

Supervision of Minilab[®] Training, Review of Drug Quality Monitoring Results, and Preparation for Upcoming Pharmacovigilance Activities

Antananarivo, Madagascar, October 9-17, 2008

Trip Report

Dr. Mustapha Hajjou
Program Manager

**U.S. Pharmacopeia Drug Quality
and Information Program**
12601 Twinbrook Parkway
Rockville, MD 20852 USA
Tel: (+1) 301-816-8160
Fax: (+1) 301-816-8374
Email: uspdqi@usp.org

Cooperative Agreement # HRN-A-00-00-00017-00
Sponsoring USAID Mission: USAID/Madagascar
Grantee: United States Pharmacopeia Drug Quality and Information (USP DQI) Program
Author(s) Name: M. Hajjou
Language: English
Date of Publication: November 26, 2008



This report is made possible by the generous support of the American people through the United States Agency for International Development (USAID), under Cooperative Agreement number HRN-A-00-00-00017-00. The contents are the responsibility of the U. S. Pharmacopeia Drug Quality and Information Program and do not necessarily reflect the views of the United States Government.

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

Dr. Hajjou traveled to Madagascar to supervise Minilab[®] training, review the drug quality monitoring report, discuss planned activities relating to pharmacovigilance, and meet with partners.

Key Words

Madagascar, training, ACTs, sentinel sites, antimalarial medicines, pharmacovigilance, NDQCL, USAID, and USP DQI

Table of Contents

<u>Acronyms</u>	4
<u>Acknowledgements</u>	5
<u>Background</u>	6
<u>Purpose of Trip</u>	6
<u>Source of Funding</u>	6
<u>Overview of Activities</u>	6
<u>Next Steps</u>	9
<u>Annex 1: List of participants</u>	10

ACRONYMS

ACT	Artemisinin-based Combination Therapy
AMM	Agence du Médicament de Madagascar
CDC	U.S. Centers for Disease Control and Prevention
CSB	Centre de Sante de Base
DIC	Drug Information Center
DULMT	Direction des Urgences et de la Lutte contre les Maladies Transmissibles
CNPM	Centre National de Pharmacovigilance de Madagascar
HPLC	High Performance Liquid Chromatography
MDA	Mass Drug Administration
MOH	Ministry of Health
NDQCL	National Drug Quality Control Laboratory
NPCM	National Pharmacovigilance Center of Madagascar
PMI	President's Malaria Initiative
PV	Pharmacovigilance
QAMSA	Quality of Antimalarials in Sub-Saharan Africa
SLP	Service de lutte contre le Paludisme
SP	Sulfadoxine/Pyrimethamine
UCTMG	University of Chinese Traditional Medicine of Guangzhou
USAID	United States Agency for International Development
USP DQI	United States Pharmacopeia Drug Quality and Information Program
WHO	World Health Organization

ACKNOWLEDGEMENTS

USP DQI staff would like to express sincere appreciation to Dr. Jean René Randriasamimanana, the Director of l'Agence du Medicament de Madagascar (AMM). Special thanks go to Dr. Yvette Rakotobe, Head of the National Drug Quality Control Laboratory (NDQCL); Dr. Donat and Dr. Lock from the pharmacovigilance unit; and all AMM staff for their availability and for coordinating the visit. Many thanks go to Dr. Alyssa Finlay, U.S. Centers for Disease Control and Prevention (CDC) resident adviser, for her time and assistance.

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

Background

With the support of USAID/Madagascar, USP DQI has been providing technical assistance to l'Agence du Medicament de Madagascar (AMM) focusing on strengthening the drug quality assurance system in the country. Areas of intervention include strengthening the national drug quality control laboratory (NDQCL) and its drug registration, establishing a drug quality post-marketing surveillance program, and helping establish and strengthen the national pharmacovigilance (PV) program.

Since the inception of the USP DQI program in Madagascar, NDQCL has tested 1,668 samples as part of the drug quality monitoring program. As a result of this activity, AMM has withdrawn 31 lots from the market. PV expertise has expanded to the regional level, and efforts are being made to bring it to the district level. In 2008, NDQCL was also involved in the Quality of Antimalarials in Sub-Saharan Africa (QAMSA) study and carried out one round of sampling and testing. USP DQI is currently conducting confirmatory testing on these samples.

The success of these programs is made possible by the dedication of AMM staff and continuous support from USAID.

Purpose of Trip

Dr. Hajjou made this trip to supervise training on Minilabs[®], review the report on drug quality monitoring, and discuss planned activities in pharmacovigilance.

Source of Funding

This trip was supported with funds from USAID/Madagascar.

Overview of Activities

Meeting at USAID Mission

Dr. Hajjou met with Dr. Alyssa Finlay, CDC Resident Adviser, to discuss pharmacovigilance activities and planned activities. The focus of the meeting was on the inclusion of sentinel sites into the PV program to report adverse drug events to the National Centre of Pharmacovigilance of Madagascar (NCPM). Currently there are two sentinel surveillance systems: 1) fever sentinel sites run by Institute Pasteur-Madagascar (IPM) and Direction des Urgences et de la Lutte contre les Maladies Transmissibles (DULMT) and 2) Twelve malaria sentinel surveillance sites for epidemic surveillance ("postes sentinel"). In 2009, the sentinel sites will be expanded beyond epidemic surveillance to include general malaria surveillance with an anticipated total of 44 sites by the end of 2009. The number of sites is expected to increase to 36 in 2009 and 66 in 2010-2012. Dr. Finlay mentioned that the IPM/DULMT fever existing sentinel sites handle considerable work, and suggested the possibility of including PV in the new malaria sentinel surveillance sites that will focus mainly on malaria because these sites will have dedicated personnel at the district level to help supervise operations at the Centre de Sante de Base (CSB) and hospital level in the target districts.

Dr. Finlay also mentioned the planned Mass Drug Administration on Nosy Be, supported by Chinese partners, using the drug Artequick. She suggested that Dr. Hajjou see it if it would be possible to focus pharmacovigilance efforts in this region during the planned Mass Drug Administration (MDA).

Meeting with the Director of AMM

The Director, Dr. Jean René, expressed his appreciation and gratitude for the continued support of USP DQI and USAID/Madagascar. Dr. Jean René was thankful for the establishment of the Drug Information Center (DIC) and expressed his wish for increased USP DQI support in pharmacovigilance and drug registration units and with training the laboratory staff to acquire additional skills. He emphasized the need for training lab staff on the use of the High Performance Liquid Chromatography (HPLC) system donated in 2007 by USP and requested that the training be provided in French. Dr. Jean René stressed the need for disseminating the information about the work achieved in drug quality surveillance and pharmacovigilance. As for drug registration, the service is in a dire situation. It has only two staff, and they need training on computerized registration systems to cope with the amount of work. Many drugs circulating in the market are not registered. Dr. Jean René mentioned that AMM is talking with customs to collaborate on the control of drugs entering the country. Based on the information that AMM will provide, customs will retain any drug that is not registered.

Because of the increased costs to run the drug quality monitoring program, the resources provided will not cover supervisory activities for the next round. Dr. Jean René announced that AMM will carry out the supervisory and monitoring activities at its own expense. However, these activities will be limited to the sentinel sites accessible by road.

Dr. Jean René informed Dr. Hajjou that he visited the facilities of the Chinese manufacturer of “Artequick”, a fixed dose combination of Artemisinin and Piperaquine phosphate. Artequick will be used in a mass treatment study in the island Nosy Be in the north of the country.

Meeting with Drug Quality Control Laboratory (NDQCL)

Dr. Hajjou met with Dr. Yvette and the lab staff to discuss the Minilab[®] training and the report on drug quality monitoring activities.

Dr. Hajjou reviewed the latest report and asked Dr. Yvette if she could gather information on the registration status of the samples collected and tested at the sentinel sites. The samples of non-registered drugs were high especially for Quinine Sulfate and Sulfadoxine/Pyrimethamine (SP). Of the 31 quinine sulfate samples and 47 SP samples, 23 and 26 were not registered, respectively. About 42% of chloroquine phosphate samples were not registered. All the ACT samples were registered except one sample.

Two samples were confirmed substandard. AMM issued decisions to withdraw the two lots from the market.

During the week, Dr. Hajjou supervised the training in basic tests using Minilabs[®] and provided the trainers with the following recommendations:

- Each trainee should carry out a full set of testing
- Samples tested during the training should be different for each pair of trainees
- Each pair of trainees should present their results to the group
- The lab should dispose of acid and alkali waste after neutralization

A total of fourteen participants received the training (see Annex). Five analysts from NDQCL conducted the training.

Meeting with Pharmacovigilance Team

Dr. Hajjou met with Dr. Donat, Dr. Sabrina, and Dr. Antha to review the planning for upcoming activities. The discussion focused on the details of the budget for the training of health workers at the district level.

The Ministry of Health (MOH) requested that NPCM participate in an upcoming study conducted by the University of Chinese Traditional Medicine of Guangzhou (UCTMG) on mass treatment of malaria using Artequick supplemented with Primaquine. The study will take place in the island of Nosy Be. The institutions implementing the study include UCTMG, the national malaria control program “Service de Lutte contre le Paludisme” (SLP), the Regional Directorate of Health and Familial Planning Diana, the district health service of Nosy Be, and IPM.

The PV team has modified the plans for the health worker training to include the district of Nosy Be; the training will take place in early November, 2008. Dr. Hajjou recommended including the district of Ambanja which will be used as a control zone in the study. The training in this district will be conducted following the completion of the training in Nosy Be. Under the supervision of NPCM staff, regional trainers will conduct the training in Nosy Be, then independently in Ambanja. Dr. Hajjou suggested designating focal points at each district to follow up with trained health workers. The monitoring of the safety of Artequick is highly important because there is a lack of data on the safety of the combination Artemisinin/Piperaquine supplemented with Primaquine. The study is also a good opportunity to assess the safety of Artesunate/Amodiaquine combination which will be used as treatment in the control zone.

Meeting with the Director of Joseph Ravoahangy Hospital

Dr. Hajjou made a courtesy visit to Dr. Bruno Andriamiarina, Director of Joseph Ravoahangy Hospital, and thanked him for selecting two physicians to run the DIC. Dr. Hajjou thanked Dr. Bruno for his collaboration and enthusiasm for the DIC and his selection of two physicians as staff to run the center. The two physicians were receiving training at the Centre Anti Poison and Pharmacovigilance of Morocco at the time of the visit. Dr. Bruno expressed his interest in more collaboration in which the DIC will play an important role.

Meeting with CDC, WHO, and the pharmacovigilance team at AMM

Participants:

Dr. Alyssa Finlay, CDC Resident Advisor

Dr. Donat, Head of CNPM

Dr. Sabrina Lock Njarasoa, CNPM staff

Dr. Luciano Tuseo, WHO Madagascar

Dr. Finlay gave an overview of the existing sentinel sites and mentioned that the workload at the IPM/DULMT Fever Surveillance sentinel sites was high; consequently, these sites may not provide efficient support for the PV program. Malaria surveillance sentinel sites, on the other hand, provide a good opportunity for integration into the program. There are 12 sentinel sites, and Global Fund Round-7 and the President’s Malaria Initiative (PMI) will support the establishment of an additional 32 sites by the end of 2009. One physician will run each site, and selection and hiring of the physicians is underway. Dr. Tuseo confirmed that 44 sentinel sites will be created by the end of 2009. The number is expected to reach 66 by the end of 2010. Although there are 111 districts in Madagascar, Dr. Tuseo indicated that staff will cover 1-2 districts each. The participants discussed the way to proceed with the inclusion of the sentinel

sites in the PV program, and it was agreed that CNPM will train the recruited physicians in Antananarivo. This training could be provided at the time when training on the malaria program and malaria surveillance is conducted.

The group also discussed the upcoming series of PV trainings for district-level health workers.

Debriefing USAID Mission

Because of scheduling conflicts, Dr. Noë Rakontodrajaona was not available to meet. Dr. Hajjou had a follow-up meeting with Dr. Finlay who was to convey the outcome of the meeting to Dr. Noë. Dr. Hajjou and Dr. Finlay discussed the results of the latest round of sampling and testing of anti-malarial drugs and the issue of non-registered drugs circulating in the market. There is a need to strengthen the drug registration unit. Dr. Hajjou indicated that the program supported by USP DQI had been fruitful but needed sustained support. The following areas identified:

- Expand PV training of health workers to other districts and sensitize the public to issues of drug safety. This year, CNPM staff will train 300 health workers in 8 of 111 districts.
- Maintain the drug quality monitoring program and include drugs other than antimalarials. The status of the quality of such drugs has been left unchecked.
- Support drug registration training in WHO's SIAMED software. A high number of drugs circulating in the market are not registered.
- Strengthen NDQCL with additional training and equipment.
- Support dissemination of information regarding drug quality and drug safety. This can be done through publications, public announcements and other media available to AMM and the DIC.

Next Steps

- Complete the training of health workers at the district level
- Conduct confirmatory testing for QAMSA study at the USP laboratory
- Follow up on DIC activities
- Follow up on drug quality monitoring activities at the sentinel sites

List of Participants in the Basic Tests Training

Nom et Prénoms	REGION
RASOANAIVO Fenomanana	Toamasina
ANDRIATSITOHAINA Haingo	Toamasina
ANDRIAMANANJARASOA Hanitriniaina	Antsiranana
RAKOTOMALALA Hanta Béatrice	Antsiranana
RAKOTOARITSIMA Tovonjanahary Ndrianjafimandaso	Tolagnaro
RAFANOMEZANTSOA Adolin	Tolagnaro
RATSIMBAZAFY Lalaina Basilisse	Mahajanga
Jonah Madimadisoa Razafindramaly	Mahajanga
RANJEVAMALALA Danny	Toliara
RAMAHELINARIVO Augustin	Toliara
RAZAFINDRASOA Tahina Harinivo	Antananarivo
NIAIN'NY FELAMBOAHANGY Lalaso	Antananarivo
RAKOTOARIMANANA Claudia Mbolatiana	Fianarantsoa
RAZAFIMAHATRATRA Heritiana	Fianarantsoa