

Laboratory training for Laboratório Nacional de Controlo da Qualidade de Medicamentos (LNCQM) staff and follow-up on program activities

**Maputo, Mozambique
April 22- May 7, 2013**

Trip Report

**Regina Okafor, MBA
Program Manager**

Promoting the Quality of Medicines

Implemented by U.S. Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852 USA
Tel: (+1-301-816-8363)
Email: rio@usp.org

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PROMOTING THE QUALITY OF MEDICINES

Executive Summary

Ms. Regina Okafor traveled to Maputo, Mozambique to train new provincial inspectors on the Minilab[®] and provide follow-up training to Laboratório Nacional de Controlo da Qualidade de Medicamentos (LNCQM) staff on Karl Fischer and High Performance Liquid Chromatography (HPLC). Advanced HPLC training was also provided. Ms. Okafor evaluated the current and three new LNCQM staff and was pleased with their progress and proficiency.

Ms. Okafor also met with USAID/Mozambique and the Director of the Departamento Farmacêutico to discuss the remaining activities for this fiscal year, and the group agreed to concrete next steps for the coming months.

Overall, the trip was successful, and PQM was able to complete the training, install all shipped equipment, and meet with in-country partners.

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About PQM

The Promoting the Quality of Medicines (PQM) program, funded by the U.S. Agency for International Development (USAID), is the successor of the Drug Quality and Information (DQI) program implemented by the United States Pharmacopeia (USP). PQM is USAID's response to the growing challenge posed by the proliferation of counterfeit and substandard medicines. By providing technical assistance to developing countries, PQM helps build local capacity in medicine quality assurance systems, increase the supply of quality medicines to priority USAID health programs, and ensure the quality and safety of medicines globally. This document does not necessarily represent the views or opinions of USAID or the United States Government. It may be reproduced if credit is given to PQM and USP.

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- Mr. Benedito Chaúque, Logistics Activity Manager for USAID/Mozambique, for his support and assistance with the logistics of the training
- Dr. Victor Machava, Head of Quality Assurance at LNCQM, for his kindness and for coordinating the training and other activities
- PQM administrative staff and editors for their assistance with logistical arrangements and for editing this trip report
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ACRONYMS

CMAM	Central de Medicamentos e Artigos Médicos
DF	Departamento Farmacêutico
DQI	Drug Quality and Information Program
HPLC	High Performance Liquid Chromatography
LNCQM	Laboratório Nacional de Controlo da Qualidade de Medicamentos
MQM	Medicines Quality Monitoring
MSH	Management Sciences for Health
NOMCOL	Network of Official Medicines Control Laboratories
PEPFAR	President's Emergency Plan for AIDS Relief
PQM	Promoting the Quality of Medicines Program
QA	Quality Assurance
QC	Quality Control
TLC	Thin Layer Chromatography
USAID	United States Agency for International Development
USP	United States Pharmacopeia
UV-Vis	Ultraviolet-visible spectrometry

Background

The U.S. Agency for International Development (USAID) and U.S. Pharmacopeia (USP) have been providing technical assistance to Mozambique through the Promoting the Quality of Medicines (PQM) program since 2010. Activities have focused on strengthening the quality control (QC) and quality assurance (QA) capabilities of Mozambique's medicines regulatory authority, the Departamento Farmacêutico (DF).

PQM conducted a rapid assessment of the QA/QC capabilities of the DF in December 2010, which revealed that the infrastructure, equipment, and staff of the DF's QC laboratory, the Laboratório Nacional da Qualidade de Medicamentos (LNCQM), were inadequate to provide QC services. The assessment also identified a lack of post-marketing surveillance of medicines quality. In 2011, PQM and the DF partnered to develop a training program to conduct basic tests on the quality of medicines and to establish a medicines quality monitoring (MQM) program.

In 2012, PQM shipped and installed a variety of laboratory equipment, supplies, and reagents necessary for a QC laboratory to adequately test medicines and conducted training on how to operate the equipment. Additionally, PQM conducted training on the proper use of USP NF as well as how to conduct compendia testing. In June 2012 the Permanent Secretary of Mozambique declared LNCQM's temporary QC lab officially open. PQM continues to support LNCQM's progress by providing technical equipment, training, and consumables still needed for the lab to operate independently. In September 2012, LNCQM officially became a member of the Network of Official Medicines Control Laboratories-Africa (NOMCOL-Africa) and hosted the second annual NOMCOL meeting in Maputo. PQM also trained LNCQM staff on dissolution, process verification testing, and Karl Fischer titration.

Purpose of Trip

Ms. Regina Okafor traveled to Maputo to:

- Train new provincial inspectors and provide follow-up training to LNCQM staff on Minilab[®] techniques
- Provide training on advanced High Performance Liquid Chromatography (HPLC) and quality management system (QMS) follow-up
- Set up equipment procured and shipped to LNCQM (Perkin Elmer UV-Vis, Erweka Disintegration and Dissolution systems)
- Discuss FY13 work plan activities with the DF
- Meet with USAID to discuss FY13 and FY14 activities

Source of Funding

This trip was funded by USAID/Mozambique through the President's Emergency Plan for AIDS Relief (PEPFAR).

Overview of Activities

Prior to beginning the training, Ms. Okafor set up the equipment procured and shipped to LNCQM (Perkin Elmer UV-Vis, Erweka Disintegration and Dissolution systems). Following the training, two Minilabs[®] were shipped to the new sentinel sites, Cabo Delgado and Tete.

The following chart provides details of the training provided during the trip:

Item	Description
Specific Objectives	<ul style="list-style-type: none"> • Train provincial staff on Minilab[®] <ul style="list-style-type: none"> ○ Basic testing of samples using Minilab[®] ○ Sample collection and labeling ○ Sample preparation ○ Data collection and reporting results ○ Sampling and testing protocol • Train staff on gradient elution HPLC <ul style="list-style-type: none"> ○ Show staff how to setup gradient instrument methods ○ Theory of gradient vs. isocratic ○ Preparing instrument prior to run ○ Processing method ○ Serial dilutions ○ Troubleshooting • Follow-up/training on previously trained techniques <ul style="list-style-type: none"> ○ Karl Fischer – hands-on practice and question/answer ○ HPLC – theory and hands-on ○ Good Documentation Practices (GDP) – evaluate notebooks
Venue/Location	LNCQM (DF)
Organizers	PQM, USAID/Mozambique, DF, and LNCQM
Sponsors	USAID/Mozambique
Trainer	Ms. Regina Okafor
Trainees	12 staff from LNCQM and 6 provincial staff for Minilab [®] training; see Annex 1 for detailed information
Agenda	See Agenda in Annex 2 for detailed information
Opening Ceremony	<ul style="list-style-type: none"> • Dra. Felicidade Macamo, Director of DF • Dra. Paula Raymundo, Director of LNCQM • Dr. Víctor Machava, Head of QA at LNCQM • Dra. Isabel Chemane, Head of QC of LNCQM • 14 trainees
Modules	<ul style="list-style-type: none"> • Karl Fischer (hands-on) • HPLC (theory and hands-on) • GDP (hands-on) • HPLC follow-up (hands-on practice) • Thin Layer Chromatography (TLC) (hands-on) • Minilab[®] (hands-on and theory)
Closing Ceremony	<ul style="list-style-type: none"> • Ms. Regina Okafor, PQM • Dr. Pedro Siteo, DF • Dra. Paula Raimundo, Director, LNCQM • All trainees <p>Certificates were given to the participants during closing ceremonies</p>
Equipment Provided	See Annex 3 for a list of supplies, reagents, and equipment provided in preparation for and during this trip



Mr. Clemente Rodrigues and Dra. Isabel Chemane of LNCQM led the Minilab[®] training for new provincial staff



Ms. Okafor demonstrates gradient elution for the trainees

Meeting with USAID/Mozambique, April 29, 2013

Ms. Okafor met with Dra. Paula Raimundo, LNCQM director; Mr. Benedito Chaúque, Logistics Activity Manager, USAID/Mozambique; and Ms. Shannon Marsh, Senior Health Commodities Advisor, USAID/ Mozambique to discuss the progress of the lab and the next steps. The following were the outcomes of the meeting:

- Ms. Marsh is new to USAID/Mozambique, so Ms. Okafor gave her an overview of PQM's scope of work in the country and the progress made thus far at LNCQM. A tour of the LNCQM lab was also given to Ms. Marsh.
- The group discussed the scope of work for this trip, the successful completion of the training, upcoming work plan activities, and how PQM will be represented during the new fiscal year budget planning meeting. If possible, PQM will attend the meeting.

Meeting with USAID/Mozambique and Director of DF, May 2, 2013

PQM staff met with the DF director, Dra. Felicidade Siteo Macamo, and Mr. Benedito Chaúque, Logistics Activity Manager for USAID/Mozambique, to discuss the outcomes of the training, work plan activities, and the next steps. The following were the outcomes of the meeting:

- The team discussed the difficulty PQM occasionally experiences with the clearance of equipment and supplies shipped to LNCQM. Ms. Okafor informed Dra. Felicidade that PQM has mitigated some of these clearance hurdles by shipping equipment from USP headquarters. However, Perkin Elmer inadvertently shipped equipment to Mozambique without proper documentation. Dra. Felicidade promised to contact the head of the procurement department to expedite clearance of the equipment.
- The team discussed the upcoming work plan activities, especially the provincial visit for evaluation and supervision of the sample collection as well as equipping the lab (Annex 4). Ms. Okafor informed Dra. Felicidade that it would be beneficial if she accompanies USAID, PQM, and LNCQM for a site visit so as to better understand the importance of the MQM activities, and Dra. Felicidade agreed to participate in the evaluation process. PQM also discussed the work plan activity of sensitizing the public to counterfeit and substandard medicines by publicizing LNCQM and DF activities. Dra. Felicidade noted that the issue of medicines quality in Mozambique is a very sensitive topic due to the poor quality of medicines in the country. In the past, PQM and DF used a media “question and answer” session to address the public; however, Dra. Felicidade informed PQM that she would have to talk to the Minister about another media session and get approval first.
- Additionally, Ms. Okafor asked about enforcement actions that the DF has taken since the MQM results were provided to them last fiscal year. PQM emphasized that MQM is only effective when proper enforcement actions are taken to remove the substandard or counterfeit medicines from the market. Dra. Felicidade informed Ms. Okafor and USAID that the DF does not have authority at this point to take enforcement actions; only the Minister has that authority. Central de Medicamentos e Artigos Médicos (CMAM), the central warehouse for medicine distribution in Mozambique, and DF must work together to ensure the proper control of medicines in the country. There also appears to be a major supply chain and procurement issue with proper procurement and distribution of medicines in Mozambique. All medicines received in the country should be tested by LNCQM, but this is not the case. Instead, the medicines are distributed to different sectors for public use. CMAM and the DF are currently working on documents stipulating requirements and punishable actions. Ms. Okafor stated that PQM is available to provide assistance, work with Management Sciences for Health (MSH), and provide WHO regulations to DF and CMAM. The country is in dire need of a functional pharmacovigilance system.
- The group also discussed PQM providing ISO 17025 training to DF and USAID in order for them to better understand the importance of accreditation for LNCQM. Dra. Felicidade was very interested in finding out more about lab accreditation and the status of LNCQM. Ms. Okafor informed the group that PQM has subject matter experts in this area who have helped many labs obtain ISO 17025 accreditation.

Conclusions

PQM is pleased with LNCQM’s progress thus far, the staff’s proficiency regarding the techniques that they have been trained in to date, and the fact that the DF followed an earlier PQM recommendation to hire additional staff for LNCQM. The training participants stated that the training was relevant to their jobs and will help them do their work better (see **Annex 4** for the participants’ evaluations).

PQM will continue to work with the lab to train any new lab personnel and furnish the lab with all necessary equipment and supplies for the continued success of the lab. A copy of this report will be provided to MSH in an attempt to collaborate and assist in training key staff of the DF and CMAM on pharmacovigilance.

Next Steps

Except as otherwise noted, the following next steps will be completed by the end of September:

- PQM will conduct a site evaluation of two sentinel sites in July/August
- PQM will provide QMS training at USP headquarters to the LNCQM QA manager in August/September
- LNCQM will complete MQM Round 1 and forward all results and data to PQM by July 2013
- PQM will evaluate MQM Round 1 sample collection, testing, and results provided by LNCQM
- LNCQM will complete Round 2 of MQM sample collection and testing at provincial sites and confirmatory testing at LNCQM QC lab. PQM would like to evaluate the outcome of MQM 2 results and decide if further confirmatory testing is required at USP headquarters.
- PQM will conduct training to stakeholders and partners on the importance of obtaining ISO 17025 accreditation
- PQM will evaluate the progress of LNCQM after the last training
- PQM will procure pertinent equipment still needed to perform critical tests this upcoming fiscal year (see **Annex 5**)
- PQM will complete training on Dissolution and PVT and conduct follow-up training in HPLC, Karl Fischer, and UV-Vis

Minilab[®] Training and LNCQM training
Maputo, Mozambique
April 21 – May 7, 2013

LNCQM Participant List

	Name	Organization
1	Clemente Alfonso Rodrigues	LNCQM Technician
2	Victor Machava	LNCQM Quality Assurance
3	Acino Paulo Mulhovo	LNCQM Technician
4	Valdemar Albano Timóteo	LNCQM Technician
5	Maria Isabel Chemane	LNCQM Quality Control
6	Antonio Romeu Cuamba	LNCQM Administrative sector
7	Atalvino Ezequiel Nhantumbo	LNCQM Technician
8	Flora Manuel Zandamela	LNCQM Technician
9	Telma Esperanca Calisto Cheveia	Being processed as new LNCQM Technician)
10	Paulo Cumbane	Being processed as new LNCQM Technician
11	Paula Raimundo	LNCQM Director
12	Laurinda Candido Xerinda*	LNCQM

* Replacing **Julio Hamisse Varineque**

Provincial Participant List

Participant	Name	Province
1	Jenita Manuel Jose de Abreu	<u>Cabo Delgado</u>
2	Fernando Mario Zunguze	<u>Nampula</u>
3	Adelina Manuel	<u>Zambezia</u>
4	Momade Pedro	<u>Tete</u>
5	Pedro Mamba Machere	<u>Sofala</u>
6	Fatima Mucaxe	<u>Maputo</u>

Agenda – Minilab[®] Training

Week 1	Topic/Activity
Monday	Opening Ceremony and Introductions Overview of agenda Resolve logistical issues Setup of Minilab [®] materials Introduction to Basic testing - presentations
Tuesday	Minilab [®] safety TLC presentation Setup of 2 working groups Group demonstration by team lead (LNCQM) Overview of contents of Minilab [®] Sample preparations Continue working sessions TLC hands-on
Wednesday	TLC working sessions Review results
Thursday	TLC working session – hands-on by trainees Individual TLC preparation Complete hands-on TLC
Friday	Complete overview of MQM sample collection, testing, review results Question/answer session Closing ceremony Certificate presentation
Week 2	
Saturday/ Sunday	Install Equipment shipped by PQM Review all consumables received and shipped March/April 2013 <ul style="list-style-type: none"> • Set up water bath • Distiller, Sonnicator, Centrifuge
Monday	Review HPLC status and proficiency of staff performance Follow-up on KF, LOD, and Good Documentation Practices (review notebooks) Question/Answer session Determine proficiency of new LNCQM staff Continue on Follow-up Start Advanced HPLC training - overview
Tuesday	Theory – How to run gradient HPLC - fundamentals USP General chapter requirements Hands-on Gradient HPLC - preparation of solutions System suitability

Wednesday	Continue Gradient HPLC Troubleshoot any problems Review results of HPLC Begin Troubleshooting of HPLC guides and tips Other Pharmacopeias
Thursday	Continue work on HPLC guides, software lessons Key staff to perform another HPLC gradient run for practice Evaluate HPLC results Complete HPLC
Friday	Evaluate all data from hands-on Assign homework to all LNCQM staff Overview of HPLC preparations Determine next training for staff

Detailed list of equipment/supplies/reagents provided

List of Equipment Provided for LNCQM for this trip			
April 2013			
Type	Make	Model	Comments
Centrifuge	Mettler Toledo	Not Applicable	Installed by PQM
2 Sonnicator	Shimadzu	Not Applicable	Installed by PQM
2 pH electrodes and filling solutions	Mettler Toledo	Multi use	Installed by PQM
Filters for water purification system	Not Applicable	Various	Installed as pre-filter
Surge Protectors	Not Applicable	Locally purchased	At LNCQM
3 UPS(Uninterrupted Power Supply)	Not Applicable	Locally purchased	Installed by PQM/LNCQM
Printer/Scanner cartridges	HP	HP (Locally purchased)	Installed by PQM/LNCQM
3 Stir/hot plates	Craftsman (from Cole Parmer)	Multi-use	Installed by PQM
Lab Notebooks	Fisher Scientific	Locally purchased	Installed by PQM/LNCQM
Lab consumables	Various	Locally purchased	Installed by company
8 UV-Vis cells	Fisher Scientific	Quartz	At LNCQM
6 HPLC columns	Waters, Phenomenex	various	At LNCQM
Digital thermometer	Not Applicable	Not Applicable	At LNCQM
Water bath	Not Applicable	Not Applicable	
1 UV-Vis	Perkin Elmer	Lambda 25	At LNCQM/Perkin Elmer S. Africa to do IQ/OQ/PQ
Kryo20 Bath Liquid	Not Applicable	Not Applicable	At LNCQM
1 Disintegration Tester	Erweka	ZT322	Installed by LNCQM
1 Dissolution Tester	Erweka	DT726	Installed by LNCQM
6 Upper Shaft (7")	Erweka	Not Applicable	At LNCQM
6 Vessel Cover	Erweka	Not Applicable	At LNCQM
6 Locking Collar For Dissolution system	Erweka	Not Applicable	At LNCQM
6 Mesh Basket	Erweka	Not Applicable	At LNCQM
6 Basket Shaft	Erweka	Not Applicable	At LNCQM

6 Paddle For Dissolution system	Erweka	Not Applicable	At LNCQM
6 Upper Shaft (15") For Dissolution system		Not Applicable	At LNCQM
Glass Vessel (1000 ml)		Locally paid	At LNCQM
1 Water Distillation Device	Erweka	DT 600	Installed by LNCQM
2 Detergent (1 gallon)	Not Applicable	Not Applicable	At LNCQM
Absorbent Mat (100 per pack)	Not Applicable	Not Applicable	At LNCQM
MQM materials			
2 Minilabs	GPHF	Not Applicable	Shipped to 2 new sentinel sites
Lab coats and writing materials	Not Applicable	Not Applicable	At LNCQM
Reference Standards			
4-Epianhydrotetracycline Hydrochloride(50 mg)	USP	Not Applicable	At LNCQM
Tetracycline Hydrochloride (200 mg)	USP	Not Applicable	At LNCQM
Furosemide Related Compound B (100 mg) (4-Chloro-5- sulfamoylanthranilic Acid)	USP	Not Applicable	At LNCQM
Furosemide Related Compound A (50 mg)	USP	Not Applicable	At LNCQM
Furosemide (200 mg)	USP	Not Applicable	At LNCQM
Quinine Sulfate (500 mg)	USP	Not Applicable	At LNCQM
Benzothiadiazine Related Compound A (100 mg) (4-Amino-6-chloro-1,3- benzenedisulfonamide)	USP	Not Applicable	At LNCQM

Participants' Evaluations

PQM Training Workshop

Follow-up Karl Fischer, HPLC Gradient Elution

April 22 – May 7, 2013

Indicator	Strongly agree	Agree	Disagree
Course objectives were relevant to my needs	6		
I was able to understand the content of the material presented	4	2	
Overall, the course was useful and will help me do my job better	5	1	
There were enough practical exercises to facilitate understanding of the course		4	2
The sequence in which the sessions were presented was appropriate for my understanding		6	
The instructors were knowledgeable on the subject	5	1	
The instructors allowed an appropriate level of participation in the class	6		

Other Comments/Suggestions:

1. Which subject or aspects of the course should not be included in future workshops?

- Avoid repetition of subjects (1)
- Karl Fischer (1)
- LOD, Karl Fischer, Disintegration, Isocratic HPLC (1)
- No comments (3)

2. What are your recommendations/suggestions for improving the course?

Increase training time and more exercises (6)

More HPLC gradient elution training and exercises, at least 2 weeks training (6)

Detailed list of equipment still needed by LNCQM for upcoming fiscal year

Equipment & Materials Needed		
Type	Model	Estimated Cost
Vortex	TBD	\$600
HPLC columns	TBD	\$8,000
FTIR	TBD	\$20,000
FTIR supplies/parts	TBD	\$5,000
Titration	TBD	\$15,000
Titration parts/consumables	TBD	\$4,000
HPLC (at least 1 more - Waters)	TBD	\$65,000
PC/Monitor/software - Waters	TBD	\$3,500
Washing Machine (Glassware)	TBD	\$11,000
Washing machine consumables	TBD	\$3,000
Laundry machine/Dryer combo (washing lab coats)	TBD	\$5,000
Security door (procure locally)	TBD	\$2,000
Various Lab reagents/solvents	TBD	\$10,000
Nitrogen Generator	TBD	\$20,000
Storage cabinets -for lab consumables	TBD	\$2,000
Waste drums	TBD	\$2,000
Total (not including overhead)		\$176,100
+ Shipping/freight (40% of total)		\$70,440
Sum Total		\$246,540