and developed the required QMS and CAPA plans in response to the gap assessment reports. PQM+ also supported the manufacturers in developing CTD dossiers for submission to the WHO PQ team for subject products.

During Q1, PY04- PQM+ supported Pakistan Manufacturer 5 during the final audit by the WHO team and provided technical assistance to develop CAPA against WHO audit observations. That manufacturer has submitted the CAPA to the WHO team. PQM+ also provided technical assistance to Pakistan Manufacturer 2, which produces amoxicillin DT, for the implementation of CAPA and the development of a dossier for WHO PQ. Another amoxicillin manufacturer, Pakistan Manufacturer 6, received support for the identification of suppliers of comparator products to conduct pharmaceutical development studies for their selected product.

Continue to develop national capacity to conduct BE studies to assess safety and efficacy of priority medical products: In Pakistan, most pharmaceutical manufacturers are generic medicines producers. This requires the manufacturer to carry out a BE study to establish comparable safety and efficacy with that of the innovator product. PQM+ selected two local BE Centers through EOI to provide technical assistance and for national capacity building to conduct BE studies within the country, as per international best practices.

In PY3, PQM+ assisted DRAP in developing the BE roadmap for implementation of the stepwise implementation of the BE studies requirement by the generic medicines manufacturers. Key steps involved developing BE guidelines, building the capacity of local BE study centers, revising biostudy rules, and shortlisting high-risk priority molecules for phase 1 implementation.

PQM+ engaged an international BE consultant to assess and train selected BE centers per international best practices. This includes development of mock protocols for BE studies.

During Q1, PQM+ provided technical assistance to DRAP to revise the guidelines and requirements for applicants for bioequivalence studies to facilitate local bioequivalence centers to secure regulatory approvals as per international best regulatory practices. Per DRAP's Biostudies Rules 2017, the BE center or sponsor (manufacturer) has to submit the GMP certificate and Certificate of Pharmaceutical Product from the country of origin issued by the authorized regulatory body of comparator product that failed to conform to international best practices. It was a challenge for the manufacturer and BE centers to secure regulatory approval to conduct BE studies locally.

This revision will facilitate manufacturers or BE centers to secure early regulatory approval and conduct BE studies within the country which will ultimately save foreign reserves as well as support manufacturers to get BE studies at a relatively low cost. The functioning of local BE centers will also help DRAP in the smooth implementation of the national BE policy, which is needed for premarket quality, safety, and efficacy of generic medicines in Pakistan. This regulatory intervention will indirectly increase the availability of quality-assured medicine.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Support DRAP for implementation of CAPA on PIC/s gap assessment and preparation of application for submission to PIC/s.
- Support DRAP during WHO audit on GBT ML3.
- Follow up with selected manufacturers for the implementation of CAPA and submission of dossier to WHO.
- Follow up with NQCL for implementation of CAPA against WHO audit observations.
- Complete the review of the draft National Medicine Policy implementation plan.
- Conduct a gap assessment of the medicine safety surveillance system in Punjab.
- Support selected BE centers to identify a sponsor for the BE study.

Europe and Eurasia Region

Central Asia/Kazakhstan

PQM+ is strengthening the medicines regulatory system in Kazakhstan by providing technical assistance to the 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 Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S), as well as to support the NCEM in establishing an RB-PMS system.

In PY4, PQM+ is helping to:

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

Progress by PQM+ Objective

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

In PY4 Q1, PQM+ continued technical assistance to the Almaty and Karaganda MQCLs to work toward and maintain WHO prequalification (PQ):

- Helped the Almaty MQCL work on the WHO PQ CAPA plan as a follow-up to the WHO PQ inspection in July 2022. The MQCL met several times with PQM+ to discuss issues related to the implementation of the CAPA plan and addressed comments from the WHO auditors. The MQCL submitted the CAPA plan to WHO on November 25. Almaty MQCL received a letter from WHO stating that they will conduct a follow-up inspection in the next six months.
- Assisted the Karaganda MQCL in continuing to prepare for the WHO audit this year with a computerized systems validation (CSV) expert visiting the lab October 17–19, 2022. During the visit, the PQM+ expert audited the existing computerized systems, developed documentation, and demonstrated a full validation of one system.

PQM+ is supporting Kazakhstan in strengthening the inspectorate and preparing for ascension to PIC/S. PIC/S membership 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. In Q1, PQM+ helped the GMP inspectorate prepare for the launch of a newly developed QMS.

- On November 15, PQM+ met with the PIC/S working group and discussed preparation for a WHO-observed inspection planned toward the end of 2023, as part of the WHO GBT regulatory inspection function. Participants discussed preparation of the coaching inspection, licensing unit, and liaison with the inspectorate, quality defect handling, and roadmap progress in preparation for PIC/S accession. The team also discussed the matrix of inspectors, trainings for inspectors, and QMS.

- On November 24, PQM+ had a call with the with the Deputy Chairman of the Committee for Medical and Pharmaceutical Control at the Ministry of Health (Committee) and and other members on bringing the national regulation in line with the licensing requirements of PIC/S. The participants discussed the requirements for licensing new sites, changes in licenses, and enforcement activities.

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 resources for sample purchasing. PQM+ is working with the NCEM to define what actionable steps can be implemented in the short and medium term to implement RB-PMS. PQM+ also reviewed the SOP on PMS developed by the NCEM and made recommendations to align with WHO's requirements.

PQM+ continued work with the NCEM's scientific-educational center (SEC), which will ensure the sustainability of PQM+'s efforts to build the capacity of the country's medicines regulatory workforce.

- SEC asked PQM+ to provide a training on adult education; specific needs will be discussed further. This training is scheduled for early 2023.

A gap identified during the WHO GBT assessment was that the Committee needs to establish the QMS according to ISO 9001, due to its involvement in the regulatory function. In Q1, PQM+ provided technical assistance to the Committee in establishing a QMS according to ISO 9001.

- PQM+ continues to provide technical assistance on the development of the QMS of the Committee, including addressing challenges related to engagement of the members from the Committee. PQM+ is looking into alternative ways to work with members, such as hiring an expert to provide direct, hands-on support.

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

PQM+ developed a questionnaire to assess the GMP training needs of the local manufacturers and provided it to the SEC for review. After reviewing with SEC and making changes, PQM+ finalized the English and Russian versions of the questionnaire. SEC will initiate a meeting with the Manufacturers' Associations to introduce the questionnaire and describe the goals of the survey in early 2023.

Priority Activities for Next Quarter

- Assist Almaty MQCL with the WHO PQ inspection and CAPA plan development and implementation.
- Facilitate a technical assistance visit to Almaty and Karaganda MQCLs by the program's CSV expert.
- Provide in-person training for Kazakhstan MQCLs on validation and verification of test methods, risk analysis, trend analysis, and business continuity.
- Continue technical assistance to the PIC/S working group in the areas outlined in the PIC/S accession roadmap.

- Continue technical assistance to the NCEM on developing approaches and procedures for RB-PMS.
- Continue technical assistance to the SEC to build capacity on workforce development.
- Assist the Committee in establishing an ISO 9001 QMS.
- Assess the training needs of the local manufacturers.
- Continue helping the NCEM prepare for the next WHO GBT assessment.

Tajikistan

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

In 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

PQM+ is providing TA to the State Surveillance Service to strengthen its medicines registration system. In PY3, PQM+ helped the MRA establish a TWG on the medicines registration function to work with PQM+ in improving the registration of medicine. PQM+ developed a registration assessment questionnaire (using the WHO GBT questionnaire as a reference), which the TWG completed. The assessment found that legal provisions, rules, and guidelines exist to support registration/market authorization and organization and management structure to support registration activities, but there is a need to improve the regulatory process and improve communication for greater efficiency in the registration system. Also needed are development and implementation of SOPs and guidance for good review practices; special medical product registration requirements and procedures for national emergencies, epidemics, and pandemics; and dissemination of product information. Based on the PQM+ assessment findings, PQM+ in Q1 helped the TWG develop one SOPs on screening applications and another on evaluating assessments. These SOPs are with the State Surveillance Service management for review.

One gap identified during the PQM+ facilitated assessment of the registration function described under sub-activity 1.1 was that the MRA has only hard copies of the product dossier submitted for registration, with no backup. These hard copies can be vulnerable in case of fire or other catastrophes. The MRA also expressed an interest in digitization and electronic organization with backup for these submitted dossiers. In PY4, PQM+ will provide TA to the state service in digitization and electronic organization with proper backups of these submitted dossiers and to establish the RIMS registration module. In Q1, PQM+ initiated discussions with the State Surveillance Service on RIMS. PQM+ is also recruiting for an internal RIMS expert.

PQM+ is supporting registration of quality assured first- and second-line TB medicines in Tajikistan through an existing national registration procedure. In PY3, PQM+ used a competitive

selection process to identify and contract a local company experienced in registration of medicines in Tajikistan to compile and submit dossiers on behalf of the manufacturers of quality-assured TB medicines. PQM+ coordinated closely with the Global Drug Facility (GDF) to identify the manufacturers of WHO prequalified TB medicines. In PY3, nine dossiers of quality assured first line TB medicines from two manufacturers (India Manufacturers 5 and 6) were submitted and accepted by MRA for registration. This is the first time WHO-prequalified TB medicines were submitted for registration in Tajikistan. The MRA has issued no significant queries so far. It is expected that the registration process will be completed by January 2023. In Q1, PQM+ joined with GDF and the national TB program (NTP) to identify and approach three manufacturers (India Manufacturers 4 and 5 and Cyprus Manufacturer 1) of quality-assured second-line TB medicines for their interest in registering their second-line TB medicine in Tajikistan. PQM+, NTP, and GDF jointly decided to initiate the registration for first-line pediatric medicines, as these were not among registered medicines in Tajikistan. For this, WHO PQed India Manufacturer 2 was approached, and they have expressed interest in registering three medicines. The local registration company started working with India Manufacturer 2 in compiling the dossiers.

In PY3, PQM+ started TA to the Dushanbe MQCL to strengthen its laboratory operations and QMS to comply with ISO 17025:2017. In PY3, PQM+ conducted a comprehensive assessment, using SATTA, a PQM+ developed assessment tool that aligns with the requirements of ISO 17025 and WHO TRS957. The assessment resulted in 74 counts of nonconformities to the standard. To identify the causes and resolve the areas of non-conformities the MQCL with the aid of PQM+ developed CAPA are in the process of resolving gaps. As part of the CAPA, in PY4 Q1, PQM+ worked with the Dushanbe MQCL to develop two SOPs one on control of documents and another on the control of records. Both were approved by management of the MQCL.

In Q1, the PQM+ director of health elements visited Tajikistan to meet with stakeholders and initiate discussions with new partners: the GMP inspection department within the State center and the Avicenna Tajik State Medical University (ATSMU), a public university in Tajikistan, to start PY4 activities.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Implement activities with MQCL according to the CAPA plan.
- Approve submitted SOPs by the State Surveillance Service and develop new SOPs.
- Initiate new activities: RIMS, GMP, and establishment of cooperation between Purdue University and the Tajik State Medical University

Uzbekistan

Uzbekistan is graduating from the Global Fund-supported procurement of TB medicines to domestically funded procurement, and the country plans to gradually increase the funding it allocates to procure second-line TB medicines. The government's strategy is to ensure that domestically produced, quality-assured medicines are available for procurement. In recent years, the Government of Uzbekistan introduced several initiatives to strengthen the local production of quality-assured medicines in the country. In support of this strategy, and generally to ensure the quality of medicines on the local market, PQM+ is assisting the Agency on Development of the Pharmaceutical Industry ("the Agency") around medicines regulatory

systems strengthening. This includes improving the medicines review and registration system, supporting MQCLs to test the quality of medicines reliably and accurately, preparing the GMP inspectorate for PIC/S accession, and introducing RB-PMS to detect substandard 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+ is working to:

- 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

In PY3, PQM+ provided technical assistance to the Ministry of Health (MoH) in development of the "pharmaceuticals and medical devices" strategic block of the MoH's Health Strategy 2030. PQM+ through desk review, working group, and meeting with various public and private sector stakeholders gathered information for the pharmaceutical and medical devices situational analysis. PQM+ identified and documented major findings from the situation analyses, challenges, and strategy recommendations for pharmaceutical strategy and medical devices block. PQM+ submitted the final pharmaceutical and medical device sector situational analysis and recommendations and a pharmaceutical roadmap for the health strategy 2030. In PY4, Q1 the World Bank, who is coordinating with the stakeholders for all eight strategic blocks, is in the process of compiling and finalizing the Health Strategy 2030 and submitting to the MoH for their approval.

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

Medicines Registration: In PY3, PQM+ provided TA to the Agency to help them to advocate to the cabinet of ministers to adopt the emergency use authorization (EUA) clause. The EUA clause is in the final draft of the resolution for approval of the cabinet of ministers. PQM+ is also preparing a training for the registration working group on how to write SOPs and implement documents and record control. This training was requested by the Agency director. The training will focus on the importance of documentation; key requirements for writing an effective SOP; and good documentation practices. The training is now planned for January 2023.

To date, Uzbekistan has registered nine products through WHO CRP. These include six WHO-prequalified TB medicines that PQM+ helped facilitate, with an application for one more medicine, clofazimine, submitted to the State Center for WHO CRP registration (South Korea Manufacturer 1) 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, Rotasiil (liquid) for gastroenteritis caused by rotavirus, and BCG for TB. This signals that the WHO CRP process is sustainable and working for products other than TB.

GMP Inspection: In PY 3, PQM+ continued to work with the newly established GxP Center, responsible for the GMP inspection. PQM+ engaged with the working group on the development

of an updated version of the GMP guideline, training programs for inspectors, and SOP on QMS and inspection process. PQM+ facilitated several meetings with the working group; reviewed and finalized QMS SOPs. In PY3 Q4, the PQM+ technical advisor also visited Tashkent and met with the senior management of the inspectorate and its various units to discuss changes in the organization structure, and redistribution of responsibilities, including area of licensing and handling of quality defects. In PY4 Q1, PQM+ facilitated the development of a strategy for licensing processes for manufacturers and wholesalers in Uzbekistan to align with the WHO and PIC/S requirements. This strategy entails cooperation between the GxP center and the Agency. The strategy is currently with the Agency leadership for review and approval.

Laboratory Testing: In PY3, PQM+ conducted training on CAPA development and monitoring for Andijan and Tashkent MQCL. Following the training, the labs developed CAPA. PQM+ facilitated a workshop to discuss, review, and finalize the CAPA. Both labs have started implementation of CAPA. PQM+ also organized an educational visit for five representatives from the two labs to travel to Almaty MQCL in Kazakhstan. Recently, the Almaty MQCL completed a WHO audit for prequalification. The delegation from Uzbekistan toured the Almaty MQCL and observed demonstration of best practices. PQM+ also provided training on best practices for the laboratory. The Almaty and Karaganda MQCLs also shared best practices and lessons learned from their preparation of WHO Prequalification. In PY4 Q1, both MQCLs received an inspection from National Accreditation Center for ISO 17025 reaccreditation. The national accreditation center became a member of the International Laboratory Accreditation Cooperation (ILAC) in September 2022. Both MQCLs received ISO 17025 reaccreditation confirmation from the national accreditation which is now internally recognized given the national accreditation center's ILAC membership. PQM+ provided TA to both MQCLs through this reaccreditation process by guiding their preparation for the inspection visit and reviewing the MQCLs CAPA to the National Accreditation Center.

In PY3, PQM+ initiated TA on 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. PQM+ completed an audit of the management system of the Agency including the state center and identified several areas for improvement to comply with the requirements of the ISO 9001:2015. PQM+ developed and finalized a report with the audit process and findings. PQM+ facilitated the development of an implementation plan to address the gaps at the state center. The implementation plan is divided into three phases: first consultations and workshops on developing policies and procedures, second implementation and, and third monitoring of these policies and procedures. In PY4 Q1, PQM+ initiated the second phase on implementation. PQM+ with the state center initiated the development of guidelines and processes for the quality management system.

Post-Marketing Surveillance: In PY3, a presidential decree on development of the pharmaceutical industry was issued and a working group was established for PMS. The working group, with PQM+ guidance, drafted regulations for PMS. The regulation, however, was not approved because of limited financial resources. PQM+ proposed to initiate a pilot for PMS, although funding will need to be addressed. As part of the first stage of the pilot, PQM+ provided training in Q1 on PMS and MedRS in Tashkent. The training provided an overview of the RB-PMS approach and a hands-on training on how to use the MedRS tool. A total of 22 staff from the State Center (the medicines regulatory agency) attended the workshop and participated in the risk estimation for 30 selected TB medicines, 14 regions/provinces, and about 130 cities/districts in the country using the MedRS tool. Plans are underway to develop a draft PMS protocol based on the data generated during the workshop. The PMS protocol will allow the PMS team within the State Center to conduct a pilot RB-PMS activity, the first of its kind in

Uzbekistan. The scope of the surveillance will focus on two selected TB medicines, sampled from Level 3 (private sector retail outlets), which includes about 11,200 facilities that are stratified based on geographical and facility risk. Sampling will draw from about 137 facilities, the calculated sample size with the facilities randomly selected. In Q1, PQM+ also conducted an orientation on sample collection and documentation. The sample collection will begin in early January.

In Q1, a delegation from the Agency visited Ethiopia to learn about their well-functioning RB-PMS program. The members of the delegation were specialists of the Cabinet of Ministers responsible for the pharmaceutical industry, the First Deputy Director of the Agency, and the heads of the newly created Department for RB-PMS. During this visit, the delegates learned about Ethiopia's RB-PMS implementation experience, including its benefits. The Agency funded the trip themselves, while PQM+ in Uzbekistan organized the visit with the Ethiopian MRA. Following the visit, the Agency developed a roadmap for the introduction of PMS in Uzbekistan, currently in its final stage of development and to be approved by the prime minister of Uzbekistan. In Ethiopia, the Agency delegation also learned about WHO GBT implementation there. The Agency developed a WHO GBT roadmap draft for approval by the prime minister.

Pharmaceutical Technology University: PQM+ is working with Purdue University to provide technical assistance to the pharmaceutical technology university at the Tashkent Pharma Park. In PY3, Purdue conducted an electronic survey to gather information from the pharmaceutical technology university and other stakeholders on their needs. Purdue designed and delivered an introductory training on pharmaceutical process and product design for 20 faculty members from the pharmaceutical technology university. In Q1, PQM+ organized an award ceremony for those who completed the training. This event — with the participation of the Director of the Agency, the Rector of the Institute, and representatives of USAID — was widely covered in the national media.

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

In PY3, PQM+ provided TA to Uzbekistan Manufacturer 2 on the prequalification of its TB drug levofloxacin. The manufacturer has completed work on laboratory-scale batches and continues to study the stability of the drug, which will last six months. A report on the evaluation of the production of finished products of levofloxacin in accordance with GMP requirements was provided. Work on the CAPA has begun. Plans are to produce three batches of production scale to validate the production processes. In Q1, the manufacturer finalized two documents, the protocol for biowaiver lot and a batch manufacturing report for 100,000 tablets. The manufacturer also produced a biowaiver lot and is working to finalize the lot for stability investigations. This stage is important because the product development work is being completed. After development, preparation for the dossier submission to WHO will begin.

The local Uzbekistan pharmaceutical industry should be GMP compliant before accession to PIC/S, and training will assist the local industry in understanding GMP requirements and achieving GMP compliance. To address this need, PQM+ procured a vendor to deliver GMP training materials to the local Uzbekistan pharmaceutical industry.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Conduct training on how to develop SOPs for the registration working group.

- Continue TA to the PIC/S working group in its preparation for the PIC/S accession, including strengthening QMS and building the GxP inspectorate staff's capacity.
- Continue to work with Tashkent and Andijan MQCL to bring their CAPA and internal audit in line with WHO PQ requirement.
- Continue TA to the Agency on compliance to QMS 90001:2015.
- Continue TA to the RB-PMS working group to conduct the RB-PMS pilot in Uzbekistan.
- Design and deliver courses for Tashkent Pharma University.
- Continue TA to Uzbekistan Manufacturer 2 on product development, and dossier preparation.
- Initiate GMP training for local Uzbekistan pharmaceutical manufacturers.

COVID-19

Bangladesh

Coordination and Operations for COVID-19 Vaccines

PQM+ is working to establish and strengthen the relationship among key stakeholders monitoring the rollout of COVID-19 vaccines. PQM+ is providing technical support to the DGDA to revise the "Registration of Human Vaccine Guidelines." This quarter, PQM+ coordinated with DGDA to finalize the draft guidelines, which are going through a final technical review. PQM+ assisted in the overall restructuring of the guidelines, helped define the appropriate process for registering any vaccine intended for full registration, and included several sections for vaccines testing and evaluation.

PQM+ is also supporting DGDA to prepare guidelines to strengthen the regulation of medical oxygen. PQM+ completed editorial review of the medical oxygen guidelines, which are now being formally disseminated by the DGDA TWG members (including relevant directors, deputy directors, and assistant directors at DGDA).

Laboratory Systems

PQM+ is working with the NCL to establish a personal protective equipment (PPE)/ medical device testing laboratory. PQM+ is providing support to NCL's newly established medical device testing laboratory with the procurement of four pieces of equipment (mask and respirator breathing resistance tester, medical gloves hole detector, universal tensile strength tester, and paramagnetic oxygen analyzer) to strengthen PPE testing. The equipment from the selected vendors is expected to be delivered in February or March. Once the equipment arrives, PQM+ will support NCL to operationalize all equipment through qualification, preparation of standard operating procedures, and training.

PQM+ is also supporting DGDA to build the NCL's capacity in vaccines testing. This quarter, PQM+ provided technical support to the vaccine testing laboratory at NCL for qualification of its RT-PCR machine (procured by the World Bank) and inverted microscope equipment (procured by PQM+). Now NCL has the capacity to qualify these two types of equipment in the future. This enhanced the capacity of NCL for testing the identity and potency of vaccines. NCL conducted pH, sterility, and endotoxin testing of the Covidshield vaccines.

Burkina Faso

Immunization readiness and implementation

PQM+ is working to support the ANRP to strengthen its adverse events following immunization (AEFI) surveillance system and build its capacity to grant regulatory approval for COVID-19 vaccines in alignment with international norms (e.g., WHO COVID-19 vaccine safety monitoring guidelines) and the country's National Vaccine Deployment Plan. In Q1, PQM+ supported ANRP to compile and collate AEFI data from June 2021 to October 2022. From the beginning of vaccination efforts against COVID-19 through September 20, 2022, 3,812,134 doses of COVID-19 vaccines have been administered in Burkina Faso. Nine hundred sixty (960) AEFI cases were notified to ANRP, with the AstraZeneca vaccine accountable for the highest AEFI incidence. While collating the data, it was evident that there is a significant discrepancy (90%)

between the AEFI notifications declared by the vaccination program (DPV) and those notified to ANRP. This is because of a clear culture of underreporting to the regulator by the health professionals. As part of its interventions, in previous quarters, PQM+ together with ANRP included training of health professionals on AEFIs and reporting channels so there is increased awareness/knowledge on what to do. Now that ANRP has the figures, the report is being used as clear evidence to further to improve sensitization on the importance of reporting to ANRP.

Out of the 960 AEFI cases, 1.9 percent (20) were serious adverse events. However, no death was recorded. Of the 20 serious cases notified, 12 were investigated and submitted to the Technical Committee for the Vigilance of Medicines, Vaccines, and Immunological Serums for causality assessment using the WHO vaccine imputability method. Of the 12 cases analyzed, 10 involved the AstraZeneca vaccine and two the Johnson & Johnson vaccine. Six cases of serious AEFI investigated were found to be associated with vaccines or vaccination. Four cases required further investigation to finalize the causality analysis. PQM+ subsequently supported ANRP to draft a report based on the information compiled. With this vaccine safety information, this report will help ANRP, and the immunization program know the vaccines that are best suited for the population and to make better decisions on the types of vaccines to be imported and used in the country.

PQM+ is also working with ANRP to build its systems for EUA. In Burkina Faso, ANRP grants marketing authorization for drugs, vaccines, and other medical products based on the expert opinion of the Technical Commission for the Approval of Health Products (CHPS). ANRP uses a short and rapid emergency approval process for the COVID-19 vaccine, but the committee had inadequate knowledge to apply the key considerations for granting this approval. ANRP therefore requested assistance to build the capacity of these technical experts responsible for providing advice on approvals in emergencies to ANRP. As a result, in addition to the regulatory guidelines for granting EUA in Burkina Faso, which PQM+ supported ANRP to draft and validate in the previous quarters, in Q1, PQM+ supported ANRP to develop four other regulatory documents for granting EUA in Burkina Faso: (1) SOP for granting EUAs, (2) work instruction reliance, (3) work instruction for accelerated approval, and (4) work instruction for recognition. While the documents were reviewed by PQM+, they were drafted by ANRP staff and other members of ANRP's experts committee for health products assessment and registration based on knowledge gained from the EUA training delivered by PQM+ in Q3 of PY3.

PQM+ is also supporting ANRP to improve its lot release function, for which no procedure is in place. For each lot of vaccines being imported into the country, the medicines regulatory authority is required to, at a minimum, review the manufacturer's lot summary protocol (LSP) and if found satisfactory, release that lot for consumption by the population. ANRP did not have the processes or the skills to perform this function. During Q1, PQM+ supported ANRP to validate its procedure on lot release.

Laboratory Systems

PQM+ is working to build the capacity of the national quality control lab, LNSP, to test COVID-19 vaccines. This quarter, PQM+ conducted a theoretical training on bacterial endotoxin testing (BET), microbial enumeration testing, biosecurity, biosafety and on waste management. Seven laboratory analysts (2 men, five women) participated. This training provided a good opportunity for laboratory analysts to understand and apply the pharmacopeia in the performance of tests on both sterile and non-sterile pharmaceutical products, including vaccines/ biological products. The hands-on training also demonstrated to the laboratory staff the importance of observing and appreciating best practices while in the microbiology laboratory. The biosafety/biosecurity

training provided the laboratory staff the opportunity to appreciate the importance of observing safe practices and best procedures for the management of wastes, including biological waste, generated in the laboratory. In addition, in December 2022, the equipment and consumables vendor started shiping some equipment and consumables to LNSP. This will continue in Q2.

COVID-19 Therapeutics

Policy, Planning, and Coordination

PQM+ is providing technical assistance across several countries to introduce and refine a COVID-19 test-to-treat (T2T) 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 10 T2T countries to facilitate registration/market authorization of two COVID-19 antivirals, both branded (Paxlovid and Lagevrio) and WHO-prequalified generic (nirmatrelvir/ritonavir co-packaged and molnupiravir capsules) versions. PQM+ is also supporting implementing partners in obtaining the necessary authorizations for importation of these same donated products. To obtain information on the regulatory approval processes in each country, PQM+ has developed and distributed a questionnaire (available in English, French, Spanish, and Portuguese) to respective countries (Bangladesh, Botswana, Côte d'Ivoire, El Salvador, Ghana, Lesotho, Malawi, Mozambique, Rwanda, and Senegal). PQM+ has received responses from nine of the 10 countries and compiled details on the documents necessary for each path of approval available in the respective country. As a next step, PQM+ is establishing a confidential non-disclosure agreement with India Manufacturer 7, which produces a generic of both products, to facilitate the receipt of documents needed for product authorization and registration as well as importation of donated products. The same agreement will be established with other manufacturers of the products, including Pfizer for Paxlovid and Merck for Lagevrio. This assistance will decrease the time it takes for treatment facilities to receive COVID-19 antivirals for use in the T2T pilot program, which will increase the ability to treat patients at risk of progression to severe COVID-19 disease.

Infection Prevention and Control

As part of its T2T program, USAID has asked PQM+ to support generic manufacturers of nirmatrelvir/ ritonavir in obtaining WHO PQ and market authorization as soon as possible. PQM+ plans to support manufacturer(s) of nirmatrelvir/ritonavir, the first of two COVID-19 therapeutics to gain FDA EUA. Under this activity, PQM+ has been tasked to identify the manufacturer(s) to receive support and validate the support needed for WHO PQ of Paxlovid. This quarter, PQM+ identified three manufacturers from India (India Manufacturers 7, 8, and 9) as frontrunners to receive technical assistance. India Manufacturer 7 did not respond to requests for potential support and Manufacturer 9's request for support was solely focused on equipment needs and exceeded the entire workplan budget. As a result, India Manufacturer 8 was determined to be the TA recipient. This company manufactures and supplies nirmatrelvir/ritonavir (Paxlovid) and is one of a few leading manufacturers applying for WHO PQ of nirmatrelvir/ritonavir. After finalizing the technical assistance recipient, PQM+ staff visited the manufacturer in India on December 5, 2022. During the visit, PQM+ validated the need to cost share in the purchase of a hot melt extruder (HME). Providing assistance with the cost sharing for an HME would expedite attaining WHO PQ and lower the initial costs of Paxlovid. PQM+

also started putting together a sub-award package for India Manufacturer 8, which is expected to be submitted in February 2023. Completing the sub-award would expedite the manufacturer achieving WHO PQ.

Ethiopia

Policy, Planning, and Coordination

PQM+ is supporting EFDA to increase access to quality-assured COVID-19 vaccines to Ethiopian citizens through facilitating the proper regulatory review and timely implementation of EUA procedures. As part of implementing this activity, in November 2022, PQM+ conducted an advanced training on EUA with special focus on BA, BE, and in-vitro/in-vivo correlation studies for emergency products that require submission of bioequivalence data for approval and market authorization. PQM+ experts trained 27 medicine and vaccine dossier assessor experts (16 men, 11 women) from the EFDA's Medicine Registration and Licensing Directorate. In addition to the training, PQM+ also took the participants on a one-day practical visit to the clinical trial site of the Regional Bioequivalence Center through which they were exposed to the practice of BA/BE from a clinical point of view. The training gave the assessors better knowledge and understanding of the evaluation necessary for BA/BE studies for those emergency medicines, potentially shortening the evaluation time for market authorization, and increasing access to COVID-19 vaccines and other related products.

Under its previous COVID-19 funding, PQM+ Ethiopia conducted a cold chain regulatory inspection from December 2021 to February 2022 which clearly showed gaps in Ethiopia's cold chain system in compliance to regulatory requirements to maintain the quality of COVID-19 vaccines and related commodities. These gaps included staff technical capacity in good distribution practice (GDP), good storage practice (GSP), good documentation practice, and quality management system (QMS) implementation. One of the recommendations PQM+ made in the assessment was to provide training for those health workers on cold chain regulatory requirements, since it is critical to ensure the safety and efficacy of vaccines. During this quarter, PQM+ collaborated with EFDA and customized existing training materials on GDP/GSP for cold chain regulation and conducted a ToT for regional regulators, EFDA branch offices, and Expanded Program on Immunization (EPI) experts to cascade the training to about 300 immunization health facilities professionals before the end of June 2023, on GDP, GSP, good documentation practice, and QMS of cold chain products such as COVID-19 vaccines. The training was conducted for 20 experts (19 men, one woman). The training taught participants to cascade these practices within their area and enable the immunization health facilities to implement proper GDP, GSP, and QMS, ensuring the quality of vaccines in their region.

PQM+ also worked with EFDA in building the technical capability of its Market Surveillance and Relevance Directorate so it will be able to detect SF COVID-19 vaccines and related commodities through its market surveillance work. In Q1, PQM+ Ethiopia provided financial support for the training of 40 staff (27 men, 13 women) from EFDA and regional regulatory bodies on intelligent market surveillance principles. The training was provided in collaboration with the Interpol, police, and custom offices. This training will help the inspectors to conduct intelligent market surveillance of such products and provide evidence for decision-making.

Pharmacovigilance

In Ethiopia, PQM+ is working to strengthen product quality defect reporting through ADR reporting. Ethiopia has a passive ADR monitoring system where health care 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. As it stands, the system is not widely used, but can be a valuable source of information if used on a regular basis. More than 15,000 AEFI reports are collected using both the active and passive reporting systems. However, these reports are not entered to WHO's global database where they can be properly captured and analyzed.

During this quarter PQM+ supported EFDA to provide a refresher training for Regional AEFI Investigation Taskforce members on how to effectively conduct investigation of serious AEFI cases following COVID-19 vaccination. The training was provided November 17 and 18, 2022, in Adama Town, Ethiopia. A total of 52 AEFI investigation taskforce members (40 men, 12 women) from different regions of the country attended the training. As incomplete investigation information has been one of the challenges that causes delays in causality assessment classification, PQM+ maintains that capacitating the regional AEFI investigation taskforce members on how to properly conduct investigations of serious AEFI cases will enable them to provide the necessary and appropriate information to the National Safety Advisory Committee. This will in turn allow the National Safety Advisory Committee to make timely causality assessment decisions and recommendations which are essential in ensuring continued public confidence in vaccination.

PQM+ also provided technical support to EFDA's pharmacovigilance center on strengthening AEFI reporting for COVID-19 vaccines by assessing the current monitoring system and identifying gaps. PQM+ coordinated with EFDA to conduct a one-day dissemination workshop in October with relevant stakeholders in the country. The national dissemination workshop focused on COVID-19 vaccine safety data and results from the assessment conducted by PQM+ and EFDA of the national AEFI monitoring system. The 92 participants (72 men, 20 women) were pharmacovigilance stakeholders from the Ministry of Health, EPI, regional health bureaus, branch EFDA, and other implementing partners. Findings from active surveillance conducted on Janssen (Johnson & Johnson) and Pfizer COVID-19 vaccines and results from an assessment result of the national AEFI monitoring system were disseminated. This served as a platform to strengthen the contribution of major stakeholders and partners in vaccine safety monitoring.

PQM+ facilitated a causality assessment workshop for the National Safety Advisory Committee. A total of 30 people (22 men, eight women) attended and reviewed and classified serious adverse events for seven COVID-19 vaccines (two J&J, four Pfizer, and one Sinopharm) and provided recommendations to the regulatory authority for an effective safety monitoring of vaccines and prevention of unnecessary patient harm. The advisory committee used the WHO online causality assessment tool and categorized five of the reports as consistent, which indicates a possibility of the adverse event being related to vaccination. Two of the reports were categorized as coincidental, with inconsistent causal association with the vaccination.

Finally, PQM+ supported EFDA's Pharmacovigilance Center with data entry of 2,100 AEFI reports from Pfizer COVID-19 vaccines to the global database (Vigiflow) through provision of technical and financial support to 40 healthcare professionals trained (by EFDA) on AEFI data entry. VigiFlow is an Individual Case Safety Report (ICSR) management system developed and hosted by Uppsala Monitoring Centre (UMC). Every day, pharmacovigilance professionals around the world support the collection, processing and analysis of adverse event reports that are critical for a national pharmacovigilance system to function properly.

Ghana

Policy, Planning, and Coordination

PQM+ received Global VAX funding to support Ghana FDA to strengthen its lot release function, to enable the production of vaccines in Ghana. In the past, FDA Ghana's lot release function was not assessed as part of the WHO GBT assessment. Given that plans for local production of vaccines in Ghana are unfolding, FDA seeks to operationalize and achieve ML3 for its lot release function. As a result, PQM+ is providing technical assistance to ensure FDA Ghana has the legal provisions, regulations and guidelines required to define the regulatory framework of independent lot release. In Q1, PQM+ reviewed and amended three regulatory documents drafted by FDA Ghana (1) *Application form for Lot Release*, (2) *General Lot Release guidelines* and (3) *Guidelines for Lot Release of COVID-19 vaccines*. In November 2022, PQM+ convened a meeting with FDA to discuss the amendments and inputs made by PQM+ to the documents so that they can be finalized and submitted for approval. These documents will be key to FDA Ghana to operationalize this regulatory function as per best international practices, and to facilitate independent lot release mainly for the planned production of vaccines in the country. The documents will also help FDA Ghana achieve its goal of attaining ML3 for lot release.

PQM+ is also working with FDA Ghana to acquire and operationalize a complete regulatory management system, such as the IRIMS, which improves and streamlines regulatory processes. With an operational IRIMS, FDA Ghana 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 the IRIMS will help FDA Ghana meet the GBT indicator (*RS09.08 - The national regulatory authority uses computerized systems to process information, manage records, and analyze data*). IRIMS will help 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. This quarter, PQM+ designed a questionnaire to assess FDA Ghana's strengths, gaps, and weaknesses to determine the feasibility to adopt IRIMS to guide the determination of the type of system that will best suit FDA Ghana's regulatory functions and existing information communication technology (ICT) infrastructure. PQM+ held a meeting with FDA Ghana to orient them on the questionnaire before it was deployed for them to complete.

Finally this quarter, to build capacity of Global VAX regulators and academics teaching relevant biomanufacturing courses, PQM+ planned a joint study tour to South Africa from December 6 to 9 that included training, workshops, and site visits to key institutions and facilities. This visit also sought to facilitate collaborative working relations among participating Global VAX regulatory agencies and enable the formation of a community of practice around the regulation of COVID-19 vaccines. PQM+ supported the participation of 10 participants (seven men, three women) from Ghana at the vaccine manufacturing workshop in Cape Town, South Africa. The participants came from FDA Ghana, University of Ghana, University of Science and Technology, DEK consortium, and Atlantic Life Science. The training workshop covered technical topics relevant to the Global VAX initiative such as quality assurance and quality control of vaccines, production of vaccines, regulatory requirements for registering vaccines and several other topics; its practical component included visits to the South African vaccine manufacturers Afrigen and Biovac. The training materials used during the workshop and provided to the participants will serve as a comprehensive set of uniform reference documents.

In addition to providing relevant training, the study tour allowed participants to establish working relationships with key individuals at WHO, Afrigen, Biovac, South Africa Health Products Regulatory Authority (SAHPRA) and other organizations leading vaccine manufacturing on the continent.

Laboratory Systems

PQM+ Global VAX funding will support the Ghana FDA to strengthen the capacity of its lab to complete independent lot release of COVID-19 mRNA vaccines. A QC testing laboratory that meets international requirements for best laboratory practices enables 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 FDA Ghana 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, the QC analysts' capacity needs further building to enable them to test the COVID-19 vaccines per the manufacturers' methods. This quarter, PQM+ issued a request for quotation for six pieces of equipment for the QC lab which was discussed, and specifications finalized with FDA Ghana. Bids were received at the end of December 2022 and are being evaluated by PQM+'s procurement department.

Kazakhstan

Immunization Readiness and Implementation

PQM+ is supporting the NCEM in strengthening vaccine surveillance systems to ensure the system can detect, investigate, and analyze AEFIs and adverse events of special interest (AESI) to ensure an appropriate and rapid response. Under this activity, PQM+ has been tasked with conducting a situational analysis of the pharmacovigilance (PV) system in Kazakhstan in alignment with the WHO's recent GBT assessment and providing related technical assistance in support of Kazakhstan's effort to reach ML3, specifically in its vigilance functions. In November 2022, the WHO Collaborating Center for Pharmacovigilance provided training on AEFI investigation and causality assessment for 15 people (two men, 13 women). The participants were staff from NCEM's PV department, staff from the Committee for Medical and Pharmaceutical Control (CMPhC) of the Ministry of Health of the Republic of Kazakhstan, and staff from the Committee of Sanitary and Epidemiological Control of the Ministry of Healthcare of the Republic of Kazakhstan. This training included modules on investigation, causality assessment, Vigi tools, signal detection, and committees for investigation of AEFI. The training was conducted virtually over a period of five days for about three hours each day.

The WHO Collaborating Center also provided a draft template of the AEFI guideline. The Kazakhstan authorities can adapt the template for their use to manage AEFI in Kazakhstan appropriately. To prepare for the WHO GBT assessment, now planned for February 2024, the WHO Collaborating Center also provided the PV department at NCEM with a list that needs to be developed to comply with the WHO GBT Indicators for the vigilance function.

In December 2022, the WHO Collaborating Center also trained the staff of the NCEM's PV department on how to conduct training for the PV processes. The trained staff can now train other people responsible for PV in their department in the future. Eight participants (two men, six women) from the PV Department took part in this training.

PQM+ is also providing technical assistance to NCEM in strengthening its lot release systems, which allow for the continuous quality and safety monitoring of biological products through a regulatory release system on a lot-by-lot basis. This is a relatively new area for NCEM, as it has not been assessed by the WHO team as a part of the WHO GBT process. In October 2022, PQM+ delivered a virtual training on control charts and trend analysis in vaccine testing and lot release, a requirement for the WHO GBT lot release function. The helped 40 NCEM staff (nine men, 31 women) develop an understanding of trend monitoring in vaccine lot testing and lot release as well as how to generate control charts and monitor lot-to lot consistency and interpret the results.

PQM+ also prepared a presentation for the senior management of NCEM and the Committee on the progress status of vaccine lot release and laboratory testing to reflect the level of readiness for the WHO GBT audit, which is tentatively planned for February 2024. These slides provided information on the stages of indicators of the WHO GBT lot release function.

In November, PQM+ provided an in-person lot release training over a period of five days. A total of 19 participants (four men, 15 women) from NCEM attended. The training helped the participants understand the lot release indicators for WHO GBT lot release and available evidence and gaps to support the indicators as well as to develop an IDP to address the gaps. The participants also developed and tested the LSP templates and checklists and learned how to review LSP for COVID-19 vaccines, as part of the lot release procedure. The IDP that was developed during the training was verified by the Head of the Quality Assessment Department on the last day of the course. This IDP reflects the remaining gaps identified by the participants and establishes the recommended actions to fulfil the requirements of all the GBT indicators and sub-indicators related to the lot release function. It provides timeframe commitments from the team for completing actions required for each of the sub-indicators. During the remainder of the quarter, PQM+ continued to hold regular meetings with NCEM to discuss the implementation of IDPs on lot release and vaccine testing. During these meetings, the PQM+ consultants discussed the implementation of these IDPs in the NCEM departments and responded to any questions from the NCEM on implementation. PQM+ has now completed all activities per its Kazakhstan COVID-19 work plan but will continue to support NCEM with lot release through its tuberculosis funding.

Kenya

Policy, Planning, and Coordination

PQM+ is strengthening the PPB and the 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 will support PPB and NQCL toward the achievement of WHO GBT ML3 for medicines regulatory authorities. In Q1, PQM+ conducted two workshops in October and November 2022 for GMP in inspection and licensing, respectively.

For the inspection workshop, PQM+ hosted 14 attendees (10 men, four women) from PPB's GMP Inspections Department. During the workshop, PQM+ and PPB reviewed, revised, and updated nine of 15 SOPs that guide inspectors on how to conduct consistent and effective

inspections at both pharmaceutical and vaccine manufacturing sites. PQM+ has scheduled a final workshop in January 2023 to review the remaining six SOPs, as well as train relevant stakeholders on the revised SOPs. For the licensing workshop, PQM+ hosted 10 participants (six men, four women) from PPB's Licensing Department and reviewed and revised three guidelines on: 1) registration and licensing of premises, 2) good pharmacy practice (GPP) and 3) internet pharmacy. These guidelines help ensure delivery of safe and adequate pharmaceutical care, including those of COVID-19 vaccines. In February, there will be a follow-up workshop to review the remaining guidelines on licensing of vaccine manufacturing facilities and for pharmaceutical representatives and provide a training on them to PPB's licensing and inspection teams.

PQM+ is also supporting PPB to establish and institutionalize a vaccines lot release function. Lot release is a new function for PPB and is critical to ensure that Kenya can support the production and release of vaccines both for internal use and for export use. Developing lot release guidelines and SOPs will enable the regulator to develop a real-time system that continuously monitors vaccine quality through review and testing. This quarter, PQM+ completed a draft lot release guideline and started planning for a validation workshop and training on the guidelines in the following quarter.

Continuous monitoring of the quality of medicines including vaccines is important for any medicine's regulatory authority. To support this, PQM+ developed a tool for RB-PMS. PQM+ is updating its MedRS tool to include a functionality for monitoring vaccines. The updated MedRS tool is expected to be available by February 2023.

In December, PQM+ hosted a successful regional workshop in South Africa, which brought together members of several African national regulatory authorities, vaccine manufacturers, and subject matter experts for learning, sharing insights, and networking. PQM+ Kenya hosted three participants, one man and one woman from PPB and one man from the NQCL, to attend the workshop, along with a self-sponsored attendee from a vaccine manufacturer, Kenya Biovax Institute (KBI). As part of their feedback, the Kenyan team found the workshop valuable and specifically enjoyed visiting the two vaccine manufacturing sites, as this was a first for them.

Laboratory Systems

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 Q1, PQM+ began work on developing a tool for the assessment of NQCL planned for February 2023. This is a self-assessment that the NQCL team will perform onsite w to review the existing processes and equipment for testing the vaccines that the local manufactures will be manufacturing. PQM+ will walk the NQCL team through the tool to ensure understanding prior to use, and jointly review the results. PQM+ will then use the results to provide recommendations on how to fill gaps in the NQCL's capacity to support lot release and testing of COVID-19 and other vaccines.

Mozambique

Policy, Planning, and Coordination

PQM+ received American Rescue Plan (ARP) funding to work with ANARME-IP to conduct a risk-based post marketing surveillance for COVID-19 vaccines in Mozambique, as well as train ANARME staff on COVID-19 vaccine dossier review and quality control testing, and emergency

use authorization. The work plan was approved in late September, and in October, PQM+ hosted a kick-off call with stakeholders from ANARME-IP and the quality control lab. During this meeting, tentative dates for training and PMS sampling were discussed. PQM+ also worked on recruiting three consultants with expertise in regulatory systems strengthening and laboratory quality control and quality assurance. These consultants will be onboarded and start work in Q2.

Nigeria

Policy, Planning, and Coordination

PQM+ received Global VAX funding to strengthen 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. As part of this work, PQM+ is conducting an assessment to identify the regulatory documentation gaps that exist and need to be addressed. This quarter, NAFDAC sent 62 legal, policy, guideline documents used for vaccines and related biologics regulation and registration to PQM+ for its subject matter experts to review as part of the gap assessment. PQM+ started the review of these documents and will continue it into the next quarter.

To build the capacity of regulators and manufacturers across the six target Global VAX countries, PQM+ arranged a joint biomanufacturing training program at key facilities and institutions in South Africa from December 6 to 9. PQM+ supported five NAFDAC staff (three men, two women), along with the Director of Vaccine Laboratory (a woman), sponsored by the Africa Medicines Quality Forum (AMQF) to attend. It was a great opportunity for learning, networking, and further insights on various aspects of vaccine manufacturing, regulatory activities, and experience- sharing from the national regulatory agencies and subject matter experts present at the workshop. Site visits to vaccine manufacturing facilities were impactful and well appreciated by the Nigerian delegates.

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+ conducted a workshop November 14 to 18 with 17 participants (nine men, eight women) from NAFDAC to provide technical assistance to revise and update NAFDAC's laboratory safety manual and 29 existing laboratory standard operating procedures (SOPs) on quality control of COVID-19 vaccines (mRNA and non-replicating viral vector) imported into Nigeria for the ongoing COVID-19 vaccination campaign. Three new regulatory SOPs on approval mechanisms (pathways) were developed by the participants with support from PQM+ for a) EUA, (b) marketing authorization through the reliance pathway and (c) the process flow (mapping) of regulatory functions for vaccines and other biologicals. In addition, six (6) new SOPs were developed for QC testing of mRNA (Moderna & Pfizer/BioNTech) and adenovirus vectors (AstraZeneca, AZD222 & Jansen, Ad26.COV2.S) COVID-19 vaccines as well as the inactivated polio vaccine.

During the workshop, PQM+ hosted a technical session with a case scenario on a typical vaccine dossier submitted to NAFDAC for registration and authorization (emergency, market, or lot release) and general overview of CTD based on knowledge gaps observed by PQM+. This activity was to prepare participants for the upcoming lot release function in-person training to be facilitated by two PQM+ subject matter experts in Q2. At the end of the workshop, NAFDAC

developed an action plan in collaboration with PQM+ for the executive approval, implementation, monitoring and evaluation of the newly developed pathways and other SOPs.

PQM+ also started to assess and compile a list of laboratory consumables and other resource support needed by the vaccine quality control lab, the Vaccine, Biologicals, and Medical Device Laboratory Service (VBM-LS), for lot release and testing of COVID-19 vaccines and other biological products. Finally, PQM+ initiated the procurement of an *Osmometer with particulate analyzer* for testing osmolality of vaccines. This is the only laboratory equipment specifically requested by NAFDAC.

Rwanda

Policy, Planning, and Coordination

PQM+ received Global VAX funding to provide technical assistance to the Rwanda FDA to strengthen its capacity to provide regulatory oversight of COVID-19 vaccines imported into the country and expected to be manufactured locally soon. This will help assure the efficacy, quality, and safety of COVID-19 vaccines and biological products used in Rwanda. Implementation was delayed given the Rwanda FDA's request for revisions to the approved workplan. PQM+ revised the work plan, which was approved by the Mission on December 1, and has resumed implementation. Despite the pause in work, this quarter PQM+ was able to support Rwanda FDA to revise the terms of reference of its existing RB-PMS technical committee to include responsibilities of newly identified members focused on the implementation of COVID-19 vaccine-related PMS activities. PQM+ also supported Rwanda FDA to kick start the revision of its RB-PMS protocol, SOPs, and guidelines to incorporate vaccine related aspects. In Q2, PQM+ plans to organize a one-day RB-PMS technical committee meeting focusing on the inauguration of the new members, election of the vice-chairperson, and validation of the revised terms of reference.

Senegal

Policy, Planning, and Coordination

PQM+ received Global VAX funding to support the medicines regulatory authority, ARP, to reach ML3. Specifically, PQM+ is working to strengthen the systems for registration and marketing authorization (MA) for biologics such as COVID-19 vaccines. In Q1, PQM+ reviewed and provided feedback on five MA documents (ministerial decrees, SOPs, and checklists) drafted by ARP as per their practices. PQM+ inputs to these documents served to ensure they align not only with the agency's processes and country context, but also reflect international best practices.

In addition, PQM+ conducted a training on evaluation of biologics dossiers to train ARP dossier evaluators on key requirements to evaluate when reviewing dossiers for biologics such as vaccines. Twenty-two assessors/reviewers (14 men, eight women) of ARP's dossier evaluation committee attended this training, including the Deputy Director of the ARP. The training provided an overview of biologicals, including vaccines and covered the principles for developing biological products, the key elements to be considered (quality aspects/pre-clinical aspects and clinical aspects), the current regulatory and scientific challenges/ opportunities during product evaluation of the biologicals, including vaccine documents as well as regional regulatory systems where harmonization and reliance are underway. PQM+ is also working to strengthen ARP's vaccine lot release function to enable production of vaccines in Senegal. The

lot release of vaccines by regulatory authorities is part of the regulation of vaccines. It involves the independent assessment of each lot of a licensed vaccine before its release to the market. The goal of this regulatory function is to ensure the quality, safety, and efficacy of biological products through a regulatory release system. Lot release accounts for the nature and inherent variability of these products and therefore is done on a lot-by-lot basis. The assessment includes reviewing the manufacturer's summary protocol and, as necessary, testing the vaccine independent of the manufacturer's quality control testing. For vaccines imported from countries with mature regulatory authorities, lot release entails reviewing the lot release certificate issued by the producing-country's regulatory authority. Senegal, as a vaccine producing country, already routinely conducts independent lot release. However, in the recent GBT assessment, WHO indicated that the ARP's procedure for lot release needs to be updated, its staff needs training on lot release, and the quality control laboratory responsible for testing the vaccine lots requires specific procedures for implementing this regulatory function.

PQM+ reviewed and amended two regulatory documents drafted by ARP for its lot release function (1) Arrête sur Libération de Lot *(Decree for Lot Release*) and (2) Procedure de Libération de lot *(SOP for Lot Release)*. PQM+ then provided a training on lot release and on evaluation of LSPs) for ARP's technical staff involved in medicines registration, lot release, and quality testing. Five key staff were trained (three men, two women) virtually. This training improved the knowledge of ARP's technical staff on the production and control of vaccines and also improved their capacity for reviewing LSPs. It also primed and prepared the trainees for a more interactive, in-person lot release training planned for Q2 of PY4.

Finally this quarter, to build the capacity of Global VAX regulators and academics teaching relevant biomanufacturing courses, PQM+ planned a joint study tour to South Africa from December 6 to 9 that included training, workshops, and site visits to key institutions and facilities. This visit also sought to facilitate collaborative working relations among participating Global VAX regulatory agencies and enable the formation of a community of practice around the regulation of COVID-19 vaccines. PQM+ supported the participation of seven participants (six men, one woman) from Senegal at the vaccine manufacturing workshop in Cape Town, South Africa. Four participants represented ARP and three were from the University of Cheick Anta Diop of Senegal. The training workshop covered technical topics relevant to the Global VAX initiative such as quality assurance and quality control of vaccines, production of vaccines, regulatory requirement for registering vaccines, and several other topics; its practical component included visits to the South African vaccine manufacturers Afrigen and Biovac. The training materials used during the workshop and provided to the participants will serve as a comprehensive set of uniform reference documents. In addition to providing relevant training, the study tour allowed participants to establish working relationships with key individuals at WHO, Afrigen, Biovac, South Africa Health Products Regulatory Authority (SAHPRA) and other organizations leading vaccine manufacturing on the continent.

Laboratory Systems

PQM+ is also working to strengthen the laboratory testing function and equip and build capacity for testing of biologics. Senegal has an 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 October 2022, PQM+ completed a rapid assessment of ARP's Direction de Contrôle Qualité (DICQ), the NQCL of the agency. The assessment covered the microbiological/vaccine testing units currently located in Dakar. The PQM+ team evaluated the physical space, staff knowledge of vaccine testing, and equipment already available for testing biological products, given DICQ's

history of testing yellow fever vaccines. PQM+ also gauged DICQ's preparedness to test COVID-19 vaccines, specifically mRNA vaccines. It was evident that DICQ lacked the necessary equipment and consumables, had inadequate laboratory facilities, and the analysts had very little capacity for testing of COVID-19 vaccines.

PQM+ subsequently worked with the DICQ technical staff to compile a list of equipment that would be required and developed the specifications for this equipment leveraging on work done in Ghana because Senegal did not have dossiers for the COVID-19 vaccines imported into the country. In December 2022, PQM+ issued a request for quotation in the national newspaper and internationally for the equipment and consumables requested by DICQ for the testing of the COVID-19 vaccines. Bids were received at the end of December 2022 and are being evaluated by PQM+ procurement department.

South Africa

Policy, Planning, and Coordination

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. To get a better idea of SAPHRA's capacity, PQM+ adapted a competency needs assessment tool from the WHO regulatory competency framework for regulators of medical products and shared it with SAHPRA in October 2022 for self-assessment. Following this, PQM+ conducted a needs assessment with all SAHPRA units, including biological, clinical trials, clinical and pharmaceutical evaluations, inspectorate and regulatory compliance, vigilance and post-marketing surveillance, regulatory decision making, as well as the two quality control laboratories. The findings will inform the design and approach to strengthening SAHPRA's competency to build an adequate regulatory system and regulatory environment to ensure vaccine production and manufacturing is compliant with national and international standards. PQM+ also conducted a rapid SWOT analysis of SAHPRA's current MA processes and procedures in October. The SWOT analysis results are being compiled as part of the needs assessment report and will be made available to SAHPRA. Results from the SWOT analysis will be used to inform the development of a training program with a clear and practical implementation plan for strengthening staff skills and expertise.

PQM+ is also tasked to provide support to SAHPRA to develop a national RB-PMS program for vaccines and medical products. Since SAHPRA is deemed an advanced regulatory authority, PQM+ interventions will focus on strengthening its foundation for initial institutionalization of an RB-PMS program. Specifically, PQM+ will focus on efforts aimed at supporting SAHPRA and a PMS TWG to be set up by SAHPRA, to establish a RB-PMS program for quality surveillance of biological products (COVID-19 vaccines) and medical products (COVID-19 therapeutics). In November, PQM+ conducted a workshop with SAHPRA to introduce RB-PMS and to review current PMS activities. The workshop included key members from SAHPRA and the two quality control laboratories currently contracted with a total of 17 participants both online and in-person (six men, 11 women). The current guideline was reviewed to include vaccines and the risk-based approach. This guideline will help set up an overarching approach to an RB-PMS program for SAHPRA. The guideline will adopt the framework for RB-PMS of medicines with adaptations to include vaccines. Also during this workshop, the PQM+ technical team reviewed SAPHRA's current implementation plan and made recommendations to align it with the revised guideline. The implementation plan sets goals and timelines for PMS activities as well as helps SAHPRA to plan the budget and resources needed for these activities. Finally, PQM+ and

SAPHRA identified members for the TWG and completed the first draft of the terms of reference for the TWG. This multisectoral group has expertise that allows objective risk assessments and decision-making for PMS activities for efficient use of limited resources.

In relation to its RB-PMS activities, PQM+ completed the hiring and onboarding of the consultant that will implement the revisions to the MedRS tool in December 2022. The MedRS tool allows countries to estimate risks related to medicines, geographical areas, and facilities within the pharmaceutical supply chain and then make informed decisions regarding which medicines to focus on, how many samples are statistically representative and where to sample from. Currently this tool is designed for RB-PMS of medicines and will be adapted with additional modules added to allow this tool to be used for the design of COVID-19 vaccine quality surveillance protocol.

Finally, to build the capacity of regulators and manufacturers across the six target Global VAX countries, PQM+ hosted a workshop on vaccine manufacturing from December 6 to 9 at key facilities and institutions in Cape Town, South Africa. The workshop included:

- 200 total participants (virtual and in person) – 191 participants registered (88 female, 106 male, 46 PQM+-sponsored);
- 32 speakers from 18 organizations;
- 56 presentations across four days; and
- Eight site visit trips over two days to two local vaccine manufacturing sites (Afrigen and Biovac).

This workshop enabled PQM+ to effectively and efficiently engage with the relevant African continental agencies and multilateral technical organizations to mobilize technical resources in support of this program and the participating African countries.

Laboratory Systems

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. PQM+ completed the baseline assessments of the labs in September 2022 and continued to finalize the reports throughout the quarter. The reports will be disseminated in January 2023. The Wits lab (a third lab) has not yet been established and was assessed to identify the gaps and needs to support SAHPRA as part of the network of labs in the future. Both RIIP®/CENQAM® and SANCLBP have robust laboratory operations and quality management systems evidenced by several third-party recognitions; namely ISO 17025 accreditation and WHO prequalification. Each laboratory's efficiency would greatly increase with the introduction of an electronic laboratory information management system (eLIMS) for sample tracking, data management, and analysis, as well as for trending of quality indicators. The primary challenges for RIIP®/ CENQAM® included communication of QC testing requests and timely receipt of test methods from SAHPRA, as well as issues related to access to and cost of reference material from suppliers. At SANCLBP, PQM+ observed challenges with the process used for decision-making and the governance structure between

SAHPRA and UFS where SANCLBP is located. Additionally, SANCLBP expressed concerns related to the lack of decision-making structure between SAHPRA, UFS, and SANCLBP.

These challenges and others are to be directed to and worked through with the appropriate SAHPRA led technical working groups. Redundancy in testing capabilities will strengthen SAHPRA's ability to effectively conduct its lot release testing and other laboratory functions. Redundancy also will enhance the sustainability of the outsourced approach as the demand for testing increases with the addition of COVID-19 vaccine testing and the increased need for quality-assured medicines that will accompany the eventual rollout of the national health insurance (NHI).

Uzbekistan

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

PQM+ is supporting the Agency in strengthening PV and vaccine surveillance systems. PQM+ is working with the Services for Sanitary and Epidemiological Well-being (SSEW), which oversees the National Immunization Program (NIP), the Agency (Uzbekistan's medicines regulatory authority), and its State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment (the State Center) and other national and international stakeholders. PQM+ is also working with the WHO Collaborating Center (RCC) in Morocco. This quarter, PQM+ introduced WHO recommended approaches for vaccines safety surveillance to SSEW, NIP, and the Agency. Building on the work to date, PQM+ continued to work with the NIP and the PV group that sits within the Agency to strengthen the vaccine safety surveillance system in Uzbekistan.

In November 2022, PQM+ facilitated a visit of three Uzbekistan officials from the Cabinet of Ministers and the Agency on the Development of Pharmaceutical Industry and the State Center on Expertise and Standardization of Medicines, Medical Devices and Medical Equipment (Agency) to the Moroccan PV Center, including the Deputy Director, Chairman of the Pharmacological Committee, and the Chief Specialist, Sports and Health Secretariat. The purpose of the visit was to learn from the Moroccan PV center about the best practices in establishing a PV center and in operationalizing AEFIs. After the visit, the Uzbekistan delegation developed a roadmap for PV for Uzbekistan. The roadmap is important because it includes action items for the Agency on i) establishing a PV Center within the Tashkent Pharma Park Cluster; ii) establishing a centralized system of receiving reports of AEFIs; iii) involving other Public Health Programs into the System of PV led by the PV Center (TB, HIV, Immunization); and iv) developing PV legislation, guidelines, SOPs, etc. including regulations for the interaction with the Immunization Program. PQM+ reviewed and provided feedback on the roadmap. The Agency finalized the roadmap and submitted it to the Cabinet of Ministers for their approval. After approval from the Cabinet of Ministers, the Agency will launch the implementation of the action items as listed on the roadmap.

Following the visit, the Agency established a link with the WHO Collaboration Center in Upsala through an agreement between the Upsala center and the Republic of Uzbekistan. The Agency also ordered software (VigiBase, VigiFlow, VigiLyze) for reporting (e-reporting system for Health care providers and patients, e-reporting system for manufacturers, Vigimobile application for AEFIs. This linkage between the Agency and the WHO Collaborating center in Upsala is important because this speaks to the Agency's commitment to report AEFIs.

Policy, Planning, and Coordination

PQM+ conducted a COVID-19 vaccine, diagnostic, and medical devices regulatory approval pathways assessment in 2021 as part of the cross-bureau activity. The assessment found that the vaccines were imported based on the waiver of registration. No regulatory framework, procedures or capacity existed for using EUA, which is a good practice for expedited authorization of the pharmaceutical products, vaccines, and medical devices during the emergencies. As a result of PQM+'s technical assistance, a concept for EUA was introduced to the Agency and PQM+ advocated for developing a regulatory framework for its introduction. In this quarter, a provision on EUA was reintroduced into the draft of the updated Resolution of Cabinet of Ministers regulating the registration of the pharmaceutical products, vaccines, and medical devices. As soon as the updated resolution with EUA is approved, PQM+ will start providing technical assistance to operationalize the EUA procedure, including creation of guidelines, standard operating procedures (SOPs), and trainings.

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

In Quarter 1, PQM+ developed a PIR (a foundational scientific document) for gentamicin injection. To do so, PQM+ consulted with Purdue's Biotechnology Innovation and Regulatory Science Center, developed a draft PIR and sent it to USAID for review. Job aides on the PIR for inspection and registration will follow.

PQM+ supported implementation of interventions identified during the consultative meetings on amoxicillin DTs and gentamicin organized by the CHTF Commodities Sub-Group:

- Held meetings with GHSC-PSM and MTaPS to refine the call-to-action paper for the key interventions identified in the consultative meetings. These interventions aim to address bottlenecks in each partner's respective area.
- Addressed feedback from the wider CHTF Commodities Sub-Group and provided feedback for the overall messaging of the paper.
- Planned a call with stakeholders for early January to review the final content and dissemination. Following the call, PQM+ will finalize a timeline and inputs required from MTaPS and GHSC-PSM for a webinar.

PQM+ will conduct a landscape assessment of regulation and supply of priority MNCH medical devices. The assessment will:

- Identify gaps in the initial country landscape sweeps of medical devices to help refine the questionnaire for the bigger landscape assessment activity.
- PQM+ is refining the concept note to share with USAID and will hold a meeting with partners to review initial data from Bangladesh and Ghana and determine the eight additional countries for the larger assessment.

PQM+ will also conduct a landscape assessment of regulation and supply of tranexamic acid for maternal health use. PQM+ has begun a background review of regulatory issues for tranexamic acid to help identify the root cause of low uptake. This assessment will help identify registration requirements and assessment processes, market authorization and inspections, and the application of risk-based approaches to regulatory functions to help identify bottlenecks and root causes for low uptake.

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

In Q1, PQM+:

- Attended the UNICEF-UNFPA-WHO suppliers meeting in Copenhagen (November 28-December 1).
- Provided a consultative review of an Implementation Toolkit for Small and Sick Newborn Care developed by the London School of Hygiene and Tropical Medicine (LSHTM). PQM+ focused on the medical supplies and devices section.
- Presented work on MCH commodities in an implementation learning seminar on the Implementation Toolkit for Small and Sick Newborn Care developed by NEST 360 and UNICEF. PQM+ was part of a session of the seminar in which PQM+, MTaPS, and PSM all spoke about our work. About 50 participants attended from international organizations such as UNICEF, academia (LSHTM), ministries of health, and other implementing partners.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Finalize review of gentamicin PIR and begin development of job aids for registration and inspection.
- Finalize a call-to-action paper for amoxicillin DT and gentamicin, present it to the CHTF commodities subgroup, and discuss dissemination plans.
- Finalize the landscape assessment tool questionnaire and begin gathering country data.
- Continue desk review of tranexamic acid.

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.

- Continued to work with India Manufacturer 1 on CAPA deficiencies for albendazole 400 mg tablets. Discussed the company's failed mebendazole BE study and Expert Review Panel (ERP) review with USAID.
- Continued to provide technical assistance to India Manufacturer 3 on praziquantel 600mg tablets; completed analysis of the samples and am awaiting the interim bioequivalence report.
- Worked with USP's legal department to review CDAs with India Manufacturer 2 (albendazole and ivermecton) and Nigeria Manufacturer 1 (mebendazole). A series of comments have been addressed and final review is underway.
- Completed a dossier review for Bangladesh Manufacturer 1 for azithromycin 500 mg. (waiting for product shipment to U.S. market for submission for WHO PQ).
- Engaged a Section 508 compliance vendor to complete testing and remediation of the NTD Dashboard tool.
- Identified potential topics for two new advanced GMP courses and will determine if resources allow for one or two robust courses to be developed with an academic partner.
- Participated in the UNICEF/UNFPA/WHO suppliers meeting in Copenhagen.
- Agreed on final edits with USAID on the NTD landscape analysis.

Priority Activities for Next Quarter

Next quarter, PQM+ plans to:

- Conduct site visits with Kenya Manufacturers 1 and Bangladesh Manufacturer 1.
- Finalize CDAs for discussions with India Manufacturer 2 and Nigeria Manufacturer 1.
- Continue working with India Manufacturers 1 and 2 and Bangladesh Manufacturer 2.
- Finalize 508 compliance remediation of NTD dashboard tool.
- Finalize NTD 1-2 page overview and disseminate.

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.

Progress by PQM+ Objective

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

In Q1, PQM+ continued supporting two pharmaceutical manufacturers of first line, four drugs 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. 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. As a result, the manufacturer submitted the 4FDC dossier to WHO. WHO accepted the dossier for full assessment. PQM+ helped 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. 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.

PQM+ is also providing technical assistance to Pakistan Manufacturer 4 for two-drug fixed-dose combination (2FDC) TB medicines. The manufacturer will produce the 2FDC in the same production line as 4FDC. PQM+ technical assistance will focus on compiling the dossier, conducting a BE study, and developing the product. In Q1, PQM+ helped identify suppliers for reference product for 2 FDC; procurement of the reference product is in progress. 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 the WHO assessment team reviewed. ACDIMA, Pakistan Manufacturer 4, and PQM+ are addressing WHO's comments on the protocol.

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

In PY3, PQM+ and USP completed the validation of methods to test for nitrosamines impurities in rifapentine TB medicine. USP finalized the laboratory report for the liquid chromatography-mass spectrometry method development/validation for the Rifapentine API and tablets. In Q1, USP completed the validation of methods to test for nitrosamine impurities in rifapentine and rifampin TB medicine. The team also completed the first draft of the training slide deck for analyzing nitrosamine impurities in rifapentine and rifampin TB medicines.

Also, in Q1, PQM+ continued to 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. During the laboratory phase, in PY3 Q4, the team successfully identified a synthesis route and demonstrated each step of the continuous manufacturing process. In Q1 of this program year, PQM+ with USAID's lead is exploring potential manufacturers to receive the technology transfer.

In PY3, PQM+ signed a non-disclosure agreement with South Africa Manufacturer 1, which currently produces two TB APIs, and is providing technical assistance to the manufacturer for WHO PQ of isoniazid API. During a visit to this manufacturer, PQM+ conducted an onsite GMP assessment of the facility and helped with preparation of the isoniazid drug master file (DMF). Next, PQM+ will work with the manufacturer to improve GMP compliance and prepare the DMF.

As part of the effort to identify additional priority TB manufacturers, PQM+ experts on a trip to India for COVID therapeutics work also visited India Manufacturer 8's facilities to assess potential collaboration in Q1. The team was able to confirm the company's capacity and capabilities to support manufacturing of TB products.

The BE study report is a critical document used as evidence to justify the interchangeability and effectiveness between two products in the dossier submitted for marketing authorization. The Regional Bioequivalence Centre Sh. Co. (RBEC) in Ethiopia is a public private partnership 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, Ethiopia Food and Drug Authority, RBEC, and PQM+. In PY3, PQM+ facilitated TWG meetings and, with RBEC, laid out a plan of action for assessing, identifying, and addressing gaps. In Q1, the TWG was finalizing a concept note for a stakeholders' workshop that, along with the desk review conducted by the TWG, will inform the technical report that will serve as a foundation to build the capacity of RBEC.

Priority Activities for Next Quarter

Next quarter, PQM+ will:

- Follow up with Pakistan Manufacturer 1 to review the updated dossier and stability data prior to submission to WHO.
- Continue to work with Pakistan Manufacturer 4 to address the gaps identified in the WHO audit for 4FDC and product development and BE for 2 FDC.
- Finalize training material on method validation to test for nitrosamine impurities for rifapentine and rifampin API.
- Finalize the work with VCU on phase 2 of the manufacturing process optimization for a priority TB product.
- Continue to provide technical assistance to South Africa Manufacturer 1 on GMP compliance and preparation of DMF for isoniazid API.
- Conduct the stakeholders' workshop to develop the technical report.
- Identify experts to conduct optimization for Rifamycin-s and to conduct a landscape analysis of South African manufacturers.

Program Support

Communications

Social media: To highlight PQM+ activities and amplify our work, PQM+ shared 40 posts this quarter via Twitter and LinkedIn. The posts earned more than 520 engagements. The most popular posts were about the Global VAX workshop in South Africa and the Ethiopia and Uzbekistan learning visit.

Success stories: We submitted one story this quarter for USAID review about Pakistan's COVID-19 vaccines activities. In addition, we wrote a legacy success story about Ghana's NQCL achieving WHO PQ.

Newsletter: PQM+ shared its ninth newsletter this quarter, which had a 43 percent open rate. This issue spotlighted the Global VAX workshop in South Africa, Kenya's surveillance systems, the RIMS products, and Uzbekistan's use of CPAR to accelerate access to TB medicines.

Website: We began to update the new website and added information about our Global VAX work, as well as three new leadership bios. We announced the website via the winter newsletter and will continue to promote it via an announcement to our contacts, social media, and emails.

Staff: PQM+ continues to recruit applicants for two full-time communications positions.