

# USP DQI Training for Ethiopian Medicines Quality Control Laboratory on HPLC, Dissolution, and Laboratory Quality Systems

Addis Ababa, Ethiopia

October 19-23, 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**

The USP DQI team traveled to Ethiopia to provide the Drug Administration and Control Authority (DACA) laboratory staff with advanced training on how to conduct HPLC and dissolution analytical testing of Lumefantrine-artemether tablets for senior analysts and basic training on HPLC and dissolution for newly hired analysts. All analysts were also trained on how to establish Standard Operating Procedures (SOPs) for analytical methods. During the training, two major SOPs were finalized.

## **Recommended Citation**

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## **Key Words**

Medicines, Quality Control, Quality Assurance, Quality Systems, HPLC, Dissolution, Standard Operating Procedure

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## **ACKNOWLEDGEMENTS**

The USP DQI team would like to thank all the participants in the training; DACA CEO, Mr. Yehelu; his Deputy and the QC lab Director, Mr. Bikila; and all those who helped make the training go smoothly.

We would also like to thank the USAID/Ethiopia staff: Mr. Richard Reithinger, PMI Manager; Mr. James Browder, PEPFAR CTO; and Dr. Negussu Mekonnen, the head of the MSH/SPS program in Ethiopia for funding USP DQI activities in the country and also for their guidance and insights.

Finally, we would like Mr. Anthony Boni and Veerle Coignez at USAID Washington for their guidance throughout the preparation stages of this training.

## ACRONYMS

ACT	Artemisinin-based Combination Therapy
AIDS	Acquired Immune Deficiency Syndrome
CTO	Cognizant Technical Officer
DQ	Drug Quality
DACA	Drug Administration and Control Authority
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
GLP	Good Laboratory Practices
HIV	Human Immunodeficiency Virus
HPLC	High Performance Liquid Chromatography
MOH	Ministry of Health
MSH-SPS	Management Sciences for Health - Strengthening Pharmaceutical Systems
PEPFAR	President's Emergency Plan for AIDS Relief
PMS	Postmarketing surveillance
QA /QC	Quality Assurance / Quality Control
QMS	Quality Management System
RS	Reference Standard
SOP	Standard Operating Procedure
TLC	Thin Layer Chromatography
USAID	United States Agency for International Development
USP DQI	United States Pharmacopeia Drug Quality and Information
WHO	World Health Organization

## **Background**

The United States Pharmacopeia Drug Quality Information Program (USP DQI) received funds from the United States Agency for International Development Mission in Ethiopia (USAID/Ethiopia) to provide technical, strategic, and operational support to strengthen the quality control of antimalarial medicines in Oromia region. The USAID/Ethiopia Office of Health, AIDS, Population and Nutrition believes that postmarketing surveillance (PMS) will contribute to the Mission's efforts in malaria diagnosis, treatment, prevention, and control under the President's Malaria Initiative (PMI).

USP DQI established a postmarketing surveillance program in five sentinel sites and conducted the first round of collecting and testing antimalarial drugs using basic tests. Selected samples from each site were also subjected to confirmatory tests in the Drug Administration and Control Authority (DACA) Quality Control (QC) laboratory.

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

## **Purpose of Trip**

The USP DQI team (“the team” or “the trainers”) was made up of Dr. Daniel Bempong, Manager of Analytical Laboratory Services, and Dr. Abdelkrim Smine and Dr. Eshetu Wondemagegnehu, USP DQI consultants. The team was to:

1. Train newly hired DACA QC lab staff on the basics of HPLC and dissolution
2. Train senior DACA QC lab staff on advanced HPLC and dissolution testing of Lumefantrine-artemether tablets
3. Train all lab analysts on drafting and finalizing standard operating procedures (SOPs) for major analytical methods.
4. Review data from the first round of antimalarial PMS in five sentinel sites
5. Discuss the FY09 work plans with DACA and USAID/Ethiopia
6. Attend the PMI partners meeting in Addis Ababa

## **Source of Funding**

This trip was supported through USAID/Ethiopia with funding from PMI and PEPFAR. A sub-contract with MSH/SPS provided additional funding.

## **Overview of Activities**

### *Opening Ceremony*

A brief opening ceremony was organized by the Director of the DACA QC lab who introduced the USP DQI team to his newly hired staff. The Director and the team gave an overview about USP DQI program objectives and future plans. They decided to split the analysts into two

groups; the first group was trained on the basics of HPLC and dissolution testing according to international standards, and the second group of senior analysts was trained on advanced HPLC and dissolution testing of the Artemisinin-based Combination Therapy (ACT) medicine Lumefantrine-artemether (please see the list of participants in *Annex 1*). Advanced HPLC and dissolution are very challenging analytical methods which require advanced knowledge of compendial testing.

#### *Training Program*

Both groups were trained on HPLC and dissolution for three and a half days. All analysts were jointly trained on writing and finalizing SOPs for one and a half days.

- **Overview of the trainings**

#### *HPLC and dissolution training - Junior Group*

Dr. Smine taught the basic course. Since the laboratory uses USP as a priority reference, Dr. Smine used the USP-NF as a model pharmacopeia and started by training the group on the general notices, showing the group the proper way of using monographs. He then reviewed with the group the most important points of USP-NF general chapter <621> which covers all chromatography systems and requirements for this analytical method.

Dr. Smine covered the instrument components and its maintenance. Acetaminophen was used for the practice session in which they were able to both run the system suitability and assay.

A similar approach as described above was used for dissolution testing using the USP chapter on dissolution <711>. For the hands-on training, the group carried out the calibration of the lab dissolution tester using prednisone tablets as per USP guidelines. The system passed the calibration.

During both trainings, Dr. Smine pointed out missing SOPs related to carrying out these two analytical methods.

Based on the evaluation sheets and verbal communications, the trainees gained a lot of knowledge from these two basic trainings, and Dr. Smine urged them to apply what they learned in their daily work in the QC laboratory.

#### *HPLC and dissolution training – Senior Group*

Dr. Bempong taught the advanced course. The team had previously been trained on basic HPLC and fundamentals of dissolution. Prior to starting laboratory work, Dr. Bempong introduced the group to the USP Non-U.S. monographs and explained that the monographs can be accessed from the USP website free of charge. He then focused attention on the USP Non-US monograph for Lumefantrine and Artemether tablets and provided detailed explanations of the various sections of this monograph. He also pointed out that the “briefing” provided for each USP Non-US monographs contains useful information, including HPLC columns used to develop and validate procedures included in the monograph. In response to a question regarding the difficulty the analysts experience in finding suitable columns for HPLC work, Dr. Bempong introduced the group to the Column Equivalency Database available on the USP website and explained that it is

a useful database for finding possible alternative HPLC columns. It became apparent from discussions that the analysts routinely proceed to test samples without first meeting all system suitability requirements. Dr. Bempong explained that not meeting all such requirements invalidates the test results.

Dr. Bempong trained the group on how to perform the gradient HPLC assay provided in the lumefantrine-artemether monograph. The system suitability requirements included in the procedure were met. The group was introduced to the preparation of standard solutions in duplicate as one way of confirming the accuracy of standard sample weighing and standard solution preparation. A sample of lumefantrine-artemether tablets was analyzed and found to pass the monograph assay requirements. Several extraneous peaks appeared in the chromatogram, and these were shown to be from the water that was used for the analysis. Dr. Bempong emphasized the importance of using HPLC grade reagents, including water, for such analysis. He also explained that the analytical balance that was used does not provide the accuracy (0.01 mg) required for the weighing performed for this analysis.

Dr. Bempong went on to train the group on the artemether dissolution method – a two-time point, three-hour dissolution procedure that uses an HPLC procedure for sample analysis. He started by explaining how multiple sampling is done in dissolution testing. He went through the calculation of amount of drug dissolved at each time point with the analysts, emphasizing in particular how previously withdrawn samples are accounted for in subsequent time points. He trained the team on inspection of the dissolution tester and accessories, and also measurements that are made prior to performing the dissolution to check for potential problems. A sample of lumefantrine-artemether tablets was tested and the students were asked to record their observations during the testing. The recorded measurements and observations were later used to demonstrate that one position (tablet) failed the test because the dissolution tester malfunctioned at that position during the test.

The analysts showed an in-depth understanding of the analytical techniques. However, some of the practices in the laboratory need to change, including laboratory data documentation, pH meter calibration, and the necessary daily checks of balances.

#### *Drafting and finalizing SOPs – all analysts*

The trainers reviewed SOPs drafted by the DACA QC lab analysts prior to the training and provided the analysts with feedback on the drafts. The trainers emphasized the need for a consistent structure for all SOPs. In this regard, the trainers proposed a general structure for all DACA SOPs.

In addition, the trainers thoroughly discussed two key SOPs with the analysts – Notebook and HPLC. The two SOPs were finalized and were ready for immediate implementation. The trainers and the DACA laboratory director agreed that following the training, other draft SOPs that have already been reviewed by USP DQI staff and found to be satisfactory would be forwarded to the director for implementation. Eight of these SOPs have been forwarded to the director.

For the trainees' evaluations of the training, please see *Annex 2*. For a list of supplies sent to the DACA QC laboratory, please see *Annex 3*.

- **Other Meetings**

*Meeting with MSH-SPS*

Dr. Smine met with Dr. Negussu Mekonnen, the head of the MSH/SPS program in Ethiopia, and gave an overview of the DACA training. Dr. Smine and Dr. Mekonnen exchanged their PEPFAR FY09 work plans, discussed program activities, and identified areas where the two programs could collaborate in 2010. Further discussions about collaboration will take place between the USP DQI Director, the Cognizant Technical Officer of the PEPFAR program in Ethiopia, and others within SPS. Dr. Smine and Dr. Mekonnen agreed to keep each other updated about future plans, especially regarding activities in pharmacovigilance and drug information.

*Meeting with DACA*

The USP DQI team was pleased that the DACA Director General, Mr. Yehelu, had visited the QC lab during the opening ceremony for the training. Dr. Smine and Dr. Bempong gave him an overview of the trainings and also discussed future training plans and the major activities planned under the new PEPFAR funds. Mr. Yehelu offered his full support and urged the Lab Director to do his best to comply with implementation plan deadlines.

Later in the week, Dr. Smine, Dr. Wondemagegenehu, and Mr. Bikila visited the new QC lab facility in DACA headquarters. Dr. Smine pointed out a few issues with the laboratory, such as safety concerns with the entry and exit doors, the size of the elevator door, and the plans for partitioning the new laboratory. Dr. Smine advised the Lab Director to hire a design professional to help with specifications about supply elements such as air, water, and electricity. Dr. Smine informed DACA that the PEPFAR work plan includes funding to cover this.

After the lab visit, the team met with the Deputy Director General of DACA and discussed the implementation plan under the PEPFAR work plan. Activities will be planned in agreement with DACA. The Deputy Director was pleased with the information and the ambitious work plan.

*Participation in PMI partners meeting*

Dr. Smine and Dr. Wondemagegenehu attended a half day PMI partners meeting in Addis Ababa. This was a great opportunity to meet with other PMI partners and learn about their work. Dr. Smine and Dr. Wondemagegenehu met with Dr. Richard Reithinger and the USAID PMI team. The team learned a great deal about the reporting systems and branding policies and received all the templates to be used in future reports.

Because of time constraints, the team was not able to give the prepared presentation at the meeting, but a copy was shared with the PMI manager (please see *Annex 4* for a copy of the presentation).

**Next steps**

- DACA will finalize and sign the implementation plan
- DACA QC laboratory will continue to make and finalize SOPs following the models
- USP DQI will review and provide comments on SOPs as they are written by QC lab staff

- Both USP DQI and the QC lab will follow up on the planned activities in the implementation plan and deliverables as per the plan deadlines
- DACA QC lab sentinel site team will finalize the first round data report and plan for the start of the new round under PMI funds.
- USP DQI will provide the necessary budget to carry out the next sampling round at the sentinel sites when the budget is finalized, reviewed, and approved.

### **Conclusion**

The workshop was successful and achieved all expected objectives. The participants of both groups were dedicated and showed a great deal of interest in learning about all aspects of the training program.

The USP DQI staff and the Director of the DACA QC lab agreed to stick to the implementation plan and carry out all duties as scheduled. The plan calls for increase in DACA QC staffing levels and performance capacities of the lab.

The gradual approach in building staffing levels and quality assurance systems in Ethiopia will benefit both PMI and PEPFAR funding programs. A stronger QC lab will help Ethiopia assure the quality of antimalarials and antiretrovirals as well as other medicines used in health programs.

### List of Participants

Addis Ababa, Ethiopia ♦ October 19-23, 2009

#### Group 1 - Senior Group

Participant	Role in DACA DQCTL
Bekele Tefera Workneh	Analyst
Tamrat Tesfaye Tofie	Analyst
Seyoum Wolde Bekele	Analyst
Getachew Genete Gebeyehu	Analyst
Heran Gerba Borta	Analyst
Kemal Hussien Seid	Analyst
Bonsamo Gobena Tegen	Analyst
Lantider Kassaye Bekele	Analyst

#### Group 2 - Junior Group

Participant	Role in DACA DQCTL
Teferi Mantegaftot Mola	Analyst
Girum Habte Beyene	Analyst
Mohammedamin Jemal Kedir	Analyst
Yehowalashet Bogale Damite	Analyst
Henok Alebachew Alemu	Analyst
Meaza Kassa Mengesha	Analyst
Habtamu Hailu Asgedom	Analyst
Nigussu Dadi Geleta	Analyst
Habtamu Beyene Guluna	Analyst
Asnakech Alemu Desalgn	Analyst
Yenenesh Kassaye Tefera	Analyst
Hailu Mamo Hailu	Analyst
Fitih Tola Negewo	Analyst
Nahom Getachew Kebede	Analyst
Afewerk Abebe Gebryes	Analyst
Nebyou Yigezy Tafse	Analyst
Getahun Bekele	Analyst
Abiy Negash	Laboratory Assistant
Asegedech Worku	Laboratory Assistant

## Evaluations

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

### A. Evaluation of Specific Aspects of the Dissolution Training

DISSOLUTION TRAINING	EXTENT TO WHICH THE TRAINING MET YOUR OVERALL EXPECTATIONS			
	Exceeded Expectations	Met Expectations	Met Some Expectations	Unsatisfactory
Inspection of equipment	6	14		
Media preparation	10	8	2	
Monitoring of dissolution test	10	10		
Sampling and sample analysis	9	10	1	
Data collection and interpretation	4	15	1	
Precautions taken before and during dissolution test	12	8		

### B. Overall Evaluation of the Dissolution Training

	Strongly Agree	Agree	Somewhat Disagree
Course objectives were relevant to my needs	10	9	
The training material helped me understand and better organize my data	9	10	1
I was able to understand the content of the materials presented	8	10	
Overall, the course was useful and will help me do my job better	13	6	
There were enough practical exercises to facilitate understanding of the course	8	11	
The pacing of the various sessions was appropriate for my understanding of course materials	7	11	1
The sequence in which the sessions were presented was appropriate for my understanding	9	9	
The instructors were knowledgeable on the subject	15	5	
The instructors allowed an appropriate level of participation	17	2	1

### C. Evaluation of Specific Aspects of the HPLC Training

HPLC Training	Extent To Which The Training Met Your Overall Expectations			
	Exceeded Expectations	Met Expectations	Met Some Expectations	Unsatisfactory
Proper use of HPLC systems	2	16	2	
Troubleshooting in HPLC	4	8	7	1
Data Collection and Interpretation	4	15	1	

## D. Overall Evaluation of the HPLC Training

	Strongly Agree	Agree	Somewhat Disagree
Course objectives were relevant to my needs	11	8	
The training material helped me understand and better organize my data.	6	12	1
Overall, the course was useful and will help me do my job better	10	9	
There were enough practical exercises to facilitate understanding of the course materials	7	11	1
The pacing of the various sessions was appropriate for my understanding of course materials	8	11	
The sequence in which the sessions were presented was appropriate for my understanding	9	10	
The instructors were knowledgeable on the subject	15	4	
The instructors allowed an appropriate level of participation in the class	13	5	

## E. Summary of Comments/Suggestions

### I. What Did You Like Best About the Course?

- Hands on practical sessions
- Instructors' enthusiasm
- Instructors' were knowledgeable
- Emphasis on precautions
- Emphasis on need to document laboratory data
- Extensive discussion of the Standard Operating Procedures (SOPs)

### II. What Did You Like Least About The Course?

- The time for the entire training was too short

### III. What Are Your Recommendations/Suggestions for Improving the Course?

- Increase the training time especially time for the hands-on practical training
- Reduce the number of analysts per group for the hands-on training
- Have the instructors around during normal working days to help implement recommended changes
- Provide training in the following:
  - Microbiology
  - HPLC maintenance and troubleshooting
  - Dissolution apparatus besides apparatus 1 and 2
  - Gas Chromatography
  - UV Spectroscopy
  - IR Spectroscopy

**List of Supplies Sent to DACA QC Laboratory**

UNITS	COUNTRY OF MFG	DESCRIPTION OF GOODS	UNIT VALUE	SUB TOTAL
10	USA	FISHER SCIENTIFIC: LAB NOTEBOOKS	23.05	230.54
2	USA	WATERS: HPLC COLUMN	599.00	1198.00
7	USA	VWR: GLASS LUER-LOCK SYRINGE	136.00	136.00
4 (1 EA)	USA	FISHER CHEMICAL: BUFFERS PH 2 (500 ML)	20.34	20.34
	USA	PH 4 (500 ML)	9.76	9.76
	USA	PH 7 (500 ML)	9.58	9.58
	USA	PH 10 (500 ML)	9.96	9.96
1	USA	ORION: ELECTRODE FILLING SOLUTIONS, ORION 910001	56.49	56.49
1	USA	ORION 810007	98.24	98.24
8	USA	VWR: STEEL CANNULAS	16.25	130.00
6	USA	VWR: SPATULA	11.27	67.62
1	USA	MILLEX: MILLIPORE SYRINGE FILTERS, PACK 250	541.37	541.37
2	USA	DURAPORE: HVLP, 0.45-µm FILTERS, PACK 50	215.81	431.62
25	USA	KIMBERLY CLARK: LAB COATS	26.86	671.5
3	USA	FISHER: LAB GLOVES (S,M,L)	23.70	71.1
1	USA	FISHER: ALUMINUM WEIGHING BOATS, 1.062 FL. OZ	28.15	28.15
1	USA	FISHER: ALUMINUM WEIGHING BOATS, 1.375 FL. OZ	41.20	41.20
1	USA	FISHER: ALUMINUM WEIGHING BOATS, 1.875 FL. OZ	38.22	38.22
1	USA	FISHER: ALUMINUM WEIGHING BOATS, 2.375 FL. OZ	6.04	6.04
1	USA	FISHER: ALUMINUM WEIGHING BOATS, 5.000 FL. OZ	19.50	19.50
1	USA	FISHER: PARAFILM	16.41	16.41
5	USA	FISHER: KIMWIPES	2.78	13.90
1	USA	FISHER: LABEL TAPE	59.95	59.95
1	USA	FISHER: PASTEUR PIPETS, PACK 250	19.67	19.67
2	USA	FISHER: BENZALKONIUM CHLORIDE SOLUTION, 1L	71.27	142.54
1	USA	VARIAN: DISSOLUTION CENTERING GAUGE	31.90	31.90
1	USA	VARIAN: DISSOLUTION DEPTH GAUGE	77.90	77.90
3	USA	USP RS: PREDNISONE	194.00	582.00
3	USA	USP RS: PREDNISONE TABLETS	224.00	672.00
2	USA	USP RS: AMODIAQUINE HYDROCHLORIDE	194.00	388.00
2	USA	USP RS: CHLOROQUINE PHOSPHATE	194.00	388.00
2	USA	USP RS: ARTEMETHER	194.00	388.00
3	USA	USP RS: LUMEFANTRINE	194.00	582.00
2	USA	USP RS: SULFADOXINE	194.00	388.00
2	USA	USP RS: PYRIMETHAMINE	194.00	388.00
2	USA	USP CATALOGS	NO CHARGE	NO CHARGE


**U.S. PHARMACOPEIA**  
 DRUG QUALITY AND INFORMATION PROGRAM

PMI Partners Meeting  
 Addis Ababa, Ethiopia ♦ October 23, 2009

**USP DQI Update:  
 Workplan and Accomplishments**

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 Consultant  
 USP - Promoting Quality of Medicines




**USP DQI : Goals**

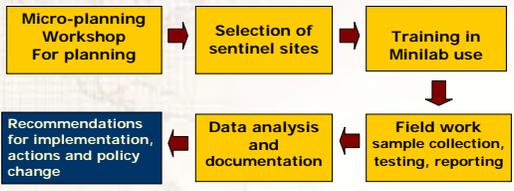
USP Drug Quality and Information Program

- ♦ **First year PMI support of USP FY08**
- ♦ **Program Targets for the year**
  - ▶ Strengthen drug quality monitoring in Oromia Region by establishing antimalarial drugs monitoring in five sentinel sites
  - ▶ Strengthen the capacity of DACA for Quality Assurance and Quality Control of antimalarials




**Framework for Monitoring**

USP Drug Quality and Information Program



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    graph TD
      A[Micro-planning Workshop For planning] --> B[Selection of sentinel sites]
      B --> C[Training in Minilab use]
      C --> D[Field work sample collection, testing, reporting]
      D --> E[Data analysis and documentation]
      E --> F[Recommendations for implementation, actions and policy change]
      F --> A
  
```

USP DQI also trains quality control labs on compendial analytical methods, such as HPLC, dissolution, and UV-spectrophotometry.




**USP DQI : Workplan**

USP Drug Quality and Information Program

Postmarketing Medicines Quality Monitoring Program MOP FY 08		
Activity	Outputs	Status
Micro-planning workshop to develop Implementation Plan, study design and protocol	<ul style="list-style-type: none"> <li>♦ Implementation Plan agreed upon</li> <li>♦ 5 sentinel sites identified</li> <li>♦ Sampling protocol developed</li> </ul>	Completed
Training in use of Minilabs <sup>®</sup>	♦ 27 DACA, ORHB, and regional DACA staff trained	Completed
Training of DACA and ORHB staff in compendial testing	♦ 8 DACA QC lab staff (GLP, HPLC, USP NF, Dissolution), 5-day training	Completed
Collection and analysis of samples	<ul style="list-style-type: none"> <li>♦ 1st round of sampling &amp; testing of all samples collected - Completed</li> <li>♦ Final report – Being finalized</li> </ul>	410 samples collected and tested



## USP DQI : Workplan

USP Drug Quality and Information Program

### Postmarketing Medicines Quality Monitoring Program MOP FY 08

Activity	Outputs	Comments
Resources for DACA lab	◆ Provided lab supplies, reference standards and reagents	Completed
Data review, and reporting and re-training	◆ Re-training needs identified ◆ Sampling strategy revisited for next rounds FY09.	Completed
Building capacity of DACA lab (FY09)	◆ Implementation Plan developed ◆ Implementation started	In progress



## Drug Quality Monitoring: Sentinel Sites

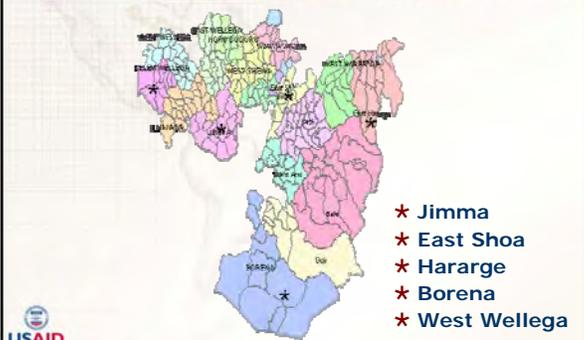
USP Drug Quality and Information Program

- ◆ **Five sites selected based on —**
  - ▶ Epidemiology, geography and demography
  - ▶ Proximity to DACA regional offices
  - ▶ Status as drug efficacy sentinel site
  - ▶ Borders with other countries
  - ▶ Cities known for existing illegal markets
  - ▶ Areas where fake, substandard drugs found



## Drug Quality Monitoring: Sentinel Sites

USP Drug Quality and Information Program



## Drug Quality Monitoring: Medicines

USP Drug Quality and Information Program

- ◆ **Medicines to be Collected and Tested**
  - ▶ Chloroquine
  - ▶ Quinine
  - ▶ Sulfadoxine–Pyrimethamine
  - ▶ Primaquine
  - ▶ Artemeter/Lumifantrine (Coartem and generic)





## Drug Quality Monitoring: Program Objectives

USP Drug Quality and Information Program

- ◆ Produce evidence-based data on quality of antimalarials in selected sentinel sites
- ◆ Demonstrate use of basic tests as effective screening tool to monitor medicines quality
- ◆ Share information with relevant authorities and stakeholders about quality and source
- ◆ Advocate for enforcement of the regulations when substandard and counterfeit medicines are found
- ◆ Strengthen quality control capacity at central and regional levels



## Samples Collected From Five Sentinel Sites in the Oromia Region

USP Drug Quality and Information Program

Product	Borena	E. Shoa	Hararge	E. Wollega	Jimma	Total
Amodiaquine	1					1
Arthem./Lumf.	26	20	12	23	23	104
Chloroquine	21	35	20	39	28	143
Sulphadoxine/ pyrimethamine	15	22	10	13	9	69
Quinine	18	14	10	27	15	84
Primaquine	1	3	-	3	2	9
<b>Total</b>	<b>82</b>	<b>94</b>	<b>52</b>	<b>105</b>	<b>77</b>	<b>410</b>



## Samples Collected From Borena Sentinel Site- by Source and Registration Status

USP Drug Quality and Information Program

Product	Source			Registration Status		
	Impt.	Loc.	UnK.	Reg.	Unreg.	UnK.
Amodiaquine	1	-	-	-	1	-
Arthem./Lumf.	26				26	
Chloroquine	1	20	-	10	10	1
Sulfadoxine/ pyrimethamine	9	3	3	5	7	3
Quinine	15	2	1	2	15	1
Primaquine	1	-	-	-	1	-
<b>Total</b>	<b>53</b>	<b>25</b>	<b>4</b>	<b>17</b>	<b>60</b>	<b>5</b>
<b>Summary</b>	<b>82</b>			<b>17</b>	<b>60</b>	<b>5</b>



## Samples Collected From E. Shoa Sentinel Site by Source and Registration Status

USP Drug Quality and Information Program

Product	Source			Registration Status		
	Impt.	Loc.	Unk.	Reg.	Unreg.	Unk.
Amodiaquine	-	-	-	-	-	-
Arthem./Lumf.	20	-	-	-	20	-
Chloroquine	1	34	-	13	22	-
Sulfadoxine/ pyrimethamine	15	7		8	14	
Quinine	9	-	5	-	9	5
Primaquine	-	3	-	-	3	-
<b>Total</b>	<b>45</b>	<b>44</b>	<b>5</b>	<b>21</b>	<b>68</b>	<b>5</b>
<b>Summary</b>	<b>94</b>			<b>21</b>	<b>68</b>	<b>5</b>



### Samples Collected From E. Harrarge Sentinel Site by Source and Registration Status

USP Drug Quality and Information Program

Product	Source			Registration Status		
	Impt.	Loc.	Unk.	Reg.	Unreg.	Unk.
Amodiaquine	-	-	-	-	-	-
Arthem./Lumf.	12	-	-	-	12	-
Chloroquine	2	18	-	11	9	-
Sulfadoxine/ pyrimethamine	10	-	-	6	4	-
Quinine	10	-	-	-	10	-
Primaquine	-	-	-	-	-	-
<b>Total</b>	<b>34</b>	<b>18</b>	<b>-</b>	<b>17</b>	<b>35</b>	<b>-</b>
<b>Summary</b>	<b>52</b>			<b>17</b>	<b>35</b>	<b>-</b>



### Samples Collected From W. Wollega Sentinel Site by Source and Registration Status

USP Drug Quality and Information Program

Product	Source			Registration Status		
	Impt.	Loc.	Unk.	Reg.	Unreg.	Unk.
Amodiaquine	-	-	-	-	-	-
Arthem./Lumf.	23	-	-	-	23	-
Chloroquine	4	35	-	5	34	-
Sulfadoxine/ pyrimethamine	9	4	-	4	9	-
Quinine	27	-	-	-	27	-
Primaquine	2	1	-	-	3	-
<b>Total</b>	<b>105</b>			<b>9</b>	<b>96</b>	<b>-</b>



### Samples Collected Jimma Sentinel Site by Source and Registration Status

USP Drug Quality and Information Program

Product	Source			Registration Status		
	Impt.	Loc.	Unk.	Reg.	Unreg.	Unk.
Amodiaquine	-	-	-	-	-	-
Arthem./Lumf.	23	-	-	-	23	-
Chloroquine	1	27	-	15	13	-
Sulphadoxine/ pyrimethamine	8	1	-	4	5	-
Quinine	14	-	1	-	15	-
Primaquine	-	2	-	-	2	-
<b>Total</b>	<b>46</b>	<b>30</b>	<b>1</b>	<b>19</b>	<b>8</b>	<b>-</b>
<b>Summary</b>	<b>77</b>			<b>19</b>	<b>68</b>	<b>--</b>



### Results of Confirmatory TLC Tests at DACA DQCL

USP Drug Quality and Information Program

Product	TLC Confirmatory Test at DACA DQCL									
	E.Showa.		W. Wollega		Borena		Jimma		East Harrarge	
	Total	failed	Total	failed	Total	failed	Total	failed	Total	failed
Chloroquine	37	7	39	8	20	-	32	3	20	6
Primaquine	3	-	3	-	-	-	3	-	-	-
Quinine	14	1	27	2	16	-	18	-	10	-
Sulfadoxine Pyrimethamine	22	-	11	-	11	-	11	-	10	-
Arthem./Lumf.	20	-	23	-	23	-	25	1	12	-
<b>Total</b>	<b>96</b>	<b>8</b>	<b>103</b>	<b>10</b>	<b>70</b>	<b>--</b>	<b>89</b>	<b>4</b>	<b>52</b>	<b>6</b>

### Summary of Quality Monitoring Results

USP Drug Quality and Information Program

Product	Total smpl	TLC at Site			TLC DQCL			Confirmatory Dissolution* DQCL			Confirmatory Assay DQCL		
		Smpl	P	F	Smpl	P	F	Smpl	P	F	Smpl	P	F
Amodiaquine	1				-	-	-	-	-	-	-	-	-
Arthem/Lumf	103	103	102	1	103	102	1				10	7	3
Sulfa/Pyrim	65	65	65		65	65	-	65	57	8	6	6	-
Chloroquine	148	148	124	24	148	124	24				36	32	4
Quinine	85	85	82	3	85	82	3				11	10	1
Primaquine	9	9	9		9	9	-				1	1	-
<b>Total</b>	<b>410</b>	<b>410</b>	<b>382</b>	<b>28</b>	<b>410</b>	<b>382</b>	<b>28</b>	<b>65</b>	<b>57</b>	<b>8</b>	<b>64</b>	<b>56</b>	<b>8</b>

### Summary of USP DQI activities in Ethiopia -2008

USP Drug Quality and Information Program

USP DQI Activity	Ethiopian partners involved	Number of staff participated or trained	Products
Assessment	DACA, MOH, MCP, WHO, SPS, Public Hospitals	NA	• Assessment report
Micro-planning workshop	DACA, NMCP, RHB, PFSA, WHO	15 participated	• PMS program designed
Basic tests PMS training	DACA, NMCP, RHB, PFSA, SPS	24 trained	• PMS plan finalized
GLP, HPLC, Dissolution training	DACA lab	8 trained	• Implementation plan for DACA lab finalized • Confirmatory testing
First round PMS	DACA, RHB, NMCP, PFSA	24 trained sentinel sites staff involved	• Sampling and basic test report
First round PMS	DACA, RHB, NMCP, PFSA	DACA lab, USP DQI	• Confirmatory testing conducted in DACA lab
Second training on HPLC, dissolution and QMS	DACA lab	8 and 12 analysts trained	• Implement Plan with DACA • Reviewed PMI future activities

### Challenges faced

USP Drug Quality and Information Program

- ◆ Delayed activities due to DACA Business Processes Re-engineering
- ◆ Procedures and guidelines not followed properly
- ◆ Staff movement (loss of trained staff)
- ◆ Hiring a large number of new analysts in DACA lab (need for re-training)
- ◆ Low level of quality control skills in DACA lab
- ◆ Lack of resources in DACA QC lab
- ◆ Slow decision making regarding enforcement actions

USP DQI ACTIONS →

- Increase frequency of USP visits to DACA lab
- Increase evaluation and monitoring
- Learn from mistakes already done and correct them
- Set yearly target for staff and monitor performance
- Establish strong QMS and enforce good lab practices

### PMI / USP DQI FY09- Work plan

USP Drug Quality and Information Program

Activities	Outputs	Target Indicators	Timeline
Drug Quality Monitoring in the five sentinel sites of Oromia region	<b>Round 1</b> <ul style="list-style-type: none"> <li>• Provide sentinel sites and DQCL with any needed reagents, supplies or reference standards</li> <li>• Review and approve sampling plans before round-1</li> <li>• Conduct first round of sampling and testing in five sentinel sites (FY09-Q2)</li> <li>• Sample, test and report sentinel sites data</li> <li>• Conduct Lab confirmatory tests according to DQI procedures</li> <li>• Monitor and evaluate the first round activity and recommend changes for second round.</li> </ul>	<ul style="list-style-type: none"> <li>• Sentinel sites ready</li> <li>• Number of samples collected</li> <li>• Number of samples tested</li> <li>• Number of samples failed to pass basic tests</li> </ul>	FY09 Q2
	<b>Round 2</b> <ul style="list-style-type: none"> <li>• Conduct second round of sampling and testing, taking in consideration any changes required from round one (FY09-Q4)</li> </ul>		FY09 Q4

**USP** USP DQI FY09 - Work plan ...cont.

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Expand to two sites outside Oromia region	<ul style="list-style-type: none"> <li>•Purchase 2-3 Minilabs</li> <li>•Identify the two new sites outside Oromia region (selection must be made in agreement with USAID, DACA, NMCP)</li> <li>•Train the sentinel sites staff on sampling and basic tests according to the same DQI procedures</li> </ul>	<ul style="list-style-type: none"> <li>• Minilabs &amp; supplies purchased and delivered</li> <li>• Sentinel sites staff trained</li> <li>•Number of samples collected</li> </ul>	FY09 Q1
	<ul style="list-style-type: none"> <li>•Conduct one round of sampling and testing the same way and at the same time than those of Oromia region</li> </ul>	<ul style="list-style-type: none"> <li>•Number of samples tested</li> <li>•Number of samples failed to pass basic tests</li> </ul>	Q4
Disseminate data and raise awareness	<ul style="list-style-type: none"> <li>•Report drug quality data and present to stakeholders</li> <li>•Collaborate with DACA and other partners (custom, police, health programs) if specific enforcement actions are needed</li> <li>•Recommend government action when substandard/ counterfeit medicines are found</li> <li>•products where appropriate</li> </ul>	<ul style="list-style-type: none"> <li>• Report presented and disseminated</li> <li>• Follow-up where appropriate</li> </ul>	Q2-Q4

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# Questions?



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# Thank You



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