

USP DQI Workshop on Basic Tests of Antimalarials using Minilabs®

Establishing Drug Quality Monitoring in Five Sentinel Sites in Ghana

Accra, Ghana
February 9-13, 2009

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

United States Pharmacopeia Drug Quality and Information (USP DQI) Program organized a mini planning workshop to select the sentinel sites and the institutions to be involved in the drug quality monitoring program. As a result, USP DQI and local stakeholders agreed to establish the drug quality monitoring in five sentinel sites. The program will be coordinated by the Food and Drug Board (FDB) and involve the Malaria Control Program, the Pharmacy Council and the regional FDB offices. USP DQI has purchased the Minilabs[®] needed to carry out program activities. During this trip, USP DQI will train the sentinel sites teams on basic tests using Minilabs[®] and will set standard procedures for antimalarial drugs selection, sampling, testing, and data reporting.

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Key Words

Quality Control, Antimalarial Drugs, Sentinel Sites, Minilab[®], Drug quality monitoring program, USP DQI, Food and Drug Board of Ghana, Malaria Control Program

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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/Ghana Mission, in particular Mr. Paul Psychas, PMI Team Leader; and Mr. Anthony Boni and Ms. Veerle Coignez at USAID Washington for their guidance and helpful insights throughout the preparation stages of the workshop. We are also thankful to Ms. BethAnne Moskov, USAID/Ghana Health Team Leader for very useful discussions we had with her.

ACRONYMS

ACT	Artemisinin-based Combination Therapy
FDB	Food and Drug Board of Ghana
NDQCL	National Drug Quality Control Laboratory
MOP	Malaria Operational Plan
PEPFAR	The U.S. President's Emergency Plan for AIDS Relief
PMI	President's Malaria Initiative
QA	Quality Assurance
QAMSA	Quality of Antimalarials in Sub-Saharan Africa study
QC	Quality Control
QHP	Quality Healthcare Partners
SP	Sulfadoxine and Pyrimethamine
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

USP DQI received funding from USAID/Ghana in FY04 (October 1, 2004 – September 30, 2005) and supported the Food and Drug Board (FDB) of Ghana in assuring the quality of medicines in the market. USP DQI equipped and trained quality control (QC) laboratory staff and also trained FDB on drug registration, installing SIAMED for the department of drug evaluation. In addition, USP DQI assessed several medicines manufacturers in Ghana.

In FY09 (October 1, 2008 - September 30, 2009), USP DQI received funds from USAID/Ghana under the President's Malaria Initiative (PMI) to assist the country with drug quality assurance (QA) of antimalarials at the peripheral level of the supply chain.

Drug quality assurance is still a major issue in Ghana because local manufacturers produce and sell products not in compliance with GMP. The QC lab staff are well trained; however, the lab facilities are old and do not offer a good working environment. Pharmacovigilance activities have been delayed, and the market is flooded with many types of antimalarial drugs.

In October 2008, a USP DQI team conducted a rapid assessment of the quality assurance and quality control (QA/QC) capacity of FDB. After meeting with all country partners, the team built a consensus about the program activities to be conducted in FY09 through the USAID/Ghana PMI program. FDB and USP DQI organized a workshop to set the plan for establishing a medicines quality monitoring program. The participants set the objectives of the program, defined roles and responsibilities of program teams, selected five sentinel sites, selected the medicines to be collected and tested, discussed the budget elements, and planned training on basic tests using Minilabs[®].

The objective of this visit were to meet with key stakeholders of the program and work together to define all the critical program elements, train staff on basic tests, and set the timeline and process to conduct two testing rounds in five selected sentinel sites in FY09.

Purpose of Trip

USP DQI staff traveled to Accra, Ghana to:

1. Meet with FDB, Malaria Control Program, Pharmacy Council, and Regional representatives of FDB and review the program elements.
2. Train the participants on medicines sampling, basic tests, and data reporting.
3. Estimate the budget needed to carry out one round of antimalarial drugs sampling and testing, including laboratory confirmation and a final report.
4. Debrief USAID about the program activities and discuss funding for next year.

Source of Funding

This activity was funded by USAID/Ghana, under the PMI program.

Workshop Overview

Item	Description
Training Objectives	<ul style="list-style-type: none"> ✓ Rationale of using basic tests to monitor the quality of antimalarial drugs at peripheral level. ✓ Basic theory about Thin Layer Chromatography ✓ Training on medicines sampling at sentinel sites level ✓ Training on Visual and Physical Inspection of medicines ✓ Training on Thin Layer Chromatography using Minilabs® ✓ Training on simple drug disintegration ✓ Training on proper reporting of drug quality data
Venue	FDB Medical Devices Laboratory, Accra, Ghana
Local Organizers	Food and Drug Board of Ghana
Opening Ceremony	Mr. Emmanuel Agyarko, Mr. Ben Botwe, Rev. Johnathan Martey, and USP DQI staff
Course Proceedings	<p>The Training was organized as follows:</p> <p>Day 1: Opening, Theory about TLC and Sampling, Logistics and Budgets. Sentinel sites and supervisory teams set up (<i>See Annex 1</i>)</p> <p>Day 2: TLC lab (amodiaquine followed by sulfadoxine-pyrimethamine)</p> <p>Day 3: TLC lab (Chloroquin, followed by Quinine Injection, and Artesunate)</p> <p>Day 4: Artesunate and fixed dose combinations of Artem/lumef testing of suppositories, suspension dosage forms</p> <p>Day 5: Review of budget, wrap up discussion, certificates, closing</p>
Participants	Twenty FDB, MCP, and Pharmacy Council staff trained. (<i>See Annex 1</i>)
Equipment Provided	All materials provided by USP DQI are indicated in the List of Supplies sent to FDB (<i>See Annex 2</i>)
Closing Ceremony	<p>CEO of FDB Mr. Emmanuel Agyarko, Dr. Smine and Dr. Hajjou, Reverend J. Martey</p> <p>Following the closing remarks, certificates were awarded to all participants who successfully completed the course.</p>
Course Outcomes	<p>At the end of the course, participants were able to:</p> <ul style="list-style-type: none"> ✓ Understand the sampling protocol and sampling plan ✓ Carry out visual inspections and TLC testing of all antimalarial drugs ✓ Carry simple disintegration ✓ Report drug quality data as established by the USP DQI program using standard procedures. <p><i>It is important to note that during the training, fake and substandard samples were found by the trainees. This fact motivated the trainees and showed that basic tests are good tool QC tools.</i></p>
Course Evaluation	Participants were asked to evaluate each of the course modules and sessions by filling out the Course Evaluation Form. (<i>See Annex 3</i>)

Overview of Activities

Opening of the Training

On the first day of the training, the CEO of FDB, Mr. Emmanuel Agyarko; his deputy, Mr. Ben Botwe; and the head of the FDB QC lab, Reverend Jonathan Martey, attended the opening ceremonies. Mr. Agyarko welcomed the USP DQI team and all the participants and emphasized the importance of monitoring the quality of antimalarial drugs at the peripheral level. He acknowledged that there may be poor quality drugs in the private sector and that some may not even be registered with FDB. He encouraged the participants to do their best to make this program successful and reach its target objectives. Mr. Agyarko finished his opening address by thanking USAID and USP DQI for their support and wished the trainees and the participants good luck with the training. Reverend Martey added that Ghana was lucky to have benefited from such USAID and USP DQI support. He ended by thanking the USP DQI team and encouraging the participants to do their best to make this training successful.

Introduction to Basic Tests and Drug Sampling

After the opening of the training, Dr. Smine and Dr. Hajjou started the training by covering the following topics:

- Introduction to basic tests and the rationale behind using this approach to monitor the quality of medicines in limited-income countries
- Theory about Thin Layer Chromatography (TLC), its advantages and limitations
- Principles of medicines sampling at the peripheral level. This topic was discussed in detail and the participants asked many questions. Some FDB lab staff are involved in the Quality of Antimalarials in Sub-Saharan Africa (QAMSA) study and helped answer many questions about the sampling experience in the regions where sentinel sites are located.
- Dr. Smine reviewed the program design done at the micro-planning workshop. All needed information about the sampling, timeline, staff involved, and the responsibilities of all parties were completed.
- Dr. Smine also reviewed the budget elements and asked the participants and Rev. Martey to work on a final draft of budgets for the five sentinel sites. The budget estimation will be completed by the end of the training.
- Dr. Hajjou and the FDB lab personnel set up and installed the training materials.

Testing Rounds

The participants agreed to carry out two complete rounds of sampling and testing in FY09. Each round will be completed within three months, including one month for confirmatory testing at the National Drug Quality Control Laboratory (NDQCL).

- First round: March 12 - May 12
- Second round: July 1 - August 30

Sampling Methodology

USP DQI staff presented the sampling guidelines used in different countries. Following group discussion, the participants agreed to adopt the critical elements about drug sampling. They also agreed that the sampling is in perfect line with the program

objectives. This must be considered a “convenient” random sampling for the purpose of monitoring the quality of antimalarials at the periphery of drug supply chains in the selected sites.

Sampling Plan

- Total of at least 100 samples/site/round
- Solid dosage form: 20 units/sample
- Injections: 5 units/sample
- Syrup: 2 units/sample
- Suppository: 3 units/sample

Targeted Medicines in term of priority

- Artesunate + Amodiaquine: 17 samples
- Artemether + Lumifantrine: 17 samples
- SP: 17 samples
- Quinine: 15
- Artemether Injection: 5 samples
- DHA-Piperaquine: 5 samples
- Artemisinin derivatives as monotherapy: 10 samples
- Amodiaquine: 5 samples
- Chloroquine phosphate: 5 samples
- Sulfamethoxyprazine/Pyrimethamine (SP): 2 samples
- Halofantrine: 2 samples

Sampling sources

- Public sector: **30 %**
- Private sector: **60 %**
- Informal market: **10%**

At the end of the meeting, the group discussed details regarding the handling of the samples and the logistics of carrying out two rounds of testing before September 2009. The participants on the sample identification code:

Project (DQI)/Sentinel site/API/Date of sampling/Serial number.

All failed and doubtful samples plus 10% of conforming samples will be sent to the NDQCL for confirmatory testing. The remaining samples will be retained at the sentinel sites for a period of time that FDB will determine. The budget required for the first round of testing was determined by FDB and MCP staff and reviewed by the USP DQI team.

Conclusion

Based on the discussions that the USP DQI team had with the participants and the reality in the field, it seems that serious effort has to be made by MCP to promote the rational use of antimalarial drugs in Ghana.

- Monotherapy is still a wide practice even though it has been banned officially for over two years.
- First-line treatment should be re-evaluated because it seems that patients take only artesunate from co-packaged Artemisinin-based Combination Therapies (ACTs). The side effects of amodiaquine were given as the cause of this practice.
- The market is flooded with all types of ACTs from manufacturers that are not pre-qualified and not known in the larger global market.
- ACTs with of all types of dosage forms are available, although studies in other countries have shown issues with their stability (suspension, suppositories, syrups, injections).
- It seems that injection of artemether alone has become a common practice as first-line treatment of patients with fever.

The Food and Drug Board of Ghana has to step up efforts to better control the quality of drugs in the market.

- No market authorization should be given for monotherapies.
- Chloroquine and sulfadoxine-pyrimethamine are still widely used, and FDB has to increase inspections and enforce compliance with MCP and World Health Organization (WHO) guidelines.
- FBD should limit the registration of too many ACTs and ACT dosage forms with questionable quality. This will facilitate the quality control of drugs in the market.
- FBD should promote procurement of medicines from trusted and pre-qualified suppliers only.
- FBD must take serious actions about manufacturers found to have substandard drugs in the market.

Debriefing of USAID

Dr. Smine met with Mrs. BethAnne Moskov, the head of the Health and Nutrition team. Dr. Smine gave an overview of the training, the program objectives, and the next steps. He pointed out the major issues listed above regarding quality assurance and rational use of antimalarial drugs in Ghana. Similar issues exist with other types of medicines and will surely affect all USAID Mission efforts in many health programs.

Dr. Smine requested that the level of USP DQI funding in the FY09¹ Malaria Operational Plan (MOP) be re-evaluated, because current levels will not sustain the activities started with MCP. The USP DQI drug quality monitoring program at the periphery level of supply chains will be effective only if it is continued for at least three years. This program will not reach its main objectives if other support is not provided to the FBD lab and drug registration unit to promote corrective action when drug quality data become available.

Mrs. Moskov promised to raise USP DQI's concerns with the PMI team and also try to convince the team in charge of HIV/AIDS to support USP DQI's drug quality work to assure the quality of HIV medicines. Mrs. Moskov suggested that the USP DQI team

¹ The FY09 MOP funds activities in FY10: October 1, 2009-September 30, 2010.

should collaborate with the Quality Healthcare Partners (QHP) program and work together to better support the country.

Mrs. Moskov said that she will be moving to work in Mali in a few months. Dr. Smine informed her that USP DQI is a PMI partner working on drug quality and pharmacovigilance of antimalarial drugs in Mali.

Next Steps

To carry out the planned activities listed above, USP DQI will:

- Review and finalize the budget and transfer funds to FBD to start the sampling and testing of the first round before the end of March 2009.
- Review the first round data and make the necessary adjustment to carry out the second round of testing.
- Work with FDB, MCP, and the PMI team to promote the necessary enforcement actions based on the first round data.
- Conduct a monitoring and evaluation visit to the sentinel sites during the second round of testing.
- Finalize the first year report of the drug quality monitoring program before September 2009.

WORKSHOP PARTICIPANTS

LABORATORY

Jemima Odonkor
Jemima Django
Araba Esiaa Thompson
Barbara Hoffman
Opuni Frimpong-Manso Kwabena
Samuel K. Kwakye
Eric Karikari-Boateng
Jonathan Y. Martey

DRUG INSPECTORATE

Geoffrey Arthur
P.K. Agyeman-Duah
Winslow Sackeyfio
Jennifer Bonnah
Seth Seaneke

REGIONAL OFFICERS (SENTINEL SITES)

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NATIONAL MALARIA CONTROL PROGRAMME

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LIBERIA MEDICINE & HEALTH PRODUCTS REGULATORY COMMITTEE

Jolo C. M. Mulbah

PHARMACY COUNCIL

Henry Saja

USP DOI PROJECT WORKING TEAMS						
TEAM	REPRESENTATION	ACCRA	HO	TARKWA	KUMASI	BOLGATANGA
Sampling Team	FDB Inspectorate	Mr. Seth Seaneke	Mr. Eric Owusu	Ms Abena Ekufua Esia-Donkoh	Mr. Joseph Bennie	Mr. Solomon Agampim
	FDB Inspectorate/Lab	Mrs. Jennifer Bonnah Mr. Winslow Sackeyfio	Mr. Azariah Nortey	Mr. George Pentsil	Mr. Patrick Acheampong	Ms. Jacqueline Asgil-Rogers
	National Malarial Control Program					
Minilab [®] Analysis Team	FDB Inspectorate	Mrs. Jennifer Bonnah	Mr. Eric Owusu	Ms Abena Ekufua Esia-Donkoh	Mr. Joseph Bennie	Mr. Solomon Agampim
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Supervisory Team	FDB Inspectorate	Geoffrey V. Arthur				
	FDB Laboratory	Samuel Kwakye				
	National Malarial Control Program	Sylvester Segbaya James Frimpong Naa Korkor Allotey				
	WHO	Edith Andrewse Annan				
	Pharmacy Council	Henry Sajah				
	Contact Person	Rev. Jonathan Martey (FDB Management)				

Supplies provided to FDB

Item	Quantity
Graduate ruler	15
Lab glass bottle, 100-ml	15
Thermometer	10
Pre-set timer	5
Spatula	15
Pair of scissors	15
Aluminum foil	2
Funnel	15
10-ml glass bottle	40
25-ml glass bottle	15
40-ml glass bottle	30
1-ml pipette	20
2-ml pipette	10
5-ml pipette	20
10-ml pipette	20
25-ml pipette	10
Pipette filler	15
Rack	15
Label tape	10
Marker	15
Pencil	15
Pencil sharpner	5
Microcapillaries	15
Hot plate	10
Adaptor plug	10
TLC plates	2
TLC developing chamber	15
Filter paper	3
UV lamp	5
TLC dipping chamber	5
Tweezers	15
Replacement batteries	16
Safety glasses	30
Protection masks	50
Gloves	6 Packs

Evaluation by Participants

Eighteen participants returned the evaluation form.

Indicator	Strongly Agree	Agree	Disagree Somewhat
1. Course objectives were relevant to my needs	15	3	
2. I was able to understand the content of the materials presented	15	3	
3. Overall the course was useful and will help me do my job better	14	4	
4. There were enough practical exercises to facilitate understanding of the course	12	5	1
5. The pacing of sessions was appropriate for my understanding of course materials	12	6	
6. The instructors were knowledgeable on the subject	17	1	
7. The instructors allowed an appropriate level of participation in the class	15	3	

Any other comments/suggestions:

1. Which topic(s) or aspects of the course should not be included in future workshops?

No Comments added

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

- **Seven participants suggested that other classes of medicines such as antibiotics and anti-tuberculosis agents should be included in the program.**
- **Some participants suggested using mini-fume hoods to avoid exposure to volatile chemicals.**
- **Other suggestions included allowing more time for the practice and the use of samples known to be substandard.**

The participant evaluations and experience of the facilitators during the course will be used to update the training materials at a later date.