

**USP DQI Workshop on GLP, HPLC, and Dissolution at DACA Quality Control  
Laboratory**

Addis Ababa, Ethiopia

January 12-17, 2009

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***Trip Report***

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## **About USP DQI**

The United States Pharmacopeia Drug Quality and Information (USP DQI) Program, funded by the U.S. Agency for International Development (cooperative agreement HRN-A-00-00-00017-00), provides technical leadership to more than 30 developing countries to strengthen their drug quality assurance programs, ensure the quality of medicines and promote public health.

USP DQI helps build local, national and regional capacity to improve the standards of drug manufacturing and distribution, reduce the impact of infectious diseases, mitigate the effects of the HIV/AIDS epidemic, and advance the appropriate use of medicines. This document does not necessarily represent the views or opinions of USAID. It may be reproduced if credit is given to USP DQI.

## **Abstract**

USP DQI conducted a training workshop on Good Laboratory Practices (GLP) and compendial analytical methods (HPLC and Dissolution) for Ethiopia's Drug Administration and Control Authority (DACA) Drug Quality Control and Toxicology Laboratory (DQCTL) January 12-17, 2009 in Addis Ababa, Ethiopia. The USP DQI team also assessed DQCTL's working conditions and provided recommendations to improve the lab staff practices, specifically to improve the laboratory documentation and operating procedures. USP DQI met with the USAID Ethiopia Mission and discussed the best plan of action to improve DACA DQCTL's working conditions.

## **Recommended Citation**

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## **Key Words**

Ethiopia, DACA, DQCTL, USP DQI, quality assurance, quality control, quality management system, malaria, PMI, HIV/AIDS, PEPFAR, GLP, HPLC, dissolution, ISO/IEC 17025:2005

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The authors wish to express their appreciation to the USP DQI administrative staff and editors for their assistance with logistical arrangements and for editing the trip report.

Finally, the authors would like to thank the USAID/Ethiopia Mission, in particular Dr. James Browder, CTO of PEPFAR, and Dr. Richard Reithinger, PMI Team Leader; and USP DQI CTO Mr. Anthony Boni and Veerle Coigneux at USAID Washington for their guidance and helpful insights throughout the preparation stages of the workshop.

## ACRONYMS

ACT	Artemisinin-based Combination Therapy
AIDS	Acquired Immune Deficiency Syndrome
BPR	Business Process Reengineering
CTO	Cognizant Technical Officer
DACA	Drug Administration and Control Authority
DCMP	Document Control Management Program
DQCTL	Drug Quality Control and Toxicology Laboratory
DQ	Drug Quality
DRA	Drug Regulatory Authority
FDC	Fixed-Dose Combinations
GC	General Chapter
GFATM	Global Fund to fight AIDS, Tuberculosis and Malaria
GLP	Good Laboratory Practices
GPNPCL	Good Practices for National Pharmaceutical Control Laboratories
HIV	Human Immunodeficiency Virus
HPLC	High Performance Liquid Chromatography
IEC	International Electro technical Commission
ISO	International Organization for Standardization
MOH	Ministry of Health
MSH/RPM+/SPS	Management Sciences for Health/Rational Pharmaceutical Management Plus/Strengthening Pharmaceutical Systems
PEPFAR	President's Emergency Plan for AIDS Relief
PF	Pharmacoepial Forum
PMI	President's Malaria Initiative
PVT	Performance Verification Test
MoH	Ministry of Health
QA	Quality Assurance
QC	Quality Control
QMS	Quality Management System
RMP	Records Management Program
RS	Reference Standard
SP	Sulfadoxine and Pyrimethamine
SOP	Standard Operating Procedure
USAID	United States Agency for International Development
USP DQI	United States Pharmacopeia Drug Quality and Information
USP-NF	United States Pharmacopeia-National Formulary
WG	Working Group
WHO	World Health Organization

## **Background**

USP DQI has been selected by the USAID Ethiopia Mission to provide technical, strategic, and operational support to strengthen the quality control of antimalarial medicines in Oromia. The USAID/Ethiopia Office of Health, AIDS, Population and Nutrition believes that postmarketing surveillance will contribute to the Mission's efforts in malaria diagnosis, treatment, prevention, and control under the President's Malaria Initiative (PMI).

USP DQI conducted a two-day Micro-Planning Workshop in July 2008 on establishing a postmarketing surveillance (PMS) program to monitor the quality of antimalarial medicines in Oromia Region. In August 2008, USP DQI organized a training of DACA Drug Quality Control and Toxicology Laboratory (DQCTL) staff as well as representatives from regional health bureaus. The PMS program was established in five sentinel sites, and the first round of collecting antimalarial drugs has already been completed at the sentinel sites level. DACA DQCTL is conducting the confirmatory testing following USP DQI protocol.

To build capacity of DACA DQCTL, USP DQI received funds from the President's Emergency Plan for AIDS Relief (PEPFAR) project under a sub-contract between USP DQI and Management Sciences for Health, Strengthening Pharmaceutical Systems (MSH-SPS) program. Under this sub-contract, it was agreed that USP DQI will train DACA DQCTL on analytical methods and good laboratory practices. USP DQI will also assist DACA DQCTL management establish an advanced quality management system and accompany the lab through a program until it becomes pre-qualified by the World Health Organization (WHO).

The objectives of this mission are to train DACA DQCTL on good laboratory practices, HPLC, and Dissolution. During the week-long training, the USP DQI team will also assess the working practices of DACA DQCTL staff, the working conditions of the lab equipment, and the needed technical assistance to complete an implementation plan including the timeline needed to bring the lab to international working standards.

## **Purpose of Trip**

USP DQI staff traveled to Addis Ababa, Ethiopia to:

1. Perform Good Laboratory Practices training – focusing on compliance with compendial requirements and improving documentation practices using HPLC and Dissolution techniques at DACA DQCTL;
2. Review DACA DQCTL working conditions and provide recommendations to improve Quality Control (QC) practices, specifically, documentary and revision procedures;
3. Organize a round table discussion with USAID, DACA, MSH-SPS, and USP DQI to discuss USP DQI approaches and the human and financial resources needed to bring the lab to international standards.
4. Meet with local stakeholders and brief them about USP DQI approaches and planned activities to strengthen the capacities of DACA DQCTL.

## Source of Funding

Funding was provided by PEPFAR-Ethiopia, under a sub-contract between USP DQI and MSH-SPS.

## Overview of Activities

### January 12-16, 2009 – GLP, HPLC and Dissolution Training

Item	Description
<b>Training Objectives</b>	<ul style="list-style-type: none"> <li>✓ Proper use of USP-NF; focusing on HPLC, Dissolution, and the General Notices</li> <li>✓ Proper use of USP RS</li> <li>✓ Proper use of USP PF</li> <li>✓ Train DACA DQCTL staff on GLP, strongly emphasizing traceability, recordkeeping, safety, reproducibility of data, organization of laboratory work, and proper use of laboratory equipment</li> <li>✓ Train DACA DQCTL staff on HPLC, UV, and Dissolution techniques according to USP-NF specifications</li> <li>✓ Review DACA DQCTL working conditions and provide recommendations to improve QC practices, specifically documentary and revision procedures</li> </ul>
<b>Venue</b>	DACA DQCTL, Addis Ababa, Ethiopia
<b>Local Organizers</b>	DACA DQCTL and USAID-Ethiopia
<b>Opening Ceremony</b>	Mr. Dawit Dikasso, DACA Deputy Director General; Mr. Wondie Woldemedhin, DACA DQCTL Director; Mr. A. Barojas & Dr. A. Smine, USP DQI; and trainees.
<b>Course Proceedings</b>	The proceedings followed the Trip Agenda. (See <a href="#">Annex 1.</a> )
<b>Participants</b>	Total of eight DACA DQCTL staff were trained. (See <a href="#">Annex 2.</a> )
<b>Equipment Provided</b>	All materials provided by USP DQI are indicated in the List of Supplies sent to DACA DQCTL (See <a href="#">Annex 3.</a> )
<b>Closing Ceremony</b>	<p>Mr. Dawit Dikasso, DACA Deputy Director General; Mr. Wondie Woldemedhin, DACA DQCTL Director; Dr. James Browder, USAID-Ethiopia HIV/AIDS Officer; Dr. Richard Reithinger, USAID-Ethiopia PMI Team Leader; Dr. Negusu, Head of MSH-SPS Ethiopia, Mr. A. Barojas &amp; Dr. A. Smine, USP DQI; and trainees</p> <p>Following the closing remarks, certificates were awarded to all participants who successfully completed the course.</p>
<b>Course Outcomes</b>	<p>At the end of the course, participants were able to:</p> <ul style="list-style-type: none"> <li>✓ Effectively perform HPLC and Dissolution analysis according to USP-NF specifications</li> <li>✓ Better understand HPLC and Dissolution troubleshooting procedures</li> <li>✓ Improve the laboratory's GLP working conditions</li> <li>✓ Utilize the USP-NF and USP PF more effectively</li> <li>✓ Identify deficiencies in lab working conditions, specifically related to key SOPs</li> </ul>
<b>Course Evaluation</b>	<p>Participants were asked to evaluate each of the course modules and sessions by filling out the Course Evaluation Form. (See <a href="#">Annex 4</a> and <a href="#">Annex 5</a>)</p> <p>The most common comment was a request to extend the time of the training and to extend these types of trainings to other lab techniques (UV, KF, GC, GC-MS, LC-MS).</p>

## Conclusions

USP DQI was extremely pleased with the dedication of the DACA DQCTL staff. All of the trainees were interested in the materials and dedicated to improving their skills and practices. DACA DQCTL staff demonstrated adequate ability to perform HPLC and Dissolution analysis and to interpret the results of testing. However, USP DQI identified various oversights by DACA DQCTL staff which result in non-compliance with USP specifications.

The following are the main deficiencies with regards to USP-NF compliance:

- Staff were not familiar with the dates of implementation of the USP-NF
- Staff were not familiar with the various mechanisms USP uses to update and make changes to official text in the USP-NF
- Staff were not familiar with the specifications of USP General Notices, General Chapter (GC) <621> Chromatography & <711> Dissolution, and USP monographs
  - For example:
    - Staff routinely fail to comply with all monograph system suitability parameters for HPLC Assay tests before analyzing their samples. Failure to meet system suitability parameters is a deviation from USP monograph requirements and invalidates the results obtained.
    - Staff did not abide by the sample withdrawal time requirements of GC <711> Dissolution

Regarding equipment and infrastructure, DACA DQCTL is very well equipped and possesses most of the necessary instrumentation and equipment to comply with internationally recognized compendial and GLP standards. However, the current lab working conditions are not adequate to ensure compliance with those standards. Of primary concern is the lack of a Quality Management System (QMS) and absence of an independent Quality Assurance (QA) unit. These system-wide shortcomings could possibly compromise the trustworthiness and validity of data produced by the lab.

USP DQI feels confident that if DACA DQCTL staff implements the lessons learned during the workshop, the QC data produced will be compliant with compendial requirements. However, the culture of the lab needs to improve, and it is imperative that management place as its top priority the improvement of the lab's working conditions to create a culture of quality.

Improving the lab's working conditions and creating a culture of quality are processes that take time, and DACA DQCTL management will have to drive the processes by ensuring they provide the appropriate amount of human and financial resources to implement a stringent QMS. Additionally, it is imperative that DQCTL staff continue to demonstrate the willingness to develop their skills, as implementing substantial changes can not occur without continual improvements from the lab staff.

As a first step, DACA DQCTL management should create an independent QA unit with staff solely dedicated to implementing a stringent QMS. However, the creation and staffing of a new department may take some time, and DACA DQCTL should not postpone the implementation of many other USP DQI recommendations. As a start, DACA DQCTL should designate one staff to

begin carrying out QA functions until a full team is established. USP DQI has prepared an implementation plan ([Annex 6](#)) that establishes recommendations and a clear path for gradual improvement toward compliance with WHO's Good Practices for National Pharmaceutical Control Laboratories (also known as GLP) and ISO/IEC 17025:2005 standards, and to enhance the capability of staff to conduct adequate QC testing.

The ultimate goal is for the DACA QC lab to submit an Expression of Interest for prequalification in the WHO Prequalification Program and then subsequently apply for ISO/IEC 17025:2005 accreditation. Obtaining WHO prequalification and/or ISO/IEC 17025:2005 accreditation will provide the Ministry of Health with a QC lab capable of producing trustworthy and valid results, and at the same time, assure that DACA DQCTL's QMS, administrative, and technical operations are functioning at the highest internationally recognized standard.

## **ADDITIONAL MEETINGS**

### **January 14, 2009 – Meeting at USAID-Ethiopia Mission**

Participants: Dr. James Browder, USAID-Ethiopia HIV/AIDS Officer; Dr. Richard Reithinger, USAID-Ethiopia PMI Team Leader; Mr. A. Barojas, USP DQI Program Manager; Dr. A. Smine, USP Consultant

This meeting was called to debrief USAID-Ethiopia staff on USP DQI activities in the country, specifically as related to the HPLC and Dissolution training.

USP DQI staff gave an overview about the training workshop and the major finding about the working conditions in DACA DQCTL. USP DQI shared the main recommendations and the priority steps in the implementation plan for DACA DQCTL. With the support of USAID, USP DQI plans to assist the lab until it qualifies for WHO GLP and/or ISO:IEC 17025:2005 accreditation.

USAID-Ethiopia expressed their desire to ensure USP DQI's objectives are realistic and recommended that the primary objective be to obtain WHO prequalification and then subsequently aim for ISO/IEC 17025:2005 accreditation. USAID-Ethiopia suggested that the implementation plan should establish a clear path for DACA DQCTL's gradual improvement toward compliance with WHO's GLP and ISO/IEC 17025:2005 standards. This plan should help DACA identify and utilize other sources of donor funding and not be solely reliant upon USAID funding. For example, it was discussed that the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM) has recently financed a new building for DACA, and it would be prudent to include in future proposals to GFATM a request to fund part of the USP DQI/DACA DQCTL implementation plan as part of the systems strengthening aid given to Ethiopia's MoH.

USAID-Ethiopia suggested that USP DQI should take in consideration DACA's recent Business Re-engineering Process (BPR) changes and see how that may affect USP DQI's plans for the lab. The USP DQI team informed USAID staff that the Director of DACA DQCTL will be changed as part of DACA BPR. USP DQI invited the new DQCTL Director to join the round table discussion that will take place at the end of the training.

## **January 17, 2009 – Meeting at DACA**

Participants: Mr. Dawit Dikasso, DACA Deputy Director General; Mr. Wondie Woldemedhin, DACA DQCTL Current Director; Mr. Bikila Bayissa; DACA DQCTL Incoming Director; Mr. A. Barojas, USP DQI Program Manager

This meeting was called to review and discuss USP DQI's trip findings and recommendations regarding DACA DQCTL's working conditions, discuss how the BPR changes will impact DACA, and visit the DACA building financed by GFATM.

USP DQI expressed gratitude to DACA management for their support in helping deliver the GLP, HPLC, and Dissolution training and congratulated DACA for the dedication the DQCTL staff exhibited throughout the entire week.

USP DQI discussed some of the key deficiencies identified during the training and stressed that the current lab working conditions are not adequate to ensure compliance with compendial and GLP standards. USP DQI reiterated that implementing a culture of quality and a stringent QMS have to be placed as top priorities of DACA management.

DACA management promises to put qualifying the lab as one of its first priority and will make sure that USP DQI's recommendations be implemented according to the implementation plan.

USP DQI and DACA discussed how the BPR will affect DACA. Currently, the BPR will not drastically change the mandate of DACA; however, there have been some modifications that will impact DQCTL's operations. Of primary importance are two points:

- Current DACA DQCTL Director, Mr. Wondie Woldemedhin, will be replaced by Mr. Bikila Bayissa. USP DQI looks forward to working with Mr. Bayissa to provide the level of support that has always been provided to the DACA laboratory. USP DQI expects that Mr. Bayissa, with the support of management and his staff, will implement the recommendations. USP DQI will also work with Mr. Bayissa to create a culture of quality in the laboratory and create a quality assurance unit within the laboratory.
- DACA's mandate will expand to include the control of foods produced in and imported into Ethiopia. DACA management indicated that, initially, the main role for DACA will be to perform documentary registration – not laboratory analysis – of foods. Nonetheless, USP DQI stressed the importance of creating a separate department to perform QC analysis of foods and to not mix QC analysis of foods and medicines.

DACA's new building, financed by GFATM, is estimated to be finished by June 2009. Once the building is completed, DQCTL will move their operations to this site. USP DQI visited the new facility and made several recommendations about the layout of the DQCTL and emphasized the importance of clearly separating the food and medicines testing. USP DQI stressed the importance of obtaining professional advice regarding the interior design, fitting, and furnishing of the new DQCTL location. USP DQI will work with DACA to ensure the final installations provide an appropriate environment for performing QC analysis. A comprehensive discussion of issues related to the future DQCTL location is contained in the implementation plan ([Annex 6](#)).

## **Next Steps**

- USP DQI will discuss and finalize the implementation plan with DACA upper management.
- USP DQI will assist DACA DQCTL in performing the first proficiency project to evaluate the effectiveness of the HPLC and Dissolution training and DQCTL compliance with compendial and GLP standards.
- USP DQI will continue to monitor the progress of DQCTL, and when the recommendations of the first stage are met, USP DQI will deliver training as part of the second stage of the implementation plan.
- USP DQI staff will continue to coordinate the drug quality monitoring program in Oromia region, compile the results of round one, and share them with country stakeholders.

## **USP DQI TRIP AGENDA**

Addis Ababa, Ethiopia ♦ January 12-17, 2009

### **Monday, January 12**

- Opening ceremony
- Introduction of participants and instructors
- Review of course objectives
- Discuss trainees course expectations
- Presentation: Introduction to Good Laboratory Practices
- Presentation: Introduction to USP-NF and General Notices
- Presentation: Introduction to Dissolution, USP-NF General Chapter <711> Dissolution & PVT

### **Tuesday, January 13**

- Prepare Dissolution Apparatus for PVT: Prednisone Tablets - Apparatus 2
- Perform PVT: Prednisone Tablets - Apparatus 2
- Review PVT Results: Prednisone Tablet Apparatus 2
- Presentation: Introduction to HPLC and USP-NF General Chapter <621> Chromatography
- Presentation: How to Interpret and Utilize USP PF
- Review USP-NF and USP PF Sulfadoxine & Pyrimethamine FDC Tablets monographs
- Prepare USP RS for HPLC Assay Analysis of Sulfadoxine & Pyrimethamine FDC Tablets
- Begin system suitability for HPLC Assay Analysis of Sulfadoxine & Pyrimethamine FDC Tablets for both USP-NF and USP PF monographs

### **Wednesday, January 14**

- Meeting at USAID-Ethiopia Mission
- Presentation: Introduction to HPLC and USP-NF General Chapter <621> Chromatography
- Review USP-NF and USP PF Sulfadoxine & Pyrimethamine FDC Tablets monographs
- Install and condition column overnight for HPLC Assay Analysis of Sulfadoxine & Pyrimethamine FDC Tablets
- Prepare USP RS for HPLC Assay Analysis of Sulfadoxine & Pyrimethamine FDC Tablets

**Thursday, January 15**

- Lab demonstration: Good weighing practices & how to properly prepare solutions
- Begin system suitability for HPLC Assay Analysis of Sulfadoxine & Pyrimethamine FDC Tablets
- Troubleshoot HPLC parameters to meet system suitability requirements for HPLC Assay Analysis of Sulfadoxine & Pyrimethamine FDC Tablets
- Review system suitability results for HPLC Assay Analysis of Sulfadoxine & Pyrimethamine FDC Tablets for both USP-NF and USP PF monographs
- Prepare Sulfadoxine & Pyrimethamine FDC Tablets Assay solutions
- Perform Dissolution Analysis of Sulfadoxine & Pyrimethamine FDC Tablets
- Inject Sulfadoxine & Pyrimethamine FDC Tablets Assay & Dissolution solutions

**Friday, January 16**

- Review Sulfadoxine & Pyrimethamine FDC Assay and Dissolution results
- Presentation: Components of an SOP
- USP DQI and lab staff to identify the needed SOPs to properly carry HPLC and Dissolution testing.
- Presentation: Review of USP Non-US Standard: SALMOUS Monograph - Artemether & Lumefantrine Tablets
- Install and condition column for HPLC Assay Analysis of Artemether & Lumefantrine FDC Tablets
- Prepare USP RS for HPLC Assay Analysis of Artemether & Lumefantrine FDC Tablets
- Begin system suitability for HPLC Assay Analysis of Artemether & Lumefantrine FDC Tablets (Note: due to time constraints this analysis was not performed)
- Q&A session and general discussion of the training
- Distribute Supplemental Training Materials
- Complete HPLC and Dissolution module evaluation forms
- Closing ceremony

**Saturday, January 17**

- Meeting at DACA

**List of Participants**

Addis Ababa, Ethiopia ♦ January 12-16, 2009

<b>Participant</b>	<b>Role in DACA DQCTL</b>
Shewatatek Hailemariam	Sen. Expert Pesticide Lab
Tamrat Tesfaye	Lab Assistant
Awot Gebre-Egziabher	Analyst
Tekalign Hailemariam	Analyst
Bekele Tefera	Analyst
Kemal Hussien	Analyst
Bonsamo Gobena	Analyst
Lantider Kassaye	Analyst

## Annex 3

**List of Supplies Sent to DACA DQCTL**

UNITS	COUNTRY OF MFG	DESCRIPTION OF GOODS	UNIT VALUE	SUB TOTAL
3	USA	PHENOMENEX: HPLC COLUMN	550.00	1650.00
1	USA	WATERS: HPLC COLUMN	550.00	550.00
1	USA	KONTES: FILTRATION SYSTEM	1482.14	1482.14
2	USA	VWR: GLASS LEUR-LOCK SYRINGE, PACK 6	136.62	273.24
3	USA	EMD: PH BUFFER	25.32	75.96
2	USA	VWR: STOPWATCH	20.49	40.98
1	USA	FISHER: STEEL CANNULAS PACK 12	133.48	133.48
1	USA	MILLEX: MILLIPORE SYRINGE FILTERS, PACK 250	521.73	521.73
2	USA	MILLEX: HVLP FILTERS, PACK 100	111.86	223.72
1	USA	KIMBERLY CLARK: DISPOSABLE LAB COATS PACK 25	154.22	154.22
3	USA	FISCHER: LAB GLOVES (S,M,L)	12.16	63.48
1	USA	FISCHER: TACHOMETER	343.15	343.15
1	USA	FISCHER: CORK RING, 1-3 L	14.28	14.28
1	USA	FISCHER: PARAFILM	10.00	10.00
5	USA	FISHER: KIMWIPES	6.17	30.85
1	USA	FISHER: LABEL TAPE – RED – PACK 3	27.84	27.84
1	USA	FISHER SCI: PASTEUR PIPETS, PACK 250	11.38	11.38
1	USA	FISHER SCI: QUARTZ UV CELLS	391.98	391.98
2	USA	VWR: DIGITAL HAND-HELD THERMOMETER	281.84	563.68
1	USA	FISHER: LAB SPECTACLES, PACK 12	36.43	36.43
2	USA	UPCHURCH: FRIT STAINLESS STEEL FILTERS	34.19	68.38
2	USA	UPCHURCH: FRIT STAINLESS STEEL HOLDERS	56.49	112.98
1	USA	VARIAN: DISSOLUTION CENTERING GAUGE	31.90	31.90
1	USA	VARIAN: DISSOLUTION DEPTH GAUGE	77.90	77.90
2	USA	FISCHER SCI: TLC PLATES – ALUMINUM BACK, PACK 50	130.73	265.46
2	USA	FISCHER SCI: TLC PLATES – GLASS 10*20 CM, PACK 50	369.13	738.26
4	USA	USP RS: PREDNISON	185.00	740.00
2	USA	USP RS: PREDNISON TABLETS	213.00	426.00
3	USA	USP RS: AMODIAQUINE HYDROCHLORIDE	185.00	555.00
3	USA	USP RS: CHLOROQUINE PHOSPHATE	185.00	555.00
5	USA	USP RS: ARTEMETHER	185.00	925.00
5	USA	USP RS: LUMEFANTRINE	185.00	925.00
3	USA	USP RS: QUININE SULFATE	185.00	555.00
3	USA	USP RS: QUININONE	576.00	1728.00
3	USA	USP RS: PRIMAQUINE PHOSPHATE	185.00	555.00
5	USA	USP RS: SULFADOXINE	185.00	925.00
5	USA	USP RS: PYRIMETHAMINE	185.00	925.00
1	USA	USP 32/NF 27	800.00	800.00
5	USA	USP PF	580.00	2900.00
4	USA	USP 31/NF 26 SUPPLEMENT	410.00	1640.00
30	USA	USP DQI MANUALS	NO CHARGE	NO CHARGE
4	USA	USP CATALOGS	NO CHARGE	NO CHARGE
25	USA	USP DQI OPERATIONAL GUIDES	NO CHARGE	NO CHARGE
30	USA	USP DQI BROCHURES	NO CHARGE	NO CHARGE
100	USA	PHOTOCOPIES	NO CHARGE	NO CHARGE

### Evaluation of Dissolution Workshop by Participants

In order for USP DQI to evaluate the efficacy of each training module and improve the level of the courses, we ask all participants to kindly provide their feedback by filling out this evaluation sheet.

#### **A- Evaluation of Specific Aspects of the Training Workshop**

DISSOLUTION TRAINING	EXTENT TO WHICH THE TRAINING MET YOUR OVERALL EXPECTATIONS			
	Very helpful	Average	Not too much	Wasted my time
Introduction to dissolution	7			
Installation of equipment	4	2		
Proper use of dissolution tester	7			
Calibration of dissolution tester	7			
Troubleshooting	6		1	
Familiarity with different sections of USP NF	7			
Monitoring of dissolution test	6	1		
Data collection and interpretation	5	2		
Data management	5	2		
Equipment proper maintenance	3	3		

#### **B- Overall Evaluation of the Training Workshop**

	Strongly agree	Agree	Somewhat disagree
Course objectives were relevant to my needs	7		
The training material helped me understand and better organize my data	6	1	
I was able to understand the content of the materials presented	6	1	
Overall, the course was useful and will help me do my job better	7		
There were enough practical exercises to facilitate understanding of the course	4	3	
The pacing of the various sessions was appropriate for my understanding of course materials	6	1	
The sequence in which the sessions were presented was appropriate for my understanding	6		1
The instructors were knowledgeable on the subject	7		
The instructors allowed an appropriate level of participation	7		

### Evaluation of HPLC Workshop by Participants

In order for USPDQI to evaluate the efficacy of each training module and improve the level of the courses, we ask all participants to kindly provide their feedback by filling out this evaluation sheet.

#### A. Evaluation of specific aspects of the training workshop

HPLC TRAINING	EXTENT TO WHICH THE TRAINING MET YOUR EXPECTATIONS OVERALL			
	Very helpful	Average	Not too much	Wasted my time
Introduction to HPLC	6	1		
Safety Issues	6		1	
Proper use of HPLC system	6	1		
Proper use of HPLC columns	7			
Troubleshooting	6		1	
Familiarity with different sections related to HPLC test in USP-NF	5	1	1	
Familiarity with monograph limits	6	1		
Data collection and interpretation	6	1		
Data management	6	1		
HPLC waste handling	4	1	2	

#### B. Overall Evaluation of the Training Workshop

	Strongly agree	Agree	Somewhat disagree
Course objectives were relevant to my needs	7		
The training material helped me understand and better organize my data	7		
I was able to understand the content of the materials presented	7		
Overall, the course was useful and will help me do my job better	7		
There were enough practical exercises to facilitate understanding of the course materials	2	4	1
The pacing of the various sessions was appropriate for my understanding of course materials	5	2	
The sequence in which the sessions were presented was appropriate for my understanding	5	2	
The instructors were knowledgeable on the subject	7		
The instructors allowed an appropriate level of participation in the class	7		

# **Implementation Plan for Enhanced Capacity of DACA Drug Quality Control and Toxicology Laboratory DRAFT**

## **1- Background**

The quality of medicines affects their efficacy and safety and, hence, their usefulness in effecting positive health outcomes for patients. Poor quality medicines have been shown to have a serious detrimental effect on public health by increasing morbidity and mortality, causing a loss of confidence in the drugs and in the health system, increasing the likelihood of drug resistance, and wasting scarce resources. Without adequate quality control, other pharmaceutical management systems put in place to manage priority diseases including malaria, HIV/AIDS, and tuberculosis will be negated. Thus, it is crucially important that investments in pharmaceutical systems, including access and availability, be accompanied by proper measures to ensure the quality of the pharmaceutical commodities. In most countries, it is the professional responsibility of the national drug regulatory authority, through the national quality control laboratory, to ensure that pharmaceutical products being used in-country meet all requirements of safety, efficacy, and quality. The drug regulatory authority relies on the quality control laboratory to test and verify that all quality attributes of a given pharmaceutical product are in compliance with pharmacopeial specifications and, thus, approved for use.

The United States Pharmacopeia Drug Quality and Information (USP DQI) Program, through a cooperative agreement with the United States Agency for International Development (USAID), provides technical leadership in the areas of drug quality and drug information to developing countries with the view of building local capacity for quality control and quality assurance of medicines. This involves training laboratory staff in pertinent analytical techniques and working with drug manufacturers to improve their compliance with Good Manufacturing Practices (GMP) guidelines and stipulations. USP DQI's GMP specialists perform assessments, address weaknesses that may be identified, and provide the tools and training needed to achieve prequalification status under World Health Organization (WHO) guidelines. Drawing upon the expertise of its staff and scientific volunteers, USP DQI develops targeted drug and therapeutic information materials for health care providers based on specific needs. In addition, USP DQI assists in establishing and equipping local drug information centers that, in turn, provide educational opportunities for health care providers in remote areas.

Following earlier assessments of the capacity of DACA's quality assurance systems – conducted by USP DQI staff in July 2005 and November 2007 – several major findings were observed that affect the ability of DACA's Drug Quality Control and Toxicology Laboratory (DQCTL) to conduct adequate QC analysis. The objective of this document is to establish a clear implementation plan for DACA DQCTL for gradual improvement toward compliance with WHO's Good Practices for National Pharmaceutical Control Laboratories (also known as Good Laboratory Practices or GLP) and to enhance the capability of staff to conduct adequate QC testing thus ensuring DQCTL will provide the Ethiopian Ministry of Health with trustworthy and valid results. The ultimate goal is for the DACA QC lab to submit an Expression of Interest for

prequalification in the WHO Prequalification Program. Later, the DACA lab could also seek an ISO/IEC 17025:2005 accreditation.

Following the round table discussion between USP DQI, USAID, MSH, and DACA that took place at the end of USP DQI training in January 2009, it was agreed that USP DQI will establish a plan of action to be implemented by DACA DQCTL in order to qualify as a WHO collaborative center in two years and obtain ISO/IEC 17025:2005 accreditation within three years. The implementation plan will begin in February 2009.

USP DQI will assist the DACA laboratory throughout this program, which will be implemented in stages, starting with the priority actions. USP DQI will monitor and evaluate the progress made, ensuring that each step of the plan and all recommendations have been implemented before the next stage takes place.

## **2- Overview of the Implementation Plan**

The following table summarizes the USP DQI proposed implementation plan for DACA DQCTL

<b>STAGES</b>	<b>PRIORITY RECOMMENDATIONS TO BE IMPLEMENTED</b>	<b>TIMELINE</b>
<b>1</b>	Train in HPLC and Dissolution; start creating an independent QA Unit; hire/appoint a QA officer; clean and organize the lab; implement the basics of GLP as directed by USP DQI; draft 10 SOPs identified by USP DQI and DACA DQCTL; inventory current equipment and glassware and prioritize needs; carry out proficiency project as agreed by USP DQI and DACA DQCTL Director	Jan 1-Jul 31, 2009
<b>2</b>	Execute all recommendations in Stage 1; USP DQI to train on GC, UV, KF or IR and GLP; draft 15 new SOPs; begin writing quality manual and continue to implement key parameters of stringent QMS; carry out a proficiency project to continue monitoring DQCTL competency	Aug 1-Dec 31, 2009
<b>3</b>	Execute all recommendations in Stage 2; USP DQI to provide two trainings (QC analytical methods and implementing stringent QMS); draft 15 new SOPs; finalize quality manual; begin establishing internal audit program; continue implementation of key parameters of stringent QMS; participate in inter-laboratory testing	Jan 1-Jun 30, 2010
<b>4</b>	Execute all recommendations in Stage 3; USP DQI will support the lab on calibration and qualification of all lab equipment; stringent QMS is established with all key parameters operational; QMS internship for one key staff member at USP headquarters; staff are well trained; all equipment is functional; continue to participate in inter-laboratory testing; lab to move to the new facility	Jul 1-Dec 31, 2010
<b>5</b>	Execute all recommendations in Stage 4; qualify the equipment after the move to the new facility; review and update SOPs to fit the new facility and adjust work flow to new facility; USP DQI to conduct QMS mock audit; submit Expression of Interest for WHO prequalification – lab is pre-qualified by end of this stage	Jan 1-Dec. 31, 2011
<b>6</b>	Execute all recommendations in Stage 5. After WHO prequalification, USP DQI assists DACA DQCTL prepare for an international ISO/IEC 17025:2005 accreditation. Develop uncertainty budget and conduct QMS audit. ISO/IEC 17025:2005 accreditation can be achieved by end of 2012	Jan 1-Dec 31, 2012

### **3- Stage Details**

The following section provides an outline representation of the USP DQI proposed implementation plan for DACA DQCTL. For the technical details of each stage please refer to Annex 1 – Implementation Plan for Strengthening DACA DQCTL – Technical Details

#### I. Stage 1

##### A. Quality Management System (QMS)

###### 1. Creating a Quality Assurance (QA) Unit

a. Assign staff member as QA officer, whose sole responsibility is implementing a QMS

###### b. Documentation

i. Write and finalize 10 identified SOPs

##### B. Cleaning and basic organization of DQCTL

1. Management commitment to maintaining a clean and well organized lab

2. Weekly lab clean-up

3. Organize lab appropriately

4. Train support staff adequately

5. Prevent environmental contamination/impact

##### C. Compliance with Good Laboratory Practices (GLP) and Compendial Standards

###### 1. GLP Standards

a. Safety

b. Documentation and Traceability

c. Equipment use (i.e. daily calibrations and proper use)

d. Handling Reference Standards, lab reagents, and solutions

###### 2. Compendial Standards

a. When using USP-NF, must comply with General Notices, General Chapters, Monographs, and Reference Standards

b. When using other compendia (EP, BP, IP, etc.) lab staff must comply with all the necessary requirements

##### D. Equipment and Lab Supplies:

1. Proper equipment handling and use

2. Inventory current equipment and glassware and prioritize needs

3. Calibrate and qualify essential equipment (Dissolution and HPLC)

##### E. Training and Proficiency Testing

###### 1. Increase DACA DQCTL Capacity

a. Effectively using USP-NF

b. HPLC and Dissolution Techniques

c. WHO Good Practices for Pharmaceutical Control Laboratories (also known as Good Laboratory Practices – GLP)

###### 2. Proficiency testing to obtain baseline competency

#### II. Stage 2

##### A. QMS

###### 1. Documentation

a. Write and finalize 15 new SOPs

b. Start working on Quality Manual

- c. Begin to develop equipment installation, performance, and maintenance program
    - d. Begin to develop records management and document control management programs
  - 2. Clearly define lab's mission and visions
  - 3. Establish Internal Data Review Process
- B. Cleaning and Organization of DQCTL
  - 1. Maintain commitment to clean and well organized lab
- C. GLP Standards
  - 1. Monitor advances from Stage 1
  - 2. Provide further GLP recommendations
- D. Training and Proficiency Testing
  - 1. Increase DACA DQCTL Capacity
    - a. Two additional analytical techniques and compliance with USP-NF requirements
    - b. Advanced GLP
  - 2. Proficiency testing to continue monitoring DQCTL's competency

### III. Stages 3 and 4

- A. Establishing stringent QMS
  - 1. Documentation
    - a. Finalize Quality Manual
    - b. Finalize all remaining SOPs
  - 2. Establish internal audit program
    - a. Establish frequency and types of internal audits
    - b. Develop Corrective and Preventive Action (CAPA) program
  - 3. Equipment installation, performance, and maintenance program is operational
  - 4. Records management and document control management programs are operational
  - 5. Quality Management System (QMS) internship for one key staff member at USP headquarters (2-3 months)
- B. Training
  - 1. Advanced lab techniques (endotoxin, LC/MS, GC/MS)
  - 2. Internal auditing techniques (process, method, and walk-through audits)
- C. Inter-laboratory testing
  - 1. USP HQ and India/China/Brazil labs, DACA DQCTL and one other ISO/IEC 17025:2005 accredited lab conduct comparative testing
    - a. Two rounds, one product per round (start with simple product and then go to more difficult product)
  - 2. Compare results

### IV. Stage 5

- A. Move to New DACA Facility
  - 1. Qualify Equipment
  - 2. Review and adjust documentation, specifically SOPs as needed

- B. Conduct QMS audit
  1. USP staff will review documentation and perform onsite audit according to ISO/IEC 17025:2005 guidelines
    - a. Develop CAPA plan according to audit results
    - b. Provide TA as needed
- C. Prepare Expression of Interest for prequalification in the WHO Prequalification Program
  1. Letter of interest
  2. Laboratory Information File
  3. Evidence of participation in proficiency testing scheme
- D. Submit EOI for prequalification in the WHO Prequalification Program
  1. Provide TA as needed based on WHO inspection

#### V. Stage 6

- A. Prepare DACA lab for ISO/IEC 17025:2005 accreditation audit
  1. Define accreditation scope
  2. Conduct a second QMS audit according to ISO/IEC 17025:2005 guidelines
    - a. Develop CAPA plan according to audit results
    - b. Provide TA as needed
  3. Develop Uncertainty Budget
  4. Identify and contract accrediting body
  5. Provide TA in preparation of audit
  6. Provide TA as needed based on audit results

### **4- General Recommendations to DACA Upper Management**

USP DQI believes that it is in the best interests of Ethiopia that DACA DQCTL should improve their working conditions to internationally recognized standards. It is well-positioned to be the regional center of excellence in East Africa. The DACA Deputy Director has assured USP DQI and USAID that qualifying DQCTL is one of the highest priorities of the DACA Director General. To achieve this goal, USP DQI makes the following recommendations:

- Strong commitment from DACA upper management is needed to implement USP DQI recommendations and implementation plan
- Allow DQCTL staff to execute the implementation plan as part of their daily duties
- Motivate and retain the staff that USP DQI trains, because they are the real value of the laboratory
- Hire additional staff as recommended during the implementation of this plan
- Provide the full moral and financial support to DACA DQCTL Director and his staff to execute this implementation plan
- Ensure that other types of training or technical assistance are consistent with the USP DQI model and implementation plan. Accepting recommendations from different institutions can be counterproductive and may lead to inefficiency. USP DQI suggests that all technical assistance given to DQCTL be coordinated with USP DQI.
- Any financial support from other donors should be welcomed and coordinated accordingly to increase efficiency and reduce duplicative efforts.

- Be open and ask USP DQI for advice on major changes and equipment purchases
- Monitor and encourage the DACA lab to meet the targets from stage to stage throughout the implementation of this plan.

## **5- Outcomes and Conclusions**

Based on the USP DQI assessment of drug quality assurance capabilities of Ethiopia, it was apparent that DACA DQCTL is not playing fully the role it should play to protect public health in the country. With the new Business Process Re-engineering of DACA and building a new laboratory facility, it is now the perfect time that the DACA DQCTL should be strengthened to operate in compliance with international standards.

When DACA DQCTL gains WHO prequalification and ISO/IEC 17025:2005 accreditation, it will not only play the major role of protecting Ethiopia's public health, but could also play major roles in quality control at the international level. The lab could engage in activities such as:

- Participating in collaborative studies with international pharmacopeias and other drug regulatory authorities
- Testing medicines for international organizations, generating additional revenues
- Collaborating closely with and participating in studies with WHO and UN agencies
- Acting as a center of excellence in East Africa to support and set standards for quality control for all regional offices in Ethiopia

The laboratory could easily generate enough revenues to be self-funded if it is ISO/IEC 17025:2005 accredited. With DACA commitment, the support of the laboratory, and with USP DQI technical support, the set target could easily be achieved within the timelines set forth in this implementation plan.

## IMPLEMENTATION PLAN FOR STRENGTHENING DACA DQCTL – TECHNICAL DETAILS (DRAFT)

### Stage 1

At this stage, USP DQI recommends that the lab immediately implement a series of urgent measures listed below. Most of these measures do not require substantial funding. However, for any support or advice, USP DQI staff will be happy to provide the assistance needed. Stage One started with the USP DQI training in January 2009 and will end on July 31, 2009.

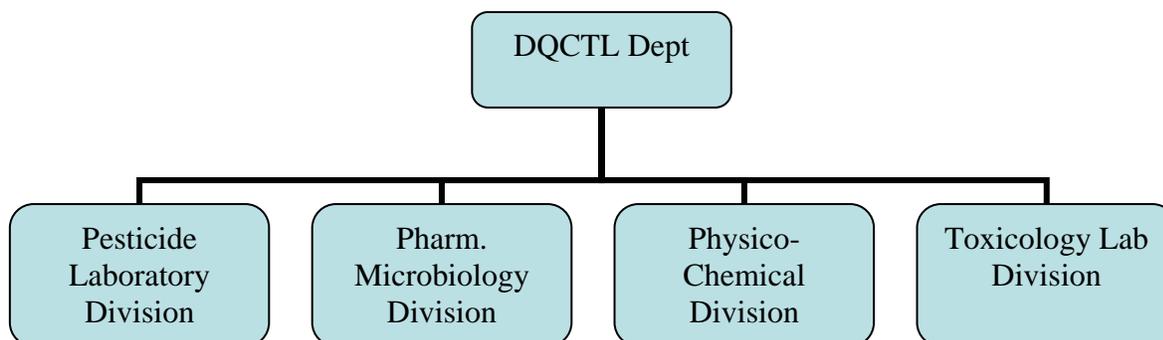
#### 1. Quality Management System (QMS)

In addition to the good laboratory practices, the Director of the lab must implement the following measures immediately.

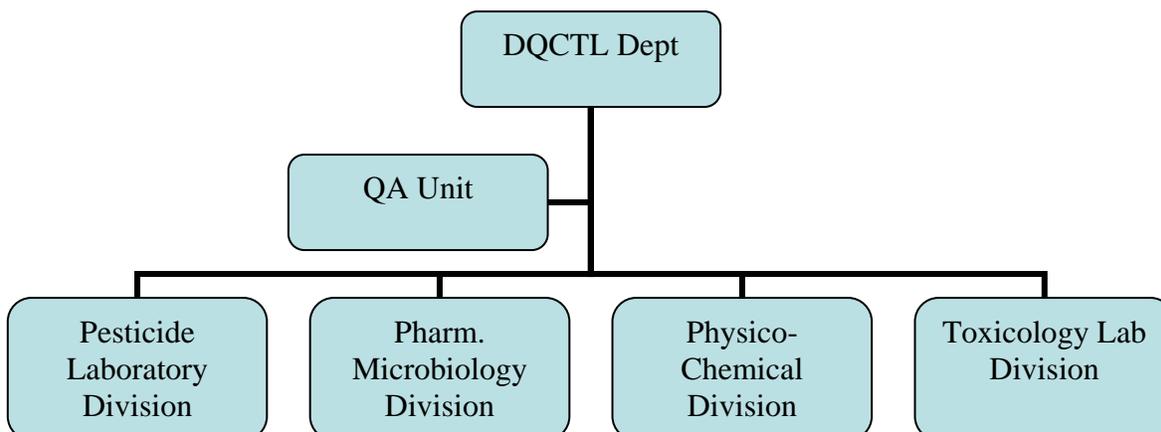
- a) Establish an independent QA Unit: the QA Unit should report directly to the DQCTL Director and have the mandate to implement the necessary changes to improve the lab working conditions.

The following organizational charts indicate the current and recommended DQCTL structures.

#### Current DQCTL Structure



#### Recommended DQCTL Structure



- b) Nominate or hire at least one person as quality assurance officer.
- c) Following the last USP DQI training, it was agreed that the lab must write and finalize the following SOPs
  - lab notebook
  - Dissolution
  - HPLC
  - Balances
  - pH meter
  - UV spectrophotometer
  - Preparation of solution
  - Thermometers
  - Stop watches
  - Documentation standards

The QA officer should write the first drafts of each these SOPs with the corresponding DQCTL analysts, subsequently review them, and then send them to USP DQI for review. After USP DQI review, the DQCTL Director should organize a training session on each of these SOPs, document the training, and issue a date by which the SOPs become official. These SOPs must be in place before end of July 2009.

- d) DACA DQCTL Director should give the lab staff the time and resources to accomplish this important task as part of their duties.

## **2. Cleaning and basic organization of DACA DQCTL**

The Director of DACA laboratory has to implement a series of measures to clean and better organize the laboratory. Management must commit to maintaining a clean and well organized lab. For example, glassware is dirty and staff waste considerable time making simple solutions or weighting a chemical products.

- a) Once a week, the whole laboratory must be cleaned and organized, and all staff must participate. The director must supervise and check if the cleaning has been done properly.
- b) Equipment and consumables should be stored in a logical manner, near where they are often used (for example, all dissolution tools, filtrations apparatus, syringes, etc. must be kept near the dissolution tester in labeled drawers). The same applies for other instruments.
- c) USP DQI recommends that the support staff collect, clean, dry, and store glassware adequately so that analysts do not waste their time looking for or cleaning glassware. Additionally, proper washing techniques ensure glassware is not damaged during the cleaning process (i.e. dissolution vessels).
- d) All windows must be closed, especially in instruments rooms. This is to prevent dust and dirt from affecting the good functioning of expensive equipment. Air conditioning units or fans could be installed in order to have a good working environment for analysts.

## **3. Good Laboratory Practices and Compendial Standards**

The DACA DQCTL must start implementing the basics of GLP, the foundation which will lead the lab to the targeted certifications. Additionally, the lab must ensure compliance with compendial requirements. During the USP DQI training in January 2009, it was apparent that the lab staff failed to comply with standards which resulted in non-compliance with USP specifications and untrustworthy drug quality data.

- a) Properly label all solutions as soon as they are made. The label must contain at least the following information: content of the solution, its concentration, the date it was made, and the analyst to whom it belongs. Containers must be kept properly closed at all time either by container closure or parafilm
- b) Start filling out equipment log books, putting in valuable information that is necessary for monitoring the performance of the equipment used.
- c) Start using laboratory notebooks instead of data sheets and use, maintain, secure, review, and sign the notebooks as per the lab SOP
- d) Comply with the basic safety rules within the lab by using the proper protections and by protecting the health of the lab personnel
- e) Calibrate the balances every day and fill our the balances log books
- f) Calibrate the pH meter everyday using proper solutions and store the pH meter in the proper solution
- g) Take care of the equipment by handling it with care and clean each instrument after use
- h) Train the lab support staff on the proper cleaning and storage of glassware
- i) Take good care of reference standards: store them in desiccators away from light and dust. Return all chemicals to the chemical storage room right after use.
- e) Store reference standards according to the storage conditions on their labels
- f) Ensure staff is using the official USP-NF text. They must stay updated with each annual volume, the semi-annual supplements, and any Interim Revision Announcements. It is very important to understand the dates of implementation of all USP-NF official texts.
- g) Staff must comply with all the requirements of USP-NF. It is imperative that staff read and comply with USP-NF General Notices, General Chapters, Monographs, and Reference Standard documents and labels.

#### **4. Equipment & Lab Supplies**

The DACA DQCTL must take better care of their equipment as properly functioning equipment is imperative to compliance with GLPs. Additionally, the lab has some minor equipment and supply deficiencies and must prioritize their needs.

- a) As mentioned above in the GLP section, proper equipment handling is essential to ensure the trustworthiness and validity of data. Each user needs to become accustomed to properly cleaning equipment after each use. This will expand the life and performance of the equipment. One of the primary objectives of weekly lab clean-ups is to ensure equipment are cleaned properly.
- b) The lab must inventory current equipment and glassware to prioritize the labs needs. The lab must purchase small lab supplies, such as spatulas, class A pipettes, pH meter solutions, calibrated weights, weighting tools, tape, markers, stickers for labeling etc. During the USP DQI training in January 2009, it was apparent that the lab is over equipped with capital equipment (GC, GC-MS, LC-MS, AA) but lacks the small lab supplies. This can lead to a considerable waste of time and often to poor lab practices.

Additionally the lab is missing some essential equipment, such as a microbalance and top loading balances.

- c) The Dissolution testers must be calibrated following the guidance provided by USP DQI staff during the training. A sticker should be placed on each dissolution tester indicating the date of the calibration. The same exercise must be repeated after six months.
- d) DACA should attempt to fix and qualify HPLC machines. USP DQI will try to help the lab troubleshoot and qualify at least the HPLCs.

## **5. Training and Proficiency Testing**

This component of the implementation plan began with the workshop on GLP, HPLC, and Dissolution delivered in January 2009.

USP DQI will organize a series of trainings following the FY08 and FY09 work plans. However, to make sure that each training has been effective and to monitor the progress made by the lab analysts, USP DQI proposes that after each training, the lab collect and test a few samples of selected medicines and share comprehensive data packages with USP DQI staff. USP DQI will provide a template of the information that will be required to submit in the data package and will then review the data package and make the necessary comments on the results.

The first proficiency sample will follow the DACA DQCTL GLP, HPLC, and Dissolution training. To monitor the effectiveness of this training, USP DQI proposes that DACA DQCTL collect three samples of three selected essential drugs (tablets and/or capsules with full monograph tests including HPLC and Dissolution).

The samples must be selected in agreement with the USP DQI Director and the Director of DQCTL from the following classes: antibiotics (cotrimoxazol); anti-TBs (fixed dose combination which has a USP monograph); ARVs (used in Ethiopia by PEPFAR – has a USP monograph); antimalarial drugs (ACT with a USP monograph). Upon completion of the testing, complete raw data packet and reports must be sent to USP DQI for review. It is important to make sure that this exercise be considered as a proficiency testing project and not drug quality control of the samples collected.

This exercise will serve as a tool to evaluate the level of proficiency and capacity of the laboratory to comply with compendial requirements throughout the varying stages of the implementation plan. At this first stage, it will serve to establish a baseline competency of DQCTL reports. Additionally, this process should enhance the performance of the lab analysts and improve communication between DACA DQCTL and USP DQI. The DACA DQCTL staff are welcome to ask questions and request technical assistance to carry out the QC tests.

### **Stage 2**

This stage will not start if all recommendations made in stage one are not fully implemented. In this stage, USP DQI will conduct another training of DACA DQCTL on two additional analytical methods and Good Laboratory Practices. USP DQI will also make a set of recommendations to continue the progress of the lab. This stage will start on August 1 and end on December 31, 2009.

## **1. Quality systems**

- a) A set of 15 new SOPs will be recommended by USP DQI based on the second DACA lab training
- b) At this stage DACA DQCTL should clearly determine the lab's mission and vision
- c) Start working on a quality manual
- d) DACA shall establish an internal review process of data generated in the lab, as well as implement the first steps of an internal audit system.
- e) Begin to develop an equipment installation, performance, and maintenance program. This program will delineate the frequency for external and internal maintenance for all equipment in the lab. The documentation related to this program should clearly define the documentary practices that need to be implemented for all equipment (including logbooks).
- f) Begin to develop records management program and document control management program.

## **2. Cleaning and Organization of DQCTL**

Always keep the laboratory as clean as possible as the lab will offer a better working environment for the analysts. USP DQI will check the changes implemented from Stage 1.

## **3. Good Laboratory Practices**

Based on the training, USP DQI will monitor the implementation of the basic good laboratory practices recommended in Stage one and will offer new good laboratory practices recommendations.

## **4. Training and evaluation**

USP DQI will train the DACA DQCTL on two additional analytical methods and advanced good laboratory practices. As in Stage 1, USP DQI will give DACA DQCTL a small project which will consist of collecting selected samples and testing them fully. USP DQI will review the results and make the necessary recommendations.

Also during the second USP DQI training, any additional training needs will be assessed and the plan for implementation will be altered as necessary as part of the work plan.

## **Stages 3 and 4**

These stages will begin after all recommendations and implementation measures from Stages 1 and 2 have been executed. These two stages will run from January 1, 2010 to December 31, 2010. USP DQI will continue to train and evaluate the progress of DACA DQCTL, with an emphasis on equipment calibration, maintenance, proper use, and qualification. Additionally, an emphasis will be made to finalize the implementation of a stringent QMS. USP DQI will train one DACA staff at USP headquarters in Rockville, Maryland.

It is expected that by the end of 2010 the lab will achieve the following:

- Adopt the culture of quality in all aspects of work
- Implement a stringent QMS, which includes:
  - Draft 15 SOPs in Stage 3 and complete the SOPs book by the end of Stage 4

- Set a clear vision and mission, ensuring management structure is adequate
- Finish the quality manual
- Have operational equipment installation, performance and maintenance, records management, and document control management programs.
- Establish an internal audit program with defined frequency and types of internal audits.
- Have a quality assurance unit of at least 3 staff
- Qualify all lab equipment and be able to provide the related documentation
- Ensure DACA DQCTL staff are well trained and carry out their daily work according to good laboratory practices and pharmacopeial standards and be able to provide the related documentation

Suggestion: for WHO prequalification, a lab needs to provide evidence of inter-laboratory testing. USP DQI will include DACA DQCTL in collaborative studies with competent laboratories to assess its competency.

It is expected that at the end of 2010, the DACA DQCTL will move to a new facility. It is imperative that the implementation plan have been executed, so that the lab is ready for a fresh start in the new facility.

## **Stage 5**

This stage will run from January 1, 2011 to December 31, 2011. This stage will last six months after moving to the new facility. The lab will participate in a new collaborative study. The target is to gain a WHO prequalification certification before the end of 2011.

USP DQI will assist DACA DQCTL with the following tasks:

- Qualify all equipment
- Review and adjust all SOPs to fit the new working environment
- Start preparing for WHO prequalification:
  - Conduct two mock audits according to ISO/IEC 17025:2005 standards, develop a corrective and preventive action plan according to audit results, and provide technical assistance as needed.
  - Prepare the necessary documentation for the Expression of Interest to the WHO Prequalification Program
    - Letter of interest
    - Laboratory Information File
    - Evidence of participation in proficiency testing scheme
- Submit Expression of Interest and provide technical assistance as needed, based on WHO inspection

## **Stage 6**

This stage will run from January 1, 2012 to December 31, 2012. Once the DACA lab has been qualified as a WHO collaborating center, efforts will continue toward gaining an international ISO/IEC 17025:2005 accreditation, which can easily be achieved within one year following a

WHO prequalification. The target is to gain ISO/IEC 17025:2005 accreditation by the end of 2012.

USP DQI will assist DACA DQCTL with the following tasks:

- Prepare DACA lab for ISO/IEC 17025:2005 accreditation audit
  - Define accreditation scope
  - Conduct a QMS audit according to ISO/IEC 17025:2005 guidelines
    - Develop CAPA plan according to audit results
    - Provide TA as needed
  - Develop Uncertainty Budget
  - Identify and contact accrediting body
  - Provide TA in preparation of audit
  - Provide TA as needed, based on audit results