Refresher Training Workshop on Basic Tests Using Minilabs®

Support for DACA Quality Control Laboratory

Addis Ababa, Ethiopia
January 20-February 6, 2010

Trip Report

Dr. Abdelkrim Smine
PQM Consultant

Sanford Bradby
Scientist IV, PQM

Patrick Lukulay
Director, PQM

Promoting the Quality of Medicines Program
Implemented by U.S. Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852 USA
Tel: (+1) 301-816-8162
Fax: (+1) 301-816-8374
Email: pqm@usp.org

Cooperative Agreement # GHS-A-00-09-00003-00
Sponsoring USAID Missions: USAID/Ethiopia – PMI & PEPFAR Programs
Grantee: Promoting the Quality of Medicines (PQM) Program
Author(s) Name: PQM Staff
Language: English
Date of Publication: March 18, 2010

This report is made possible by the generous support of the American people through the United States Agency for International Development (USAID), under Cooperative Agreement No. GHS-A-00-09-00003-00 (PMI and PEPFAR Initiatives). The contents are the responsibility of the Promoting the Quality of Medicines Program, implemented by the U. S. Pharmacopeia, and do not necessarily reflect the views of USAID or the United States Government.

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.

Abstract

PQM has been supporting the Ethiopian Drug Administration and Control Authority (DACA), the Ministry of Health, and the Oromia Regional Health Bureau strengthening their drug quality control capabilities. In 2009, PQM has established in collaboration with USAID and local stakeholders five sentinel sites in Oromia region to monitor the quality of antimalarial medicines. The program is supervised and run by the quality control and toxicology laboratory of DACA.

One full round of sampling and testing of a total of 410 antimalarial samples was completed in 2009. The final draft report has been completed however it was necessary to repeat testing carried out at some sentinel sites in order to ensure adherence to the sampling protocol.

The objective of this refresher training is to retrain the sentinel sites staff on all program steps and discuss all challenges faced during the previous round in order to get clean and usable data according to the program guidelines and the PQM protocol.
The objective of the visiting chemist was to strengthen drug quality testing at the Product Quality Assessment Directorate (PQAD) lab of DACA.

With respect to PEPFAR funded PQM activities, the PQM director travelled to Ethiopia to work with DACA management to finalize the implementation plan and MoU with DACA for all PEPFAR funded activities in FY 10. He and the PQM consultant in Ethiopia also conducted a rapid assessment of the new medicines proclamation or Act and assessed DACA's medicines registration process in preparation for a joint PQM WHO training of DACA medicine registration staff. The PQM director also took the opportunity to meet with the new PEPFAR logistics advisor, Ms. Elina Sverdlova

Key Words

DACA, Oromia, Sentinel sites, antimalarial Drugs, Medicines Quality Monitoring, ISO 17025, GLP, quality systems, standard operating procedures, accreditation, PQAD

TABLE OF CONTENTS

Acknowledgements 4
Acronyms 5
Background 6
Purpose of Trip 6
Source of Funding 6
Overview of Activities 7
Annex 1: Daily Implementation Plan for Mr. Bradby at PQAD 12
Annex 2: Updated PQAD Equipment List 13
Annex 3: Observations of lab practices, gaps, and recommendations 17
Annex 4: PQM/DACA Meeting Agenda 24
Annex 5: Review of Medicines Registration Capacity 25
Annex 6: Implementation Plan for Strengthening DACA Capacity 32

ACKNOWLEDGEMENTS

The authors would like to thank:

- the participants in the workshop for their valuable input and fruitful contribution in discussing all challenges and for coming up with solutions to improve the program

- Dr. Richard Reithinger and Mr. Jamie Browder for their support of this program

- the Director of QC lab of DACA, Mr. Bikila Bayissa, and all DACA management for their support and assistance during this visit and training

- PQM administrative staff and editors for their assistance with logistical arrangements and for editing the trip report

- Mr. Anthony Boni and Ms. Veerle Coignez at USAID/Washington, D.C. for their guidance and helpful insights throughout the preparation stages of the workshop

ACRONYMS

DQ	Drug Quality
DACA	Drug Administration and Control Authority of Ethiopia
GLP	Good Laboratory Practices
ISO	International Organization for Standardization
MCP	Malaria Control Program
MOH	Ministry of Health
MOU	Memorandum of Understanding
MQM	Medicine Quality Monitoring
NGO	Non-governmental organization
ORHB	Oromia Regional Health Bureau
PEPFAR	President's Emergency Plan for AIDS Relief
PMI	President's Malaria Initiative
PQAD	Product Quality Assessment Directorate
PMS	Post-market surveillance
QA	Quality Assurance
QC	Quality Control
SOP	Standard Operating Procedure
USAID	United States Agency for International Development
PQM	The Promoting the Quality of Medicines Program
WHO	World Health Organization

Background

In February 2008, PQM conducted a rapid assessment of Ethiopia's pharmaceutical quality assurance systems and drug information centers. PQM and USAID/Ethiopia agreed on priority actions to be taken to strengthen drug quality assurance in the country.

Five sentinel sites were chosen and a drug quality monitoring program established in Oromia region. Management Sciences for Health (MSH) Strengthening Pharmaceutical Systems provided Minilabs®, and staff from the National Malaria Control Program, DACA, and DACA regional bureaus were trained on drug sampling and basic tests.

The first round of sampling and testing of antimalarial drugs in the five sites – including laboratory confirmatory testing – was completed. In order to avoid similar challenges faced during the first round, PQM and the DACA QC lab agreed to conduct refresher training for all sentinel site staff.

In 2010, PQM received funding from the President's Emergency Plan for AIDS Relief (PEPFAR) program through USAID/Ethiopia to strengthening DACA's capacity. An implementation plan listing all activities and deliverables for FY10 was drafted. The activities are divided into three areas: strengthening drug registration practices; training and preparing the QC lab for ISO 17025 standards; and creating an accreditation plan for the QC lab to meet ISO 17025 in two years. All three objectives involve purchase, upgrade, or servicing of equipment and supplies.

Purpose of Trip

PQM staff had different objectives for this trip:

Dr. Abdelkrim Smine

- Conduct a refresher training workshop on basic tests using Minilabs®
- Identify, discuss, and correct all challenges faced during the first round
- Finalize a draft report of the first round from all sentinel sites in Oromia region
- Meet with USAID to discuss and finalize FY10 work plans

Mr. Sanford Bradby

- Follow up on the implementation plan for DACA QC lab
- Establish a complete list of all lab equipment
- Review and upgrade the chemical database
- Review and finalize selected Standard Operating Procedures (SOPs)

Dr. Patrick Lukulay

- Finalize the implementation plan and sign a contract with DACA
- Sign an MOU with Oromia Regional Health Bureau (ORHB)
- Gather information to register USP as an NGO in Ethiopia
- Meet with the new PEPFAR logistics advisor

Source of Funding

These activities were funded by USAID/Ethiopia, PMI and PEPFAR programs

PART I: PREPARATION FOR THE SECOND ROUND OF MEDCINE QUALITY MONITORING AT SELECTED SITES IN OROMIA REGION

Overview of the Training Workshop

Medicines to be collected and tested: Sulfadoxine-pyrimethamine, Chloroquine, Artemether-Lumifanthrine, Primaquine, and Quinine

Training Modules: Medicines sampling, visual and physical inspection of medicine packages and dosage forms, Thin Layer Chromatography, simple disintegration, and data management and reporting

Training participants: The participants were from DACA's National QC lab and regional branches as well as the Oromia Regional Health Bureau (ORHB)

Training Venue: The DACA National QC lab in Addis Ababa

Trainers: Dr. A. Smine, PQM consultant; Mr. S. Bradby, Scientist IV, PQM

Training Highlights

Monday, January 25, 2010

The director of the DACA QC lab, Mr. Bikila Bayissa, chaired the opening ceremony and explained the importance of the medicine quality monitoring (MQM) program. He emphasized the importance of conducting the second round well, learning from mistakes and challenges faced during the first round.

Presentations

Dr. Smine gave a presentation on drug quality assurance and discussed all of the definitions related to the program. In his second presentation, Dr. Smine focused on quality control of medicines and the rationale of using basic tests in countries with limited resources. He discussed some of the success stories regarding the approach of using basic tests as a first line of defense against the threat of counterfeit and substandard medicines. The participants discussed each step and senior staff added their comments and challenges faced in the field. Dr. Smine urged participants to work together and learn from each other to be able to carry out good and unbiased sampling.

At the end of day, the PQM team brought in the Minilabs® and reviewed all the components and safety measures. The group discussed the challenges faced during the first round of MQM and agreed on how sampling should be done in the future.

Tuesday, January 26, 2010

The first two TLC runs were conducted in a step-by-step manner to allow the trainees to learn the "good practices" in each step. The trainees were asked to follow the Minilab® manuals. The groups were able to carry out four full TLC analyses of three different antimalarials. After each step, the PQM team and senior program staff reviewed each TLC plate and made comments for improvement. By the end of Tuesday, all participants were able to run TLC individually.

Simple disintegration was also carried out on one sample as a demonstration for all participants. Visual and physical inspections were carried out on all samples tested. Appropriate forms were also filled out by each team as part of the training.

Wednesday, January 27, 2009

Dr. Smine and Mr. Bradby reviewed all program steps with the participants and discussed future activities. The trainees were provided with PQM written guidelines and tools to carry out the next round and were confident about completing the round without problems. Dr. Wondemagegnehu and Mr. Bayissa identified the staff to be involved in each of the sentinel sites and nominated a focal point for each team. A supervisory team will be made up of senior staff from the DACA lab, ORHB, PQM, and USAID.

Meeting with MSH

The PQM team met with Dr. Negussu Mekonen, head of the MSH office in Addis Ababa, and gave a short overview about the training and the objectives of this trip.

Briefing of USAID/Ethiopia

Dr. Smine met with PMI team leader Mr. Richard Reithinger to give an overview of the training and the plan for the next round of MQM. They discussed the challenges from the first round in FY09 and what PQM did to overcome the obstacles and get good quality data in FY10. It is expected that two MQM rounds will be carried out in FY10, if the first round is done according to program guidelines. Following the successful completion of that round, the program will expand to two new sentinel sites outside the Oromia region.

Dr. Smine gave Mr. Reithinger a draft report of data from the first round of FY09 and answered all questions related to the study and its findings. Mr. Reithinger requested that additional information about manufacturers of failed samples should be added to the report and also asked to visit 1-2 sentinel sites during the next round. Dr. Smine agreed to coordinate this visit as part of planned supervisory visits to monitor and evaluate the quality of work at the sentinel sites level.

Conclusion

PQM has retrained and provided sentinel site staff with all needed guidelines, tools, and skills to allow them to carry out the next round of MQM. PQM has also procured and shipped all necessary supplies, reference standards, and materials. Mr. Bayissa and his staff have submitted a budget, which was reviewed and approved by PQM. The first round of FY10 will start in March.

Next Steps

- Sample antimalarials according to the revised protocol and guidelines
- Conduct basic tests using Minilabs® at the sentinel sites and send all data to central DACA lab
- Confirm all TLC at central DACA lab
- Conduct confirmatory testing using compendial methods following PQM protocol
- Draft and share final report before end of May 2010

PART II: FOLLOW-UP ON IMPLEMENTATION PLAN FOR THE PRODUCT QUALITY ASSESSMENT DIRECTORY LAB OF DACA

Overview

As part of the implementation plan to strengthen drug quality testing at DACA, PQM staff will go to work with Product Quality Assessment Directory (PQAD) staff on a rotating basis. Mr. Bradby, PQM Scientist IV, with 15 years experience working with pharmacopeial laboratory procedures, was sent as part of this plan.

Mr. Bradby met with Mr. Bikila Bayissa and the Quality Assurance Officer, Awot Gebreeyziabh, to review and update the implementation plan into a daily interaction schedule with goals and objectives, located in *Annex 1*. With the assistance of the QA Officer, Mr. Bradby then interacted daily with the lab staff to generate the outputs.

The updated equipment list with current location, operational status, possible calibration location, and preventive maintenance information is found in *Annex 2*. A summary of observations of lab practices, gaps, and recommendations is found in *Annex 3*.

With the assistance of Dr. Smine and the PQAD QA officer, four SOPs (Balances, pH meters, UV Spectroscopy, and Personnel Training) were updated, implemented, and read and understood by the laboratory staff.

Conclusion

Mr. Bradby met with Bikila Bayissa; Awot Gebreezyiabh; Lantider Kasaye, Physiochemical Division Head; Seyoum Wolder, Toxicology Division Head; and Afewrle Abebe, Microbiology Division Head to discuss the observations, outputs, and the next steps.

Next steps

- PQM: provide equipment logbooks and blank labels
- PQM: provide Microsoft Access database to strengthen PQAD's chemical inventory system.
- PQM: assist with strengthening PQAD's lab cleaning program
- PQM: assist with developing PQAD's safety program
- PQM: provide information on expiration dating
- PQAD: develop lab floor map for identification of equipment location
- PQAD: complete updating equipment list
- PQAD: assign and affix identification numbers to all equipment

PART III: DEVELOP AND FINALIZE LETTERS OF COLLABORATION BETWEEN ETHIOPIA HEALTH AUTHORITIES AND PQM

Overview

One of PQM's key activities in Ethiopia involves strengthening DACA and its labs in quality assurance and quality systems. In carrying out these activities, the Ethiopian

government has mandated that all NGOs operating in the country develop a memorandum of understanding (MoU) with the respective health authorities so that the activities of NGOs can be identified and their impact in the country documented. To comply with this requirement, Dr. Lukulay travelled to Ethiopia to discuss proposed activities for PEPFAR funded work with DACA management and ORHB staff, to brief ORHB staff on PQM activities to date, and to sign a letter of agreement for all PMI funded activities.

Letter of Collaboration between PQM and DACA

Dr. Lukulay and Dr. Eshetu Wondemagegnehu met several times with the DACA management to discuss the implementation plan for PEPFAR funded activities in Ethiopia. After several reviews, the implementation plan was finalized and a signing ceremony was held. The four main activities are 1) technical assistance in quality control of pharmaceuticals, 2) technical assistance toward ISO accreditation, 3) post-market surveillance of the quality of select antiretrovirals and 4) technical assistance in drug registration including training abroad (in African or Asian countries) of select DACA staff in medical device registration, traditional medicines registration, and clinical trial review. The implementation plan (see *Annex 6*) was developed into a letter of collaboration and signed by the Director General of DACA, Mr. Yehulu Alamneh and Dr. Patrick Lukulay. A copy of the signed letter of collaboration was also sent to USAID.

Letter of collaboration between Oromia Regional Health Bureau, DACA, and PQM

Dr. Lukulay met with staff of the ORHB and briefed them about PQM activities funded by PMI to date. He reminded them that the post-market surveillance of the quality of antimalarials started about two years ago with input from staff of the ORHB, DACA, MSH/SPS, WHO, and USAID. He shared the accomplishments to date and proposed sharing quarterly reports with the bureau to keep them informed in a timely manner. After the meeting, Dr. Lukulay drafted a letter of collaboration between DACA, ORHB, and PQM. The letter of collaboration has been updated to clearly stipulate the roles and responsibilities of all parties and will be sent to ORHB in March.

Assessment of DACA Drug Registration

In preparation for technical assistance to DACA in the area of drug registration, Dr. Lukulay and Dr. Wondemagegnehu conducted a rapid assessment of DACA's drug registration guidelines and procedures. They interviewed key staff and reviewed guideline documents. They issued key findings of their assessment and made recommendations (included in *Annex 5*).

Meeting at USAID

On February 2, Dr. Lukulay attended the USAID HIV/AIDS Partners' Meeting in Addis Ababa. USAID staff briefed participants about the following:

- All NGOs operating in the country must register in order to continue to receive USAID funding
- New quarterly and semi-annual report templates based on the next generation indicators were discussed. The quarterly and semi-annual report should contain information about accomplishments, challenges, and future planned activities

All USAID partners were asked to develop MoUs with the respective Ethiopian government agencies with whom they work. PQM has now developed an MoU with DACA and sent the paperwork to USAID.

In his trip debrief at USAID, Dr. Lukulay met the new PEPFAR logistics advisor, Ms. Elina Sverdlova, who arrived in Ethiopia from Nigeria. She was briefed about PQM program objectives in general and PQM activities and mandate in Ethiopia. Ms. Sverdlova welcomed Dr. Lukulay to Ethiopia and pledged to work closely together to provide the necessary support to DACA. She emphasized the importance of drug quality and welcomed PQM as an implementing partner for PEPFAR.

Annex 1 Daily Implementation Plan for Mr. Bradby at PQAD

:

Ser No	Date	Activities	Out put
1	Wednesday (20-01-10)	Preparing plan on daily basis Lab visit Identification of lab equipment Compare equipment list & ID Observations of actual lab practices	Daily basis plan All lab equipment identified Gaps identified
2	Thursday (21-01-10)	Sort equipment by calibration type By the lab By local calibrating agency Foreign calibrating agency Prepare master calibration file Observations of actual lab practices	List of equipment to be calibrated Prepare master calibration file Gaps identified
3	Friday (22-02-10)	Identify equipment that are out of use & need preventive maintenance Prepare preventive maintenance schedule Observations of actual lab practices	List of equipment to be calibrated Prepare master calibration file Gaps identified
4	Monday (25-01-10)	Observations of chemicals, reagents, and different lab supplies storage, handling and tracking system Identification of gaps	Gaps identified
5	Tuesday (26-01-10)	Prepare procedure for chemicals, reagents and different lab supplies storage, handling, and tracking system Observations of actual practices	Correct Draft procedure for storage, handling, and tracking system for chemicals, reagent and lab supplies
6	Wednesday (27-01-10)	Evaluation the water purification system Observation of glassware cleaning and storage practice	Recommendation for acquiring validated water purification system. Recommendation for Proper procedure for glassware cleaning and storage
7	Thursday (28-01-10)	Observations on storage and waste disposal Observations on the general safety precautions in the lab Preparing draft time table for fulfilling the gaps identified	Gaps identified Recommendations on the proper lab safety procedures Prepared time tables
8	Friday (29-01-10)	Discussion with the lab staff (gaps identified and recommendations) Discussion with the lab Mgt (gaps identified and recommendations)	Common understanding on the recommendations

Annex 2 Updated PQAD Equipment List

#	Current Room location	ID #	Description & part #	Manufacturer	serial #	status	preventive maintenance needed?	where calibration will be done
1	hallway	na	reference standard refrigerator	add	add	in use	na	na
2	hallway	na	reference standard freezer	add	add	out of use	na	na
3	wet chemistry	PAY-ATA-01	Automated Titrimetric Apparatus 685 Dosimat	Metrohm	add	in use	na	by the lab
4	wet chemistry	na	electronic balance	Satorius	add	in use	na	local calibrating agency
5	wet chemistry	na	centrifuge, GR 412	Juan	add	out of use	na	na
6	wet chemistry	na	Powder sieve analyzer	add	add	in use	na	na
7	wet chemistry	S1	orbital shaker	add	add	in use	na	na
8	wet chemistry	na	flask shaker	add	add	in use	na	na
9	wet chemistry	na	hot water bath	Wertheim	add	in use	na	na
10	wet chemistry	na	pH meter	SevenMulti	1229225872	in use	na	by the lab
11	wet chemistry	na	pH meter	Hannan	add	out of use	yes - battery change	by the lab
12	wet chemistry	MB-SW-01	shaking water bath	add	add	in use	na	by the lab
13	wet chemistry	na	pH meter	Hannan	add	out of use	yes - battery change	by the lab
14	wet chemistry	na	Hood, Labcon	Labcon	add	in use	na	by the lab
15	wet chemistry	na	Hoods Asecos	Asecos	add	out of use	yes	by the lab
16	Dissolution	OHY-DIS-002	dissolution apparatus Pharma Test	Pharma Test	add	in use	yes	by the lab
17	Dissolution	PHY-FT-001	friability tester	add	add	in use	na	by the lab
18	Dissolution	na	stopwatch	add	add	in use	na	by the lab
19	Dissolution	na	stopwatch	add	add	in use	na	by the lab
20	Dissolution	SD-1	suppository disintegration tester	add	add	out of use	yes	foreign calibrating agency
21	Dissolution	PHY-DIS-01	Dissolution tester	add	add	in use	yes	by the lab
22	Dissolution	PHY-DT-001	Disintegration	add	add	in use	yes	by the lab
23	Dissolution	PHY-DT-002; D-2	Disintegration tester	add	add	out of use	yes	by the lab
24	Spectroscopy	na	UV-1800	Shimadzu	A11454602239	in use	yes	by the lab
25	Spectroscopy	na	UV-1800	Shimadzu	A11454602220	in use	yes	by the lab
26	Spectroscopy	na	vacuum pump	add	add	in use	yes	na
27	Spectroscopy	O_3	Oven	add	add	in use	na	by the lab
28	Spectroscopy	F_1	Furnace	add	add	in use	na	by the lab
29	Spectroscopy	na	vacuum oven and pump	add	add	in use	yes - pump oil change	by the lab
30	Spectroscopy	na	rotovap	Heidolph PVT	add	in use	na	na

#	Current Room location	ID #	Description & part #	Manufacturer	serial #	status	preventive maintenance needed?	where calibration will be done
31	LCMS	LC-1	LC-1 LCMS system	Shimadzu	add	out of use	na	foreign calibrating agency
32	LCMS	na	nitrogen generator	Claind	add	out of use	yes - filters	foreign calibrating agency
33	LCMS	na	air generator	Atlas Copro	add	out of use	yes - filters	foreign calibration agency
34	HPTLC	na	TLC scanner	Camag	120316	in use	yes - lamp change	foreign calibrating agency
35	HPTLC	na	TLC Linomat	Camag	120232	in use	na	foreign calibrating agency
36	HPTLC	na	TLC lightbox S/N 1205	Camag	1205	in use	na	na
37	HPTLC	na	TLC automatic devloping chamber	Camag	add	in use	yes - water for humidifier changed	foreign calibrating agency
38	HPTLC	na	air compressor	General Electric	160201	in use	yes - filter or oil change	na
39	HPTLC	na	TLC Spray Cabinet	Camag	111019	in use	na	na
40	HPTLC	na	Thermolyne	Thermolyne	199/744	in use	na	na
41	HPTLC	na	dry heating bath	Thermolyne	199/745	in use	na	na
42	Dark room	na	water circulator	add	3692520	out of use	na	by the lab
43	Dark room	na	UV light, model G8T5	P.W Allen & Company	add	in use	na	na
44	HPLC	PHY-HPLC-001	HPLC system	add	add	in use	yes	by the lab
45	HPLC	PHY-HPLC-002	HPLC system	add	add	in use	yes	by the lab
46	HPLC	PHY-HPLC-003	HPLC system	add	add	in use	yes	by the lab
47	HPLC	PHY-HPLC-004	HPLC system	add	add	in use	yes	by the lab
48	HPLC	PHY-HPLC-005	HPLC system	add	add	in use	yes	by the lab
49	HPLC	na	HPLC system - column wash use only	add	add	in use	na	na
50	GCMS	PHY-GC-02	Gas Chromatograph	Shimadzu GC-2010	add	in use	yes	by the lab
51	HPLC	na	HPLC system Conductivity and Electochemical detectors	Shimadzu	Conductivity detector, S/N 00927; Electochemical detector, S/N 01004; Control module, S/N 19557; Column oven and injector, S/N 04661; pump 1, S/N 02177; pump 2, S/N 02179	out of use	yes	by the lab
52	GCMS	na	hydrogen generator	add	add	in use	yes	foreign calibrating agency
53	GCMS	GCMS-1	Gas Chromatograph, Mass Spectroscopy	Shimadzu	add	in use	yes	by the lab
54	GCMS	na	Uniterruptible Power system	Comet	70FE4900N	in use	na	na

#	Current Room location	ID #	Description & part #	Manufacturer	serial #	status	preventive maintenance needed?	where calibration will be done
55	GCMS	na	Hydrogen and Nitrogen generator	Claind	1068	in use	na	foreign calibrating agency
56	GCMS	PHY-GC-01	GC	Trace	add	out of use	yes	by the lab
57	GCMS	na	GC	Buck Scientific	add	out of use	yes	by the lab
58	GCMS	na	Fandis Thermal management type code N2, S/N 000676	Fandis	000676	in use	na	foreign calibrating agency
59	Condom Quality 1	na	oven, type T58136	Fermake	3-837	in use	na	by the lab
60	Condom Quality 1	na	oven	Carbolite	add	in use	na	by the lab
61	Condom Quality 1	na	LRX condom tester	Lloyd instruments	030975	in use	na	foreign calibrating agency
62	Condom Quality Test room 1	na	Electric Hole Tester,Type M1101	Valendor	EHTH2/1	in use	yes - electrolyte change and electrode wire change	by the lab
63	Condom Quality 1	na	Accurate Inflation System Type M301	Valendor	S/N's: ATS H 3/1, ATS H 3/2, ATS H 3/4, ATS H 3/5, ATS H 3/6	in use	na	by the lab
64	Condom Quality 1	na	electronic balance, Model # 422, Bursting system calibration unit	Scandinavian Scale Company	030290	in use	na	local calibrating agency
65	Condom Quality 1	na	air filtration unit	Domnick Hunter	253973003	in use	yes filter change	na
66	Condom Quality 1	na	water leakage tester, model number WLT#4/1 and pump	add	add	in use	na	by the lab
67	Condom Quality 1	na	electronic balance AAA250L	Adam	AE048A110371	in use	na	local calibrating agency
68	Condom Quality 1	na	condom thickness tester, model ID-C1I 2 DS	Valendor	02291	in use	na	by the lab
69	Condom Quality 1	na	Condom length and diameter tester	Valendor	add	in use	na	by the lab
70	Condom Quality 1	na	Feeler (thickness gauges) blades, P/N: THC H 1/3	Valendor	add	in use	na	by the lab
71	Condom Quality 1	na	condom length tester P/N LMH - 3/1	Valendor	add	in use	na	by the lab
72	Condom Quality 1	na	Conductivity Leak Tester	Enersol	ECFC5-AC001	in use	yes	by the lab
73	Condom Quality 1	na	condom cutter for tensile strength test	Enersol	add	in use	na	na
74	Condom Quality 1	na	condum thickness tester, P/N 12.5MM/0.001, instrument base: P/N ACT.01.30F7	Enersol	A280005	in use	na	by the lab

#	Current Room location	ID #	Description & part #	Manufacturer	serial #	status	preventive maintenance needed?	where calibration will be done
75	Condom Quality 2	na	condom automatic inflation tester #1	Enersol	080303040	in use	na	by the lab
76	Condom Quality 2	na	condom automatic inflation tester #2	Enersol	080303060	in use	na	by the lab
77	Condom Quality 2	na	condom automatic inflation tester #3	Enersol	060504686	in use	na	by the lab
78	Condom Quality 2	na	condom automatic inflation tester #4	Enersol	080303020	in use	na	by the lab
79	Condom Quality 2	na	condom automatic inflation tester #5	Enersol	080303004	in use	na	by the lab
80	Condom Quality 2	na	condom automatic inflation tester #6	Enersol	080303090	in use	na	by the lab
81	Condom Quality 2	na	condom automatic inflation tester #7	Enersol	080303078	in use	na	by the lab
82	Condom Quality 2	na	condom automatic inflation tester #8	Enersol	080303124	in use	na	by the lab
83	Condom Quality 2	na	Pressure tester calibration unit, ABB	Enersol	8641/	in use	na	foreign calibrating agency
84	Condom Quality 2	na	Feeler guages THG/0.03-0.5; P/N 184-3025	add	FL 91 on box and guage	in use	na	foreign calibrating agency
85	Condom Quality 2	na	Feeler guage, 0.07 mm,	add	add	in use	na	by the lab
86	FTIR Room	ORF-530/PP	Spectrofluorometer	add	add	out of use	yes - change of lamp	foreign calibrating agency
86	FTIR Room	ORF-530/PP	Spectrofluorometer	add	add	out of use	yes - change of lamp	foreign calibrating agency
87	FTIR Room	PHY-FTIR-001	FTIR Model: Spectrum ONE	Spectrum	add	in use	yes - change of lamp	foreign calibrating agency
88	FTIR Room	PHY-FTIR-002	IR Prestige-21	Prestige-21	add	out of use	yes - change of lamp	foreign calibrating agency
89	FTIR Room	MP1	Melting Point Apparatus, model SMP3	Stuart Scientific	5060	in use	yes - internal mirror cleaning	by the lab
90	FTIR Room	na	Flow meter (?) Shimadzu	Shimadzu	add	in use	na	foreign calibrating agency
91	FTIR Room	P-1	Optical rotation	add	add	in use	na	by the lab
92	FTIR Room	na	Polax -L optical rotation	Polax	add	out of use	na	by the lab
93	FTIR Room	na	Pellet Press, Specac, P/N not indicated on instrument, no S/N	Specac	add	in-use	na	by the lab
94	FTIR Room	na	Pellet Press, Shimadzu P/N SSP-10A, S/N 310314301027	Shimadzu	310314301027	in use	na	by the lab
95	FTIR Room	na	vacuum pump, Telstar	Telstar	add	in use	yes - oil change	na
96	AA Room	na	Atomic Absorption Instrument, AA-6500	Shimadzu	add	out of use	na	foreign calibrating agency
97	AA Room	na	CA-112, water cooling unit	Eyela	add	out of use	na	foreign calibration agency
98	AA Room	na	Jun-Air pump, P/N 1412620	Jun-Air	558349	out of use	na	na

Annex 3 Observations, relevant GLP section, and Recommendations

Subject group	Observation	WHO GLP	Recommendation
Equipment	Calibration status not indicated on equipment in use. Re-qualification dates not indicated on instrument. Examples: re-qualification dates not indicated on HPLC's, dissolution apparatus, or drying ovens. Uncertified weight set in balance room, set has visible corrosion, checked 1000-g weight, and it weighed as 995 grams. Analysts not aware of calibration status of instrument in use.	12.2 All equipment, instruments and other devices requiring calibration must be labeled, coded or otherwise identified to indicate the status of calibration and the date when re-calibration is due.	Decide if calibration will be done in lab, locally, or with foreign assistance. Focus on developing as many in-house calibrations as possible, obtain other calibrations from local or foreign sources as needed. Apply calibration labels indicating dates. Train chemists to be aware of calibration status of the instruments they are using. Consider developing a calibration team – initially this team will carry out calibrations done in lab. These team members can also receive External training by instrument manufacturers to perform annual calibration and routine maintenance procedures.
Equipment	Instruments in use past requalification dates. Example: • Adam electronic balance calibration date: 25/11/2008, due date: 25/11/2009. • Both Satorius balances in weighing room are past the re-qualification date.	12.6 (b) Balances are to be checked daily…and re-qualification should be performed annually using certified reference weights.	Perform and document re-qualification using certified reference weights, update instrument labels.
Equipment	Different instrument ID labels in use. Example: Two labels seen on Disintegration tester: "PHY-DT-002" and "D-2" Instruments without unique identification numbers. Example two identical Hanna pH meters without ID numbers	12.1 Each item of equipment, instrument or other device used for testing, verification and/or calibration must, when practicable, be uniquely identified.	Assign and apply ID's to all instruments in all areas of PQAD. Remove all previous versions.
Equipment	Unknown location of equipment	12.8 (d) Records must be kept of each item of equipment... and the current location	Develop lab map of rooms, update equipment file with location.
Equipment	Instrument logbooks not assigned for all instruments in use. Unclear entries regarding multiple instruments in the same logbook. Different types of logbooks, inconsistent use of logbooks- some also have testing data in them.	12.8 Records must be kept of each item of equipment, instrument or other device used to perform testing… It is also recommended that records should be kept and additional observations made of the time for which the equipment, instruments or devices were used.	Assign logbooks for all instruments. The logbook should be located in immediate vicinity of the instrument to facilitate concurrent documentation. Multiple instruments can be assigned to a single log book. Examples: • an HPLC system • a balance located in a hood • a group of electronic thermometers. Distribute consistent logbook throughout PQAD. Train chemists in use of logbook versus worksheet and notebook. Logbook entries should be reviewed monthly to address inconsistent entries.
Equipment	Numerous examples of unmarked broken or inoperative equipment. Examples: • Outside the HPLC room on floor: A box of inoperative pH meters. • In Instrument Room 1, a Hannon portable pH meter has tape labeled as being "suspect". • In the Wet Chemistry Room: The Asecos ventilation Hood is broken but observed sample prep in	12.11 Equipment, instruments and other devices, either subjected to overloading or mishandling, giving suspect results, shown to be defective or outside specified limits, must be taken out of service and clearly labeled or marked.	Begin to label inoperative equipment with out of service labels/signs. If possible, remove inoperative equipment away from work areas. Train chemists to clearly label defective equipment and to record instrument-related information in the equipment logbook.

	the hood.		
Documentation	Solutions observed with improper or no labeling, examples: • Mobile phase bottles on HPLC instruments in use with incomplete labels. • The titration burets hold unlabeled solutions. Example: The buret labeled as "0.1 N EDTA" has a solution bottle that is unlabeled. There is no evidence of the actual contents of the bottle, or the age. • Unlabeled or partially labeled bottles with solutions seen in use on HPLC systems.	10.5 The labels of reagent solutions prepared in the laboratory must clearly specify: (a) name; (b) date of preparation and initials of technician/analyst; and (c) expiry date or re-test date, as justified.	Perform refresher training as group session. Remove and discard unlabeled buret solutions. For long-term storage, rinse the burets with water to prevent the formation of crystals in the lines and buret piston as the solutions evaporate. Label solutions concurrently as they are prepared.
Documentation	Reagents observed with improper or no labeling. Examples: • A vial of Valproic Acid secondary reference standard was observed on the return cart in the hallway near the reference standard storage room. The vial had no unique tracking number, no received date, and was past the indicated retest date of 02/2009. • No expiration date on reagents in chemical storage areas unless assigned by manufacturer.	11.3 An identification number should be assigned to all reference substances, except for pharmacopoeial reference substances. 11.4 A new identification number must be assigned to each new batch. 11.5 This number must be marked on each vial of the reference substance.	Develop system to track secondary standards and to allow assigning of identification numbers. Label vials with identification number. Assign expiration date at time of receipt.
Documentation	Inconsistent use of laboratory notebooks: • Information required by the PQAD Notebook SOP was not recorded at the beginning of each new analysis. • Instructions for Keeping Research Records not signed • Table of Contents not completed • Project name, Notebook number, "Continued On" and "Signature and Date" sections not completed on every page • "Read and Understood" not signed off • Errors not properly annotated, completely blotted out, or over written without signature, date, or explanation • When reviewing notebooks, variations of this comment heard: "The first page was signed, why sign the other pages?	15.5 The analytical worksheet must provide for the following information: (b) page numbering, including the total number of pages (including annexes); (c) the date of the test request; (d) the date on which the analysis was started and completed; (e) the name and signature of the analyst;	The current PQAD notebook SOP requires specific information such as sample name and method to be recorded in the notebook at the beginning of each new analysis. Also, it is required to underline these headings. Suggest group refresher training should be held to review the Notebook SOP to promote consistent use of notebooks and analytical worksheets. Errors should be crossed out with one line, dated, explained, and signed. The analysts should understand their notebooks and worksheet may have legal significance and complete documentation on all pages is necessary.
Documentation	Chromatography Report Form observations:	15.5 The analytical worksheet must provide for the following information:	Add equipment ID number Require analysts to use instruments with current

	• Instrument not sufficiently identified – analysts recorded "HPLC", but which instrument was actually used? • The form does not require analysts to indicate the instrument calibration is current. • The form does not require the identification of the reference standard used. • Incomplete identification of reagents used in analysis.	(h) the identity of the test equipment used… (k) the identification of reagents and solvents employed; (n) any deviation from the prescribed procedure, which must be approved and reported, 11.6 The identification number should be quoted on the analytical worksheet every time the reference substance is used. In case of pharmacopoeial reference standards the batch number and/or the batch validity statement should be attached to the worksheet.	calibrations or submit deviation forms as part of a quality improvement program. Assign ID numbers to all secondary reference standards and record on vial and in form. Define required information for identification of a reagent (for example, name, manufacturer, lot number, date manufactured, date opened, date of expiration). Train analysts to record this information consistently.
Cleaning	Insufficient or ineffective cleaning of lab: Examples • Dust on lab equipment • Dust on lab benches • Dirt and dust visible on floors • Animal (mouse?) feces on HPLC bench top • Dissolution vessels with interior surfaces covered with scratches Comment(s) heard: Inconsistent washing of glassware. Dishwasher machine does not always clean lab glass sufficiently.	2.3 The laboratory must establish, implement and maintain authorized written standard operating procedures (SOPs) including, but not limited to administrative and technical operations, such as: (n) cleaning of laboratory facilities, including bench tops, equipment, work stations, clean rooms, (aseptic suites), glassware;	Establish a regular lab-wide cleanup period. Suggestion: commence with an hour a week to establish then once a month sessions. All lab personnel should be required to participate during the clean-up time period, and supervisors should create teams to address the specific cleanup issues such as removal of all broken equipment from a room or cleaning around sensitive equipment. Remove dust on a daily or weekly basis to prevent buildup. Specific cleaning equipment should be readily available: • dusting equipment • vacuums, • mops Specific dishwashing equipment should be readily available: • soft brushes for cleaning dissolution vessels. • long-length bristle brushes. The dishwashing team should not use abrasive cleaners on lab glassware. Chemists may need to use acid solutions to remove stubborn stains without scratching the glass surfaces. Long-necked and irregular glassware may need to be hand-washed instead of dishwashing machine to ensure consistent cleaning. Wash pipettes with a pipette washer for consistent cleaning. Perform final rinse of glassware with lab-grade water.
Waste (lab chemical & supplies)	Acidic, basic, organic and other potentially poisonous solutions are disposed down the drain because lack of disposal options. Four or five hypodermic needle tips were observed in sink.	7.6 Procedures must be in place for the safe removal of types of waste including toxic waste (chemical and biological), reagents, samples, solvents and air filters. 21.3 …Staff must be aware of methods for the safe disposal of unwanted corrosive or dangerous products by neutralization or deactivation … 21.2 (e) special care must be taken, as appropriate, in handling, for example, highly potent, infectious or volatile substances;	• Establish waste disposal officer and waste disposal team with members from each lab division. • Begin to develop SOP for waste disposal. • Neutralize acidic and basic wastes before disposal. • Consider use of on-site incinerator to burn off organic wastes. • Establish use of suitable containers for collecting and disposing sharps and other potentially infectious materials.

Water system	The quality of the water used for lab testing is not validated. (distillation system) • Distillation system provides insufficient water for all lab activities, for example, the lab glassware is washed with regular tap water. Distilled water must be brought by hand to the glass washing room as the five systems there are broken. • No backup water purification systems. • No program to sanitize the water storage tanks on a regular basis to ensure no microbiological films are present. • Water quality is not validated.	***Water*** 10.10 Water should be considered as a reagent. The appropriate grade for a specific test should be used as described in the pharmacopoeias or in an approved test, when available. 10.11 Precautions must be taken to avoid contamination during its supply, storage and distribution. 10.12 The quality of the water must be verified regularly to ensure that various grades of water meet the appropriate specifications.	PQAD is in need of at least two sustainable, repairable, validated systems are needed. These systems can be taken to the new lab building when the lab moves in the near future. USP: *Purified Water* is also to be used for all tests and assays for which water is indicated...*Purified Water* must meet the requirements for ionic and organic chemical purity and must be protected from microbial contamination. The minimal quality of source or feed water for the production of *Purified Water* is Drinking Water. This source water may be purified using unit operations that include deionization, distillation, ion exchange, reverse osmosis, filtration, or other suitable purification procedures. Purified water systems must be validated to reliably and consistently produce and distribute water of acceptable chemical and microbiological quality…these systems require frequent sanitization and microbiological monitoring to ensure water of appropriate microbiological quality.
Chemical Storage	Dirt and dust observed in chemical storage areas, on floors, boxes, and reagent bottles. No quarantine area for newly received reagents or to hold expired chemicals until disposed. Glass bottles of organic solvent observed perched on cardboard box in HPLC room and in storage rooms.	2.2 The laboratory facilities must have adequate safety equipment located appropriately and measures must be in place to ensure good housekeeping. 2.3 The laboratory must establish, implement and maintain authorized written standard operating procedures (SOPs) including, (e) the internal labeling, quarantine and storage of materials;	Chemical storage areas are not exempt from good housekeeping. These areas are kept under lock, but regular access needs to be given to cleaning staff as needed to ensure good housekeeping Establish quarantine area. Move bottles to stable location for long-term storage.
Chemical Storage	Reagent/Solvent boxes are stacked to the ceiling in areas, making it very difficult to apply first-in/first out rule. Current store room practice is to stack intermingled boxes of reagents and solvents where space is available. Observed stacks with both boxes of acid and bases in them. Comment heard: the solvents are in their original packing containers, so we try to store them as they are.	7.9 The storage facilities should be well organized for the correct storage of samples, reagents and equipment. 7.11 …The laboratory must provide separate rooms or areas for storing flammable substances, fuming and concentrated acids and bases, volatile amines and other reagents, such as hydrochloric acid, nitric acid, ammonia and bromine. 10.14 The person responsible for the store is responsible for looking after the storage facilities and their inventory, and for noting the expiry date of chemicals and reagents.	Designate areas for storage of categories as in 7.11 and begin to separate the reagents chemical storeroom areas categories in preparation for move to new lab. Stack boxes with sufficient space to allow rotation or access to oldest reagents first to ensure they are distributed first to chemists. Additional shelving could be placed down the center of some storage rooms to allow more efficient use of space.
Chemical Storage	Received date and expiration date not marked on all regents when received as boxes are not opened. The boxes are used to facilitate storage by stacking.	**10. Reagents** 10.1 All reagents and chemicals, including solvents and materials used in tests and assays, must be of appropriate quality. 10.14 The person responsible for the store is responsible for looking after the storage facilities and their inventory, and for noting the expiry date of chemicals and reagents.	Established method to ensure all incoming reagents are marked. Suggestion: For boxes not opened at time of receipt, clearly label the outer box with date of receipt and expiration date. Later, when the box is opened for distribution to the chemist, the chemical store man can mark the actual received date on the bottle and distinguish it from the opening date.
Chemical Storage	Unsafe placement of glass bottles. Examples: • In HPLC room: Organic solvent observed perched on cardboard box.	.2 The laboratory facilities must have adequate safety equipment located appropriately and measures must be in place to ensure good housekeeping.	Train staff to not haphazardly place bottles on containers that may collapse at any time. Chemical storage room should be subject to regular inspections (monthly) to ensure items are stored as safely

	• In storage room: Plastic and glass reagent bottles observed perched on cardboard boxes	10.14 The person responsible for the store is responsible for looking after the storage facilities and their inventory, and for noting the expiry date of chemicals and reagents.	as possible.
Chemical Storage	No program to address special handling and storage requirement s for peroxide-forming reagents	7.2 The laboratory facilities must have adequate safety equipment located appropriately and measures must be in place to ensure good housekeeping. 10.14 The person responsible for the store is responsible for looking after the storage facilities and their inventory, and for noting the expiry date of chemicals and reagents. 21.3 …Peroxide-free solvents should be used.	Store organic peroxides in separate areas. Establish tracking procedure to ensure timely disposal of potentially explosive peroxide solutions.
Chemical Storage	Storage area: • Water damage from ceiling leak. Boxes directly under the leak were moved, but stacked boxes to the left or right could be affected. • Water damage from rain that entered open window. • Observed some windows in storage room are open, others are closed.	***Laboratory storage facilities*** 7.9 The storage facilities should be well organized for the correct storage of samples, reagents and equipment. 10.14 The person responsible for the store is responsible for looking after the storage facilities and their inventory, and for noting the expiry date of chemicals and reagents.	Lift boxes from floor (place on pallet, cover boxes next to leak with plastic sheets, eliminate source of water leak. The opening and closing of windows should be monitored and adjusted as needed.
Chemical Storage	Regular electrical light switches in storage areas for organic solvents and in chemical reagent storerooms.	7.2 The laboratory facilities must have adequate safety equipment located appropriately… 21.2 (h) adequate insulation and spark-proofing must be provided for electrical wiring and equipment, including refrigerators;	Install spark-resistant switches in areas where appropriate.
Chemical Storage	Comment: a set of reagent bottles on the floor in the HPLC area are private reagents, purchased by a person for use in specific test and are sitting on the floor until the person reclaims them. The chemists know these reagents are not for their use.	10.2 Reagents should be purchased from reputable, approved suppliers and should be accompanied by the certificate of analysis, and the material safety data sheet, if required.	The status of these chemicals should update as soon as possible by either removing them or returning them to the owner.
Chemical Storage and receiving	Comment: it typically takes 6 months to a year to receive chemicals and supplies. I observed the receipt of a large shipment of lab supplies; however, not all reagents should be brought in bulk and stored in the lab due to safety concerns.	A time gap exists between the need for chemicals and their receipt. A gap exists between the storage ability of the lab and limited storage space. Both gaps could be addressed by a program that allows as-needed purchase of reagents, especially dangerous reagents.	The PQAD should request DACA place a bid to establish a limited time length, low amount contract with a trusted vendor to allow purchase of limited amounts of hazardous reagents as needed on a timely basis. For example, the bid could be for an open one-year purchase order for chemical supplies not to exceed $5,000. This will allow PQAD to respond quickly to the testing needs of clients.
Safety	Personnel safety equipment observations: • Analysts routinely work without safety glasses. • Safety glasses seen as "uncomfortable." • Visitors in lab areas without eye protection. • Open toe-shoes seen in lab areas. • Protective rubber aprons unavailable. • Face shields unavailable.	21.2 (d) staff must wear laboratory coats or other protective clothing, including eye protection. 7.2 The laboratory facilities must have adequate safety equipment located appropriately 21.2 (d) staff must wear laboratory coats or other protective clothing, including eye protection; 21.2 (e) special care must be taken, as appropriate, in handling, for	Establish areas in physicochemical, condom, and microbiology labs where protective glasses use is mandatory. Obtain and Post signs at entrances to areas. Obtain safety glasses for analysts and visitors. Ensure policy applies to all visitors, dishwashing, maintenance and contractors staff in safety zones. Obtain additional safety equipment to allow analysts to safely work with different hazards.

		example, highly potent, infectious or volatile substances;	Perform refresher training each year
Safety	Observed unsecured cylinders of gas. Locations: • Outside the LCMS room, two free-standing cylinders of gas in hall area. • In HPLC area, one free-standing cylinder of gas. • Two cylinders of gas were placed in rack but the restraining safety strap was not connected. • Multiple cylinders of gas are located in the microbiology lab area. • No carts observed for moving cylinders of gas.	7.13 Gases also should be stored in a dedicated store, if possible isolated from the main building. Wherever possible gas bottles are to be avoided in the laboratory and distribution is preferred from the external gas store. If gas bottles are present in the laboratory, then they should be safely secured. 7.2 The laboratory facilities must have adequate safety equipment located appropriately	Obtain cylinder clamps or restraint. Obtain carts for moving gas cylinders. Train staff to always secure cylinders.
Safety	First Aid Kits are possibly inadequate - no eye wash solution. Locations on bench or in office shelf could be easily covered. Safety shower area blocked with large boxes, glass desiccators in shower floor area, Shower water flow not checked on regular basis.	7.2 The laboratory facilities must have adequate safety equipment located appropriately 21.2 (k) first-aid materials must be provided and staff instructed in first-aid techniques, emergency care and the use of antidotes.	Obtain first aid kits with eye-wash capability. Mount first aid kits on wall for established location and to prevent obstruction to access. Keep all safety equipment accessible. Establish logbook indicating safety shower water flow is checked monthly.
Safety	Lab areas do not have eye wash stations.	21.3 …Water showers should be installed	Ensure staff knows regular sinks can be used to wash eyes in case of accidents.
Safety	Broken glassware in use. Broken glassware disposed in regular trash container.	21.3 …Staff must be instructed in the safe handling of glassware…	Establish if broken glassware is to be disposed or repaired. Establish area to collect potentially repairable glassware.
Safety	Analysts are unaware about the location fire extinguishers. Staff not sure about use of fire extinguishers.	21.2 (c) staff must be familiar with the use of fire-fighting equipment, including fire extinguishers, fire blankets and gas masks;	Provide group training fire-extinguisher use. Give hands-on training in the use of the fire-extinguishers. Provide annual safety training refresher training.
Safety	Large glass bottles of organic solvents observed being carried around by hand. Unprotected and unlabeled glass bottles of waste on floor in HPLC areas.	21.2 (e) special care must be taken, as appropriate, in handling, for example, highly potent, infectious or volatile substances;	Obtain sufficient safety bottle carriers for regular daily use. Obtain sufficient safety containers to protect glass bottles in use. Train staff to place glass bottles in safety containers on floor as unprotected glass can be easily broken by accidental contact during daily cleaning, walking, etc.
Safety	No spill cleanup station, no spill cleanup specific items such as caustic and acid neutralizers or spill containment/absorbent materials. Large mercury thermometer observed perched on a piece of equipment placed on top of cabinet near ceiling. Analysts seen preparing and working with organic solvent solutions in non-functional hood.	7.2 The laboratory facilities must have adequate safety equipment located appropriately 21.3 …Staff must be aware of methods for the safe disposal of unwanted corrosive or dangerous products by neutralization or deactivation…	Establish spill response team. Obtain spill cleanup materials for acid, bases, organics, and mercury. Establish locations for spill cleanup materials. Establish padded storage drawer(s) for mercury thermometers. Analysts should not use malfunctioning equipment – where are the solvent vapors going?
Safety	Insufficient lighting; fluorescent bulbs in overhead light fixtures are burned out. Examples: • In titration room, 4 of 6 bulbs were burned out. • In spectroscopy room, 1 of 4	7.3 The environmental conditions, including lighting…are to be appropriate to the functions and operations to be performed.	Establish regular (monthly) checks of lighting.

	bulbs is working.		
Safety	No safety signs in lab. Comment: safety signs are hard to obtain in Ethiopia.	21.3 … Warnings, precautions and instructions must be given for work with violent, uncontrollable or dangerous reactions	Possible signs • Safety shower • Eye wash stations • First aid kit • Fire extinguisher • Safety glasses needed • Authorized personnel only • Exits • After hours contact information in case of accident
Safety	No established file of chemical hazards Analysts unaware of hazards of reagents they are using.	21.2 (a) safety data sheets must be available to staff before testing is carried out;	Establish Material Data Safety Sheets (MSDS) file. Make file accessible to chemists (place in library). Continually update as new chemical shipments arrive.
Safety	Dishes, cups, water and beverage containers observed in laboratory areas.	21.2 (b) smoking, eating and drinking in the laboratory must be prohibited;	Establish areas where food and eating are permissible, train staff to know and respect the areas.

Annex 4: PQM/DACA Meeting Agenda

1. Approve and sign Memorandum of Understanding (MoU)

2. Finalize and approve implementation plan
    - Training of DACA staff overseas
    - Generator to be purchased (Proforma invoice)

3. Lab ISO accreditation plan
    - USP staff rotation (lab feedback)
    - Hiring consultant for the lab
    - Moving lab to the new building

4. Equipment Service
    - Supplied by Shimadzu Equipments
    - Other suppliers' equipments (quotation)

5. Antimalarial drugs quality monitoring (in Oromia region)
    - Responsibilities of DACA and ORHB
    - Money transfer of the 1st round
    - Minilabs and lab supplies

6. Laboratory furnishing specification
    - Current status
    - Contact and payment

7. Drug registration process assessment and training

8. Others

Annex 5: A Review of the Medicines Registration Capacity of the Food, Medicine, and Health Administration and Control Authority

1. Introduction

A rapid assessment of the medicine registration capacity of the new Food, Medicine and Health Administration Authority (FMHAA) of Ethiopia was carried out by a USP-DQI Team to identify main gaps and develop plan of action to address these gaps.

The assessment was carried out using a checklist developed by the USP DQI Team (A copy of the checklist was given to the Product Registration and Licensing Directorate in advance of the assessment to enable them prepare the necessary information for the assessment). Additional information was collected during discussion with the staff of the Directorate and review of documents provided by the Directorate.

2. Result of the assessment

2.1 Availability of legal instruments

2.1.1 Primary regulation

There is a new proclamation, "Proclamation No 611/2009 which defines the scope, powers, and duties of the new Food, Medicine and Health Administration and Control Authority (FMHACA) (Annex 1).

The Proclamation defines medicine as "any substance or mixture of substances used in the diagnosis, treatment, mitigation or prevention of a disease in human and includes narcotic drugs, psychotropic substances and precursor chemicals, traditional medicines, complementary or alternative medicines; poisons, blood and blood products, vaccine, radioactive pharmaceuticals, cosmetics and sanitary items and medical instruments.

The Proclamation defines the **scope of the authority** to include the following:

- setting standards in relation to food, medicine, environmental health, health professionals, health and health related institutions;
- licensing and regulating trans-regional food and medicine production, import, export, distribution, promotion and storage of food and medicine and quality control laboratory;
- registering and licensing scarce health professionals;
- registering and licensing health professionals coming from abroad to deliver health service;
- licensing and regulating specialized health institutions;
- monitoring and regulating trans-regional environmental health services;
- undertaking quarantine service with concerned bodies at entry and exit ports; and
- other regulatory activities with respect to trans-regional food, medicine, health and health related services and institutions.

PART TWO of the Proclamation provides the Authority the **power and duties** to evaluate and register medicines on the basis of registration requirements, and renew,

suspend and revoke such registrations. In addition, it has the following duties and responsibilities with respect to medicines.

- prepare and submit to appropriate organ health regulatory standards for safety, efficacy, quality and proper use of medicines;
- issue, renew, suspend and revoke certificate of competence for medicine processing plants, quality control laboratories, medicines importers, exporters, and distributors;
- initiate policies and legislation to strengthen the quality of medicines;
- serve as medicine information center;
- identify ingredients that caused death or ill health due to medicine residue or adulteration of medicine and take appropriate measures by conducting investigation on sample ingredients;
- organize quality control laboratories as needed to carry out its duty;
- issue import and export permits for medicine, raw materials and packaging materials;
- prepare pharmacopoeia for the country, structure the medicines included in the pharmacopoeia into different categories, revise the pharmacopoeia whenever necessary;
- undertake and coordinate post marketing surveillance in order to ensure the safety, efficacy and quality of medicines that are put into use and take appropriate measures;
- authorize conducting clinical trial, monitor the process, evaluate the results and authorize the use of the result in such a way that it benefits the public; suspend or stop the clinical trial where necessary;
- monitor and control manufacture, import, export, distribution, prescribing, dispensing, use, recording and reporting of narcotic drugs, psychotropic substance and precursor chemicals, prevent their abuse and report same to the International Narcotic Control Board;
- issue, renew, suspend and revoke license to complementary and alternative medicine practitioners and health professionals coming privately or in group from abroad to deliver health service;
- ensure proper disposal of expired medicine and their raw materials;
- control illegal medicine and take appropriate measures;
- provide the necessary support to state regulatory bodies on medicine.

PART FOUR section 13 of the proclamation stipulates that:

- no medicine shall be produced locally or imported and put in use unless it is duly registered by the executive organ after being tested for its safety, efficacy and quality.
- the Authority may, in unforeseen circumstances, give permits for the importation and use of medicines not registered.
- certificate of registration of a medicine shall be renewed every four years where the medicine continues to meet the requirements of registration

PART Four, section 14, 15, 16 and 17 of the Proclamation deal specifically with quality standards, clinical trials, packaging and labeling, poisons, radiopharmaceuticals and pesticides respectively.

Part TEN section 49 deals with complaints handling in particular with respect to denial, suspension or revocation of a certificate of competence or license. The complaint may be lodge within 30 days from the date of decision to the grievance hearing body established by the appropriate organ. The body receiving a complaint is required to render its decision within 30 days.

2.1.2 Secondary regulations

The Authority has prepared draft regulations for the interpretation and administration of the Proclamation. The draft regulations are currently being discussed in a workshop to finalize them. The final draft will be submitted to the Council of Ministers and approval. The Team was unable to review the draft regulations since copies were not made available.

Observed gaps:

- There is no mention in the Proclamation about the organizational structure of the Authority and to which executive branch of the government it is supposed to report (the supervisory body).
- It is not also clear if the Authority is autonomous in managing it is finance, recruiting its staff or making technical decisions. The sources of funding of the authority are not clearly indicated in the proclamation. It is also unusual that the definition and control of medicines does not include veterinary pharmaceuticals. The Proclamation does not have provisions dealing the following (it is not also clear if they are covered in the regulations):
    - defining the criteria for registration of products;
    - requiring renewal of applications for marketing authorization;
    - listing requirements for handling variations
    - setting time limits for processing applications
    - dealing with waiver
    - setting the fees for registration/giving power to set fees
    - dealing with confidentiality of information
    - on transparency and accountability, and
    - for an independent administrative and judiciary appeals system.

3. Presence of an official organizational structure

The Team has received a copy of the organizational chart but it is not clear if it is official or not (Annex 2).

Organizationally the Product Registration and Licensing Directorate comes under the supervision of the Deputy Director General for Standard and Licensing.

The Directorate is responsible for registering medicines, foods, and complementary medicines other products specified in the Proclamation as well as for conducting GMP inspection. The Directorate has under it two teams (see Annex 2):
a) Foreign manufacturers marketing authorization team, and
b) Local manufacturers marketing authorization team

Observed gaps

- From the structure it is not clear if the same two teams are going to handle the registration of medical devices, alternative and tradition medicines, blood and biological products, foods, etc.
- The Team believes that assessment of dossiers of different products such as products containing new chemical entities, complementary medicines medical devices, biological products will requires different expertise.

4. Availability of capacity

The Directorate for Product Registration and Licensing currently has 11 fulltime staff working on product dossiers assessment and GMP inspection. Two of the pharmacists have MSc. Degree whereas the rest have B. Pharm Degree (Annex 3). The staff have received in-house training on GMP inspection but have not received formal training on dossiers assessment and GMP inspection similar to the one provided by WHO.

In addition he Authority has a medicine advisory committee that looks into new additions to the national list of medicines.

Observed gaps:

- Discussion with staff working in the Directorate has revealed that there is limited capacity (in terms of number, qualifications, technical expertise and professional mix) to evaluate and review dossiers and conduct GMP inspection.
- There is urgent need to build the capacity of the staff to enable them carry out effective and efficient product dossiers assessment and prevent any compromise of product quality, safety and efficacy. The following areas require special expertise:
    - Assessment and GMP inspection of blood and blood products
    - Assessment of vaccines, and other biological products
    - Assessment of radio pharmaceuticals
    - Assessment and GMP inspection of medical devices, etc
- There is provision in the Proclamation for the establishment of the medicine advisory committee. It is not at all clear if the external experts (medicine advisors) have the ability and expertise to assess dossiers. It is not also clear if the functions, responsibilities and timeframe are written down in any official document.

5. Availability of written guidelines, procedures and guidance materials

The Team was informed that guidelines and procedures dealing with medicine registration are posted on the Authority's website but they need updating and further improvement. The following sample guidelines were made available during the discussion:

- Guidance for submission of applications
- Guidelines on data and information to be submitted in support of application for marketing authorization (format and content)
- Reporting form for assessors

Observed gaps

There are no guidelines or guidance materials on the following

- Guidance on exemptions and fast-track registration
- Guidance for assessors on how to assess applications
- Procedures for assessing applications for variation of MAs?
- Procedures for assessment based on specific requirements of specific classes of products (e.g. generics, products containing new active substances, new strengths, etc.)
- Guidance giving instructions, in which situations inspections (all kinds) are organized to verify the data;
- Procedures for data archiving, data confidentiality and release for the public,
- Procedures requiring active monitoring of adverse medicine reactions and reporting findings to the MRA
- Guidelines on timeframes for processing applications
- Procedures for meetings with applicants and other interested parties
- Procedures/tools for assessment of: a) the Quality part of the dossier b) the safety part of the dossier c) the efficacy part of the dossier
- Guidance on content of product information leaflets
- Guidelines on conditions attached to issued marketing authorization e.g. validity, post-license trials, prescription only medicine, pharmacy only medicine, etc.
- Written criteria for selecting external experts
- Guidance of pharmacovigilance
- Guidelines on managing conflict of interest for all working in medicine registration
- Code of conduct for external experts and internal staff

6. Other issues that transpired during discussion:

- The Team was informed that most of the medicines manufactured locally are not registered with the Authority.
- Almost all the local manufacturers do not comply with GMP requirements.
- The Authority issues certificates of registration for companies and the registration is valid for five years. There is no annual retention fee. In the certificate conditions for the distribution and use of the medicine such prescription only medicine etc are not mentioned. The certificate also mentions the name of the sole agent but its responsibility is not indicated.
- A product registered under the name of a particular sole agent can also be imported into the country by other two additional importers provided they get the agreement of manufacturer of the product. However, the two additional importers have no special responsibility. It is not therefore clear who will be liable if any thing wrong goes with a particular batch of a product and who will be responsible for the recall of the product.

- Guideline needs to be very clear that donated medicines ought to go through quality control testing
- During the assessment the Team was informed that staff working in DACA branch offices and other unites also join the GMP inspections abroad despite the fact that these staff are not trained in GMP inspection and GMP inspection is not part of their job description. The reason given for this is that GMP inspection abroad is considered as incentive for staff. GMP inspection within the country should be done by staff from the registration and quality control laboratories and the inclusion of other staff who have no experience or who would not be using the expertise in their current jobs should be limited or curtailed

Conclusion:
The Directorate of Registration and Licensing does not have the necessary capacity to carry out its functions effectively and efficiently. Guidelines, procedures and guidance materials for staff and external experts as well as for clients need to be developed and implemented.

Recommendations
- The Proclamation needs to be comprehensive and regulations to implement and interpret the various provisions of the Proclamation should be developed in consultation with stakeholders.
- The proclamation should define the members of the medicine advisory committee, their functions and their term of office.
- The organization structure of the new Authority should be streamlined or delineated to reflect the various functions the authority is supposed to undertake, in particular with respect to the registration of medicines, food, complementary medicines and other products.
- A plan for human resource development should be developed and implemented, and the number of staff increased.
- Strategies such as staff rotation, job enrichment and multi-skilling should be applied to increase the efficiency of the staff.
- The number of staff in Drug Evaluation and Registration should be increased and their skills developed further and external expertise should be used to strengthen the assessment and decision making process. There should be attempt to recruit other professionals e.g. medical doctors to carry out assessment of dossiers
- Guidelines, written criteria and standard operation procedures should be developed and disseminated.
- There should be written guidelines for exemption of registration and for fast track registration
- Registration of products should be extended to locally manufactured products and products imported for the public sector, and the list of registered products should be readily available to stakeholders.
- GMP guidelines according to international norms should be put in place and used as a basis for GMP inspection and product registration. They should apply equally to all manufacturers (local as well as foreign manufacturers).

- There should be guidelines for staff and external experts to manage conflict of interest and ensure confidentiality. All staff and members of external expert committees should be required to declare their interests in writing and sign an agreement to respect confidentiality
- The consultation process with stakeholders for guidelines and procedures should be strengthened
- An appeal system providing different independent options and clear procedures for clients should be put in place and made available to all clients and the public
- Certificate of registration should indicate the conditions for the registration of the medicine and the obligations of the sole agent. The two additional importers should also be responsible for the product they import. This would require revision of the existing guidelines

Annex 6: Implementation Plan
Strengthening DACA Capacity

Timeline	Activities/Tasks	Responsible	Deliverables	Indicators
I	Strengthening of DACA QC laboratory			
26 Oct –25 Dec. 010	1. DQCL to be provided with power generator **1.1** Identify power need to run basic tests and operate analytical equipment 1.2 Prepare technical specifications 1.3 Sending technical specifications to DACA 1.4 Approve the technical specification 1.5 Execute purchase 1.6.Installation, operation and maintenance training g	DQCTL/USPDQI USPDQI Winner company/ DQCL	➢ Power generator capacity required identified ➢ Timely execution of purchasing process	➢ Submitted document Technical evaluation report ➢ Operating generator made
May –Jun. 2010	2.0 DQCL to be provided with Laundry Machine Identify the type needed Prepare technical specifications Prepare tender document & call for open tender Identify winner & Execute purchase Installation, operation and maintenance training	USPDQI & DQCL	➢ Laundry machine capacity required identified ➢ Timely execution of purchasing process	➢ Submitted document Technical evaluation report ➢ Operating Laundry machine made
28 Dec. 09 – 15 Jan. 010	3.0. USPDQI staff to assist the DQCL in the implementation of good laboratory practices process towards to Iso standards* 3.1 Develop the process map to ISO 17025 3.2 Identify major activities 3.3 Identify gaps in adherence to good laboratory practices 3.4 Prepare and/or Review additional draft SOPs, Training on Quality Systems Identification of trainees Preparation of training materials and site Conduct training	USPDQI and QA officer of the QCL	➢ Developed internal audit schedule and conducted internal audit ➢ Prepare and disseminate audit reports with recommend corrective actions/measures	➢ Audit report with identified gaps and recommended corrective actions

Timeline	Activities/Tasks	Responsible	Deliverables	Indicators
	Study tour to ISO17025 accredited labs SOPs 3.5 Follow up on previous USP training, implementation of finalized SOPs and recommend for the next step 3.6 Prepare report on progress towards ISO 17025			
15 Nov - Mar. 12, 2010	4. Laboratory Instruments/ Equipments maintenance and calibration 4.1 Make inventory of lab instruments/equipment that need calibration & maintenance 4.2 Identify maintenance needs 4.3 Request for spare parts and services needed 4.4 Call for quotations and identify winner 4.5 Calibrate analytical equipment/instruments	USP/DQI & DQCL	➢ List of lab. equipment/instruments that need maintenance and calibration ➢ Analytical equipments and instruments serviced ➢ Analytical instruments/equipment calibrated	➢ No of analytical equipments maintained ➢ No of equipment/ instruments calibrated
25 Jan –12 Feb. 010	Consultant to prepare furnishing specifications for the new laboratory Prepare TOR for consultant One-day visit by consultant to the new DQCL to identify furnishing need Consultant to design and prepare specification or furnishing the lab. to meet ISO 17025 requirements Consultant to discuss the design and specifications with DACA and DQCL Consultant to submit final design and specifications to DACA	USP/DQI, DQCL and Consultant	➢ Prepared TOR ➢ Laboratory furnishing design and specifications that comply with ISO 17025	➢ Laboratory furnishing design and specification prepared submitted
May to June,2010	Move the lab to the new laboratory building	DQCL & USPDQI		

Timeline	Activities/Tasks	Responsible	Deliverables	Indicators
	6.1 List lab instruments/equipment hat should be moved to the new lab. building Identify companies capable of reinstalling and qualifying the lab instruments equipments Identify company that can pack and transport the lab instruments/equipments to the new lab building with no rise to the Instruments- Move instruments/equipment to the new lab building Reinstallation of the lab instruments/equipments maintain lab instruments/equipments which need maintenance **5.2** Qualify the analytical instruments/ equipments (IQ, DQ,/PQ) **5.3** Calibrate analytical equipment	Respective manufacturers of lab equipments		
	Training of analysts			
	Local training			
01-12 Marc. August 2010	7.1 Training of analysts on analytical techniques GC-spectrophotometer. ET-IR e. Identify analysts to be trained Identify trainer Identify training site Prepare training materials Conduct training	USP/DQI and DQCL	➢ Provide lab analysts with the basics of GC,FT-IR etc ➢ Provide training on managing troubleshooting in such techniques	➢ Number of people trained in quality systems ➢ Quality system training materials developed
	7.2 Training on analytical techniques HPLC and Dissolution Basic techniques in HPLC and Dissolution test Hands-on training on HPLC & dissolution testing using Arthemeter/Lumefantrine tablet	USP/DQI and DQCL	➢ Train junior staffs on basic analytical principles and techniques on HPLC and dissolution testing ➢ Improve competency of analysts on	○ Number of trained analysts ○ Types of analytical training offered ○ improvement in technical competency of the laboratory staff

Timeline	Activities/Tasks	Responsible	Deliverables	Indicators
			analytical techniques, HPLC and Dissolution	
		USPDQI and DQCL	➢ develop training material quality system ➢ Provide training	➢ Improvement in quality system ➢ Improvement in the performance of the lab
	7.4 Train DACA lab staffs on maintenance of lab. equipments (HPLC, spectrophotometer, dissolution apparatus, etc) Identify analytical equipment that need maintenance Identify the trainees Identify trainers Execute training	USPDQI & DQCL	➢ Training materials on maintenance of equipment ➢ Hands on training on maintenance of analytical equipment	➢ Number of analysts trained on lab equipment maintenance ➢ No of equipment maintained (as part of training)
	Training aboard			
March – June 2010	7.5 Training of laboratory staffs abroad: 3 staffs on Advanced analytical technique 3 Staffs on Laboratory management based on ISO 17025 Identify analysts to be trained Identify trainer Identify training site		➢ Train 6 analysts abroad	➢ Number of lab equipment maintained ➢ Number of qualified lab instruments/equipment no of calibrated analytical equipment ➢ Number of calibrated analytical equipment
II	Strengthening of drug registration			
Feb 2010	8. Assess DACA capacities of Drug registration	USPDQI, Consultant	➢ Undertake Registration	➢ Registration Strength and gaps identified
	9.1 Develop proposal to assess capacities			

Timeline	Activities/Tasks	Responsible	Deliverables	Indicators
	9.2 Carry out registration capacity assessment 9.3 Bench mark with standard on drug Registration 9.4 Identify gaps and way forward	and DACA USPDQI	capacity assessment and ➢ Identify strength and gaps	
Mar 2010	10. Provide training on drug registration both theoretical and practical (two round multi sources, new chemical entity, including bio-equivalence and bioavailability 10.1 Develop training materials 10.2 Conduct training on drug registration especially giving much emphasis to the gaps identified during the assessment 10.3 Provide on hand training on drug Registration	USPDQI DACA WHO	➢ Theoretical and practical training on drug registration of drugs and medical devices conducted	➢ Number of evaluation and registration experts trained
June – July 2010	11. Training on GMP inspection of drugs and medical devices (two rounds) including clinical trial monitoring or inspection 11.1 Develop training materials 11.2 Conduct training on GMP inspection especially giving much emphasis to the gaps identified during the assessment 11.3 Provide field training on GMP inspection	USPDQI DACA WHO	➢ Theoretical and practical training on GMP inspection conducted	➢ Number of experts trained
April - May 2010	12.0 attachment Training of 4 staffs on GMP inspection, Clinical trial monitoring, Marketing authorization of medicine and medical device and MA of alternative medicine (TOT)		➢ Provide training for 4 professionals abroad	➢ Number of trained staff
Feb – May 2010	13.Trianing on soft ware and computer 13.1 Identify trainees 13.2 Conduct train soft ware and computerized tools	USPDQI DACA	➢ Provide, and install soft ware and tools and provide training	➢ New soft ware installed and number of staff trained
III	Strengthening of post marketing surveillance program			
	Sub-Total			

Timeline	Activities/Tasks	Responsible	Deliverables	Indicators
Mar. - June. 2010	Establish a pilot PMS program on ARV's and OI Drugs in the country 14.1 Develop PMS protocol on the pilot program 14.2 Develop time schedule & budget break down 14.3 Allocate resources to carry out the pilot PMS 14.4 Train and Collect samples of ARVS and drugs for opportunistic infection in the country 14.5 Carry out lab testing on the samples 14.6 Compile and write report	DACA, USAID partner USPDQI	➢ Protocol for PMS of ARVs and drugs for opportunistic infection ➢ Resources for PMS of ARVs and OI drugs ➢ Laboratory supplies * however, regulatory action and related decisions are the responsibility of DACA	➢ No of samples collected and tested ➢ PMS on ARVs and drugs for Opportunistic infection result reported
IV	15. Promote enforcement action by DACA, and its branches			
Jan – April 2010	15.1Attachment Training of inspectors for 2 experts inspection including recall and compliant handling 15.2 Develop guidelines for recall and compliant management	USPDQI DACA	➢ Train inspectors on how to use evidence based data to undertake and promote appropriate action	➢ Number of inspectors trained
Jan – August 2010	16. Promote awareness based on PMS data. 9PSA, DOC, Films using mass media 16.1 Contract out mass media 16.2 Disseminate information through mass media	DACA/ USPDQI	➢ Disseminate information on PMS data, PSA, DOC films using mass media	➢ Number of time and types of Mass media session

Timeline	Activities/Tasks	Responsible	Deliverables	Indicators
Jan – August 2010 every three month	17.0 Project monitoring and evaluation 17.1 develop and approve monitoring and evaluation tool on the basis of deliverables, and indicators 17.2 Review the thematic using monitoring and evaluation tools 17.3 Prepare report and conduct review meeting quarterly 17.4 Take corrective measures	DACA USPDQI PEPFAR	➢ Develop tools and conduct monitoring and evaluation ➢ Conduct review meeting and take corrective measures	➢ M and E Tools developed ➢ Number of review meeting and Corrective measures undertaken
	Grand Total			

* One staff from USPDQI will spend 2 weeks, every other month for six months