USP DQI Training on Basic Tests and Sampling Procedures for Establishing Antimalarial Drug Quality Monitoring in Uganda

Kampala, Uganda
May 16-27, 2008

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 and the National Drug Quality Control Laboratory (NDQCL) of Uganda conducted a training workshop on basic drug analysis tests using GPHF Minilab® kits in Kampala, Uganda May 16-27, 2008. This training course was designed to prepare the participants to carry out post-marketing surveillance study of antimalarial medicines in Uganda.

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Key Words

Drug quality, medicine, Minilab®, pharmacovigilance, malaria, Uganda, PMI, USP DQI, USAID

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ACKNOWLEDGEMENTS

USP DQI would like to thank USAID-Uganda; the Executive Secretary of the NDA of Uganda, Mr. Apollo Muhairwe; the Head of the NDQCL, Dr. Anthonia Nakamya; and her staff for their assistance in providing this training.

USP DQI would also like to thank Mr. Anthony Boni, USP DQI's Cognizant Technical Officer, and his team in Washington, D.C. for their support and advice.

ACRONYMS

ACT	Artemisinin-based Combination Therapy
FDC	Fixed Dose Combinations
GC	Gas Chromatography
GPHF	Global Pharma Health Fund (Minilab® kit provider)
HPLC	High Performance Liquid Chromatography
MOP	Malarial Operational Plan
NDA	National Drug Authority
NDQCL	National Drug Quality Control Laboratory
PMI	President's Malaria Initiative
QAMSA	Quality of Antimalarials in Sub-Saharan Africa
QA	Quality Assurance
QC	Quality Control
SP	Sulfadoxine-pyrimethamine
TLC	Thin Layer Chromatography
USAID	United States Agency for International Development
USP DQI	United States Pharmacopeia Drug Quality and Information program
USP-NF	United States Pharmacopeia National Formulary
UV	Ultra-Violet Spectroscopy
WHO	World Health Organization

Background

In late June 2005, the United States Government announced a five-year, $1.2 billion initiative – the President's Malaria Initiative (PMI) – to rapidly scale up malaria prevention and treatment interventions in high-burden countries in sub-Saharan Africa. PMI began in 2006 in three countries – Uganda, Tanzania, and Angola – and will expand to 15 countries by 2010.

Within PMI, USAID requested USP DQI to support Uganda in their efforts to assure the quality of antimalarial drugs. The National Drug Authority (NDA) of Uganda assumes the functions of quality control, pharmacovigilance, post-marketing surveillance, and drug information, but has a limited capacity to perform these functions. PMI provided financial support to NDA to increase its ability to ensure the quality and efficacy of malaria-related commodities.

Under first-year PMI funding from USAID/Uganda, USP DQI assessed the drug quality control system in the country and identified weaknesses and areas where USP DQI could assist the NDA and the National Drug Quality Control Laboratory (NDQCL). In collaboration with the NDQCL, USP DQI selected, purchased, delivered, and installed the laboratory equipment the NDA needed for testing antimalarial medicines and insecticides. To strengthen Uganda's drug quality control capability, USP DQI trained NDQCL staff on Good Laboratory Practices and major testing methods, such as HPLC, Dissolution, UV, and GC, according to international pharmacopeias and other official methods of analysis.

In June 2006, PMI and USAID/Uganda-funded partners met to discuss work plans, review milestones, and identify priorities for the program's second year. USP DQI planned to establish or improve existing pre-marketing authorization and post-marketing surveillance activities, which can reduce the prevalence of poor quality antimalarial medicines and insecticides circulating in the country market.

In July 2007, the Uganda Ministry of Health, in partnership with USAID/Uganda, invited PMI and USAID/Uganda-funded partners to the PMI Stakeholders Meeting for an update on the progress of PMI activities and to discuss the proposed plan for the program's third year. All implementing partners were also invited to attend the concurrent PMI partners progress review meeting.

Purpose of Trip

Dr. Davydova and Mr. Sanford Bradby traveled to Uganda to:

- Provide a training workshop for 25 attendees on the use of basic tests to conduct field studies to detect counterfeit and substandard antimalarials.
- Demonstrate the appropriate sampling and documentation procedures to report quality control issues for antimalarials.
- Provide technical assistance to NDA and NDQCL staff to identify quality control problems regarding antimalarials.
- Provide technical assistance for the production and distribution of basic test reports on a regular basis to the antimalarial quality control program and the national quality control laboratory.
- Provide technical assistance to NDA and NDQCL staff in identifying sentinel sites in four provinces where the Minilab® systems will be located.

- Provide technical assistance to NDA and NDQCL staff in developing plans for two rounds of antimalarial drug testing and for analyzing and reporting findings from using the Minilab® systems.
- Meet with NDA and USAID to discuss the current USP DQI work plan and the upcoming work plan for fiscal year 2009.

Source of Funding

This trip was supported with funds from the USAID Mission in Uganda.

Overview of Activities

Friday, May 16, 2008
USP DQI staff arrived in-country and met with the NDQCL Lab Director, Dr. Anthonia Nakamya, to discuss and finalize plans regarding the upcoming training workshop. Later, the USP DQI staff met with the Executive Secretary of the NDA, Mr. Apollo Muhairwe, to discuss the workshop and current issues regarding drug quality in Uganda.

Sunday, May 18, 2008
USP DQI staff researched a controversial local news article (*Annex 1*) regarding drug quality in Uganda, which was released Saturday, May 17. Weaknesses were noted in the article, such as a small sample size (for example, only three samples of one particular antimalarial drug found in Uganda were tested) and a non-representative sample area (the samples for Uganda were collected from Kampala, not nation-wide). The weaknesses were later discussed with workshop trainees to help them better plan their nation-wide pharmacovigilance study.

Monday, May 19, 2008
An opening ceremony was held to welcome the workshop trainees (*Annex 2*) and to present the goals and expected outcomes of the workshop. Afterwards, the workshop trainees were taken to the lab, given a safety tour, and introduced to the Minilab® system. Each trainee was given a training manual that included the methods and forms to be used in the workshop as well as contact information, additional background materials, and the workshop evaluation form.

Tuesday, May 20, 2008
The USP DQI team commenced the hands-on portion of the workshop by dividing the trainees into five groups, with analysts of different experience levels in each group. This was done to assure the less-experienced trainees gained knowledge from the experienced trainees.

For the first sample tested – amodiaquine hydrochloride tablets – emphasis was placed on complete documentation, proper solution labeling, good laboratory testing procedure, calculations, and reporting. Each trainee individually performed the visual inspection and the TLC procedures. Documentation was checked for completeness and hands-on instruction in laboratory techniques, such as pipetting, was given. Different strengths tablets of amodiaquine hydrochloride were tested and the calculations related to the procedure were done in a group manner on a flip chart; then the simple disintegration procedure was demonstrated and performed by each group.

Wednesday, May 21, 2008
Each trainee individually tested artesunate tablet samples in the morning. In the afternoon, each group tested artemether samples and began using teamwork to share the preparation of solutions. However, trainees individually prepared and tested their own TLC plates to strengthen their technical ability.

Thursday, May 22, 2008
Each group was asked to divide the solution preparation tasks. This was done to simulate working together in the field and reinforce consistent results as each trainee prepared and tested their own TLC plate using the shared solutions. The dividing of tasks gave an exercise in communication, proper labeling, and sharing of resources. The trainees performed the five different procedures needed to screen these artemisinin-based combination therapies (ACTs) and fixed dose combination (FDC) antimalarials:

- Sulfadoxine/Pyrimethamine tablets
- Mefloquine tablets
- Quinine sulfate tablets
- Coartem tablets (artemether and lumefantrine)

After the testing was completed, Dr. Davydova had a summary meeting and asked each group to discuss their findings. One group found a substandard (less than 80%) lumefantrine sample.

Friday, May 23, 2008
The Minilab® systems were inventoried for completeness and repacked for shipment to the sentinel sites. These presentations were made to the trainees:

- David Ekau gave a "Presentation on Sampling," a discussion of the observations and real-world issues encountered on a recent sample collection trip. Mr. Ekau contracted malaria while on this collection trip.
- Dr. Davydova gave a presentation on "Good Sampling Planning" in which she discussed the sampling protocol in detail.

Dr. Davydova reviewed the workshop goals to ensure the outcomes were met. During the closing ceremony, Certificates of Accomplishment were handed out to all the participants who completed the workshop. Representatives from the NDA, USAID, and the press attended.

Meetings

Tuesday, May 20, 2008
Dr. Davydova met with the lab director, Dr. Antonia Nakamya, to discuss the budget for the next three months of the program. Dr. Davydova then met with David Ecru and Dr. Nakamya to update the sampling strategy and the location of the Minilab® sentinel sites. The attendee from one of the sites was unable to make the training, so that site location was changed.

Wednesday, May 21, 2008
Dr. Davydova and Dr. Nakamya traveled to the NDA to meet with the information department and to discuss pharmacovigilance activities. They met with Moses Ogaa, Drug Assessment and Registration Officer, and discussed:

- Future post-marketing surveillance activities

- Newly developed software
- Upcoming training of inspectors by a consultant

Dr. Davydova and Dr. Nakamya traveled to USAID/Uganda to meet with the PMI staff. The regular contact, Betty Nakamiya, was on a trip, so they met with Rachael Cintron, Population, Health & Nutrition Officer, Health HIV/AIDS & Education Officer, Health Team Leader; and Dr. Patrick Okello, Program Management Specialist, and discussed:

- An update on USP DQI activities in Uganda
- Future pharmacovigilance activities

The USAID staff requested the work plan for the following year to be sent to them at a later time for planning purposes.

Monday, May 26, 2008
Dr. Davydova attended meetings at NDQCL to plan testing of samples collected for the quality of Antimalarials in Sub-Saharan Africa (QAMSA) study with the Minilab®.

Tuesday, May 27, 2008
Dr. Davydova met with NDQCL staff to continue planning for the QAMSA study and post-marketing surveillance study. Dr. Davydova also met with NDA staff (*Annex 3*) working at the National Pharmacovigilance Center (NPC) to discuss progress, gaps, and proposed activities. The Center was established at the NDA in the Department of Drug Information in 2005.

Next Steps

- The monitoring of the quality of antimalarial drugs at the central and the periphery areas (Hoima/Lira, Jinja, Mbarara, and Tororo) will begin. One round of collecting and testing will be completed before the end of the fiscal year. USP DQI will collaborate with NDQCL on the testing of drugs collected, the data will be reviewed, and a report will be shared with the partners.
- In collaboration with the NDA, the FY09 work plan will be finalized in accordance with the Malaria Operational Plan (MOP).

Annex 1

News Article on Drug Quality in Uganda released May 17, 2008

SATURDAY Vision

Vision Group INNOVATION AND EXCELLENCE VOL.2 No.020 Saturday, May 17, 2008 Price: Ush1,200 (Ksh60 TzSh900 RF600)

FAKE MALARIA DRUGS ON SALE

BY CHARLES WENDO

MORE than a third of the anti-malarial medicines sold in Kampala are either counterfeit or are not strong enough to cure the disease, a survey has revealed.

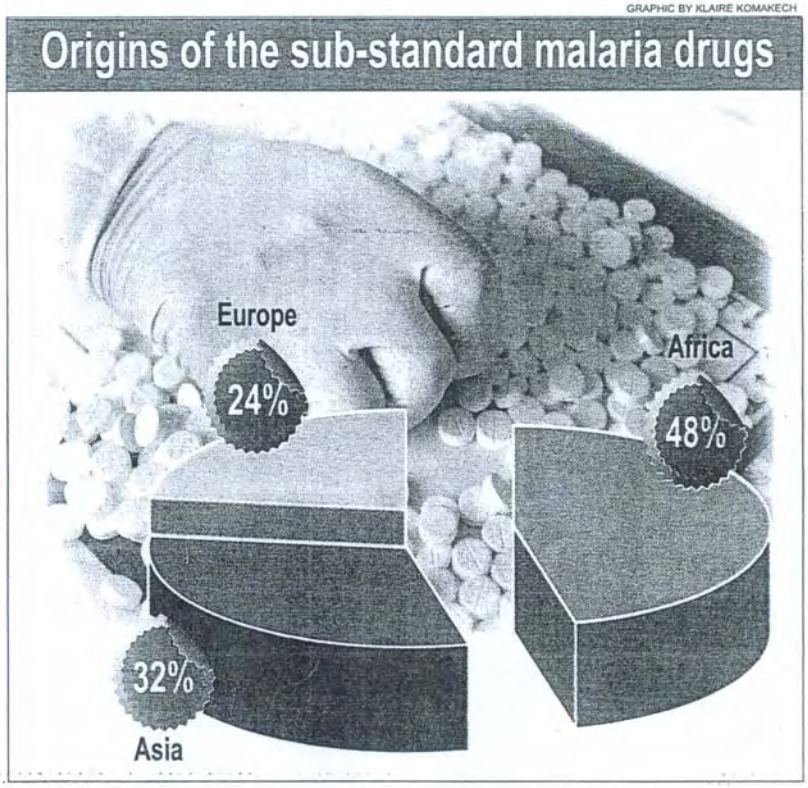
Because of this, scientists warn, malaria could easily become resistant to the new generation of medicines that have replaced chloroquine.

"We did not quantitatively estimate the public health impact of this crisis, but it must be staggering," the researchers wrote in the online journal *Public Library of Science* last weekend.

Should malaria become resistant to the new drugs, the researchers warn, sub-Saharan Africa could suffer another surge of the disease, as was the case in the 1990s.

TURN TO PAGE 3

GRAPHIC BY KLAIRE KOMAKECH



Annex 1, continued

FROM PAGE ONE

Sub-standard malaria drugs being sold

"SUBSTANDARD drugs not only endanger lives today, but also jeopardise future malaria treatment strategies by accelerating parasite resistance," said Roger Bate of the American Enterprise Institute, who led the research.

In the study, research assistants posing as ordinary customers bought various antimalarials from randomly selected pharmacies in Kampala.

They found that 35% of the drugs sampled were either fake or had less quantities of ingredients than required.

Similar tests were done in Ghana, Kenya, Nigeria, Rwanda and Tanzania. Kenya appeared to have the highest percentage of inefficient drugs (38%), followed by Uganda and Ghana (35%), Rwanda (33%), Tanzania and Nigeria (32%).

The drugs sampled were sulfadoxine-pyromethamine (commonly known as fansidar), amodiaqine (commonly known as camaquin), mefloquine, artesunate, artemether, dihydro-artemisinin and artemether-lumefantrine (commonly known as Coartem).

Overall 48% of the sub-standard drugs were made in Africa, while 32% were made in Asia. Contrary to popular belief that European drugs are of high standards, the researchers found that 24% of the sub-standard drugs were of European origin.

Even expensive drugs were found to be sub-standard. For instance, dihydro-artemisinin costs between sh8,000 and sh10,000 per adult dose, yet, two thirds of the samples were found to be sub-standard.

It is not clear how the sub-standard medicines enter the Ugandan market. The National Drug Authority (NDA) says it tests every batch of anti-malaria medicines imported into the country. Similarly, NDA says it tests every batch of anti-malarial manufactured locally.

"To find 35% of pharmacies selling sub-standard anti-malarials raises a lot of questions given the quality control measures of NDA", comments Dr. Richard Odoi Adome, an NDA board member.

"In the past, we asked the manufacturers and importers to give us samples for testing. But we discovered that some would give us only good samples and sell something different. Now we take our own sample from each batch at a random."

Adome suspects the sub-standard medicines are smuggled into the country, bypassing NDA's testing system. Such smuggled medicines are more likely to be found in drug shops than in registered pharmacies, he believes.

The Uganda Pharmaceutical Society acknowledges that there are counterfeit drugs in Uganda but doubts the researchers' figures.

"NDA is very vigilant at entry points though I can't say it is 100% perfect," said the society's secretary general, Swaibu Mukiibi. "I advise the public to buy medicine only from registered pharmacies. To buy from the small shops is to abet the problem."

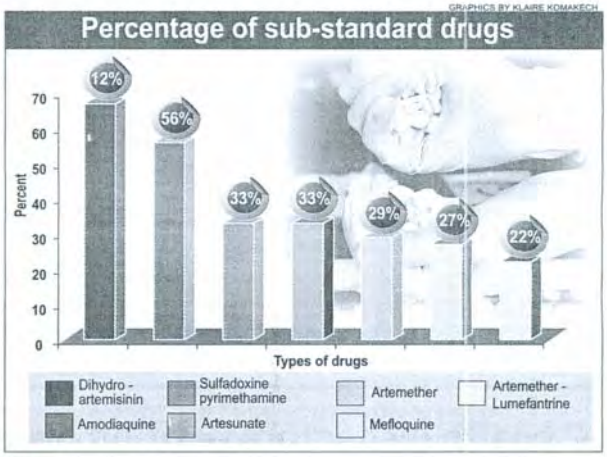
He adds that the public perpetuates the problem by looking for cheaper options. "Usually counterfeit drugs are cheaper."

Dr. Francis Epetait, shadow minister for health, thinks the researchers' figure might be an under-estimate.

"It is not enough to test the medicines at the point of entry into the country," he says.

The Pharmacy Bill on medicines regulation, currently before Parliament, will not solve the problem unless the Government puts in place mechanisms for routine sampling and testing in pharmacies and drug shops, he argues.

GRAPHICS BY KLAIRE KOMAKECH

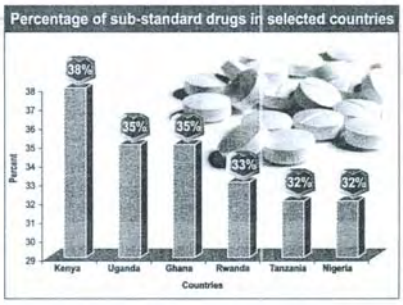


"Uganda has become a dumping ground, not only for medicines but for other products as well," he says. "We have failed to enhance an institution that would help us in quality control."

A source in NDA said they do not have the capacity to do routine sampling and testing of medicines, technically called post-market surveillance.

NDA has a hi-tech laboratory but not the human resources and funding that is required to go around the country sampling drugs.

The drug authority has only eight drug inspectors countrywide, regulating the over 400 pharmacies. Three of the inspectors are in Kampala and five are upcountry.



"UGANDA HAS BECOME A DUMPING GROUND, NOT ONLY FOR MEDICINES BUT FOR OTHER PRODUCTS AS WELL. WE HAVE FAILED TO ENHANCE AN INSTITUTION THAT WOULD HELP US IN QUALITY CONTROL."

Dr. Francis Epetait, shadow minister for health

Annex 2

Workshop Participants

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30	Ms. Sarah Kainza	n/a
31	Ms. Judith Nyanzi	n/a
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33	Ms. Lynn Ninsiima	n/a
34	Mr. Frank Nyakahuma	n/a
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Annex 3

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