

Strengthening Drug Quality Assurance Systems in Mali: Workshop to Establish an Operational Pharmacovigilance Program and Training in Drug Registration, Good Laboratory Practices, and Basic Pharmacopeial Testing

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Trip Report

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About USP DQI

The Drug Quality and Information (DQI) Program is implemented by the United States Pharmacopeia (USP) and funded by the U.S. Agency for International Development (USAID) (Cooperative Agreement HRN-A-00-00-00017-00). The DQI Program 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. 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

USAID/President's Malaria Initiative selected USP DQI to assist Mali in strengthening its medicines quality assurance. In September 2008, a DQI team conducted a three-day assessment of drug quality assurance and drug quality control capabilities of Mali. After identifying the gaps, DQI developed a work plan to strengthen the national drug regulatory authority (Direction de la Pharmacie et du Médicament or DPM), the national quality control laboratory (Laboratoire National de la Santé or LNS) and to help establish an operational pharmacovigilance program.

Dr. M. Hajjou and Mr. S. Bradby traveled to Bamako, Mali to provide training to the staff of the Drug Quality Control Laboratory (DQCL) at the LNS, to facilitate training on the appropriate use of WHO's SIAMED software in drug registration and drug import verification, and to facilitate a workshop to establish an operational pharmacovigilance program.

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Key Words

Dissolution, DPM, HPLC, Good Laboratory Practices, LNS, pharmacovigilance, SIAMED

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The team would like to thank the participants in the laboratory training and the drug registration training for their dedication and all the participants in the pharmacovigilance workshop for their contributions and inputs.

The authors would like to thank Dr. Daouda Touré for coordinating the activities. The DQI team would also like to express their sincere gratitude to USAID PMI Malaria Advisor Mr. Sixte Zigirumugabé for his support and assistance during this trip.

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ACRONYMS

CAPM	Centre Anti Poison et de Pharmacovigilance du Maroc
CNAM	Centre National d'Appui à la lutte contre la Maladie
CNRP	Centre National de Référence de Pharmacovigilance
DPM	Direction de la Pharmacie et du Médicament
DQ	Drug Quality
DQI	Drug Quality and Information Program
LNS	Laboratoire National de la Santé
MOH	Ministry of Health
DQCL	Drug Quality Control Laboratory
PMI	President's Malaria Initiative
PNLP	Programme National de Lutte contre le Paludisme
QA	Quality Assurance
QC	Quality Control
USAID	United States Agency for International Development
USP	United States Pharmacopeia
WHO	World Health Organization

Background

In December 2005, Mali was selected as one of the fifteen countries to receive President's Malaria Initiative (PMI) funding. United States Pharmacopeia Drug Quality and Information Program (USP DQI) was selected to implement the PMI program relating to drug quality and pharmacovigilance. The DQI Program conducted an assessment of Mali's medicines quality control and quality assurance (QA/QC) capabilities in September 2008. Following the assessment, DQI developed and proposed a work plan focused on strengthening the national drug control laboratory, drug registration processes, and the safety of medicines.

The drug quality control segment included providing the laboratory with basic equipment and training in pharmacopeial testing methods and basic principles of good laboratory practices. As for strengthening drug registration processes, DQI proposed to facilitate the training of staff from the Direction de la Pharmacie et du Médicament (DPM, the drug regulatory authority) on drug registration and drug import verification using the World Health Organization's (WHO) SIAMED software. Regarding the strengthening of drug safety, DQI proposed to facilitate a micro-planning workshop to establish an operational pharmacovigilance program.

Purpose of Trip

USP DQI staff traveled to Bamako, Mali, to:

1. Meet with DPM, WHO-Mali, USAID/Mali, and the Laboratoire National de la Santé (LNS, the national quality control laboratory) to discuss the topics of the visit and prepare the planned activities.
2. Train the national laboratory staff on Good Laboratory Practices and compendial testing using High Performance Liquid Chromatography (HPLC) and Dissolution.
3. Facilitate training of drug registration officers from DPM in drug registration and drug import verification using WHO's SIAMED software.
4. Facilitate a micro-planning workshop to establish an operational pharmacovigilance program.

Source of Funding

This activity was funded by the USAID Mission in Mali, PMI Program.

Overview of Activities

I. Preparation and discussion of the planned activities

The DQI team briefed Mr. Sixte Zigirumugabé and Mr. Bob de Wolfe at USAID/Mali on the planned activities. The team inquired about the lab supplies that DQI shipped for the training and was informed that the consignment was cleared and the delivery was expected the following day. Mr. Zigirumugabé emphasized the importance of working closely with DPM. He also recommended collaborating with SPS. Mr. Wolfe talked about SINO, a contraceptive implant manufactured in China. It represented a cheaper alternative to another implant that USAID procured in the past. Mr. Wolfe asked whether USP DQI could assist with the WHO prequalification of the manufacturer.

The DQI team and Dr. Daouda Touré, focal point for pharmacovigilance activities, met with Pr. Ousmane Doumbia, Director of DPM, and discussed the planned activities. Pr. Doumbia assured the DQI team of his support and willingness to provide any assistance needed.

The DQI team visited LNS and met with Pr. Benoit Yaranga Koumare, Director of LNS, and Dr. Djibril Tamba Konate, in charge of drug quality control activities. Pr. Koumare welcomed the DQI team. He indicated that he was very enthusiastic about the program with USP DQI and hoped that this collaboration will help to strengthen the capacity of LNS to reach higher levels of competency. The group went through the training manual and discussed the content of the training; the group also discussed future activities including the possibility of establishing a countrywide postmarketing surveillance program. Pr. Koumare welcomed the idea and indicated that he will discuss it with the scientific board which was going to hold its meeting the same week of the training at LNS.

Dr. Hajjou and Dr. Daouda Touré met with Pr. Abdel Kader Traore, Director of the Centre National d'Appui a la lutte contre la Maladie (CNAM). The Ministry of Health designated CNAM to host the national centre of pharmacovigilance called the Centre National de Référence de Pharmacovigilance (CNRP). Dr. Hajjou emphasized the importance of CNAM's role in the preparation of and the participation in the workshop. He invited Pr. Traore to the coordination meeting intended to finalize the agenda of the workshop. Pr. Traore reiterated his willingness to actively contribute to the discussions and indicated that there was a need to well define CNRP's role in the national pharmacovigilance program.

Dr. Hajjou met with Dr. Minkaila Maiga, Advisor on Essential Medicines at WHO/Mali, to describe the planned activities. The discussion focused on the pharmacovigilance workshop. Dr. Maiga indicated that CNAM needs to be strengthened and its role in pharmacovigilance well defined. He also indicated that all the health programs should be involved. Dr. Maiga and Dr. Hajjou agreed emphasis should be placed on strengthening the pharmacovigilance system at the central level before building capacity at the regional level.

Workshop coordination meeting

Participants in the meeting: Dr. Minkaila Maiga, WHO-Mali; Pr. Abdelkader Traoré, CNAM; Dr. Aïssata Touré Diallo, DPM; Dr. Fanta Sangho Sango, DPM; Dr. Safoura Berthé Cisse, National Malaria Control Program; Dr. Daouda Macan Touré, DPM; Pr. Rachida Soulaymani, CAPM; Dr. Houda Sefiani, CAPM; Dr. Mustapha Hajjou, DQI

The aim of the meeting was to finalize the agenda and the terms of reference of the workshop. It was decided to reduce the time of the plenary presentations to dedicate more time to the working groups. Two presentations, one on the status of pharmacovigilance in Mali and the other on the ministerial order regarding the structure of pharmacovigilance, were added. The terms of reference were modified to put more emphasis on developing an action plan and a new reporting form, and defining the flow of reporting.

II. Laboratory training

The training was conducted in English and French. Ten participants from LNS attended.

Item	Description
Training Objectives	<ul style="list-style-type: none"> ✓ Training on basic principles of Good Laboratory Practices ✓ Training on appropriate use of USP NF: General Notices ✓ Training on Dissolution ✓ Training on management of Dissolution data ✓ Training on HPLC ✓ Training on management of HPLC data
Venue	LNS, Bamako, Mali
Local Organizers	DPM and LNS
Course Proceedings	<p>The Training was organized as follows:</p> <p>Day 1: Opening, Presentation on Good Laboratory Practices</p> <p>Day 2: Presentation on the appropriate use of USP General Notices Dissolution: Physical calibration of Dissolution tester</p> <p>Day 3: Dissolution testing of Amodiaquine Tablets HPLC: system suitability</p> <p>Day 4: Calculations and review of Dissolution data HPLC: Assay of Amodiaquine Tablets</p> <p>Day 5: Calculations and review of Assay data General discussion</p>
Participants	Ten staff from DQC trained.
Lab supplies Provided	All materials provided by USP DQI are indicated in the List of Supplies sent to LNS
Closing Ceremony	Following the closing remarks, certificates were awarded to all participants who successfully completed the course.
Course Outcomes	<p>At the end of the course, participants were able to:</p> <ul style="list-style-type: none"> ✓ Understand and apply the basics of Good Laboratory Practices ✓ Understand and apply USP General Notices ✓ Carry out Dissolution testing following pharmacopeial methods ✓ Carry out HPLC testing following pharmacopeial methods. <p><i>It is important to note that during the training, a substandard sample was found by the trainees. The sample failed the Assay test.</i></p>
Course Evaluation	Participants were asked to evaluate each of the course modules and sessions by filling out the Course Evaluation Form.

Discussion and recommendations:

- According to the participants, all the training modules were useful. They suggested a follow-up training and an evaluation of staff capabilities for planning future training.
- During the training, the DQI team noticed the lack of appropriate glassware for reagents and samples preparation. Other small laboratory supplies were also lacking. The DQI team suggested to the laboratory manager to prepare a list of laboratory supplies needed.
- The DQI team recommended that staff should not access the room currently used as a lunch room through the laboratory. This will avoid transferring food to the laboratory. The exit door of this room was not used to either enter or exit the lab. The team suggested that a separate room should be used for food. This will permit two exits for the lab.
- The DQI team provided recommendations on the arrangement of equipment and laboratory supplies to make the best use of the space available.

III. Drug Registration Training

Mr. Imed Lassoued and Mr. Youssef Khedher, WHO experts from DPM-Tunisia, conducted the training. Nine participants from DPM attended.

Item	Description
Training Objectives	<ul style="list-style-type: none"> ✓ Installation of the new version of SIAMED software ✓ Training in SIAMED to issue Marketing Authorization License (MAL) ✓ Training on Import Verification module
Venue	DPM, Bamako, Mali
Local Organizers	DPM
Course Proceedings	<p>Day 1: Review of drug registration procedures at DPM Review of data previously entered into SIAMED Installation of the new version of SIAMED</p> <p>Day 2: Training on SIAMED Acquisition of data Rejection, deletion, modification, and renewal of MALs Import verification: acquisition of invoices, search into data, and printing of reports</p> <p>Day 3: Training on SIAMED Generation and printing of model letters Search into registration data to generate printable reports</p> <p>Day 4: Practice Day 5: Practice, General discussion</p>
Participants	Nine staff from DPM.
Course Outcomes	At the end of the course, participants were able to: Understand and appropriately use SIAMED software for drug registration and drug import verification.
Course Evaluation	Participants were asked to evaluate each of the course modules and sessions by filling out the Course Evaluation Form.

Recommendations to DPM:

- Designate specific tasks to each staff member
- Develop a working plan to enter all data from old and new dossiers
- Contact WHO experts in Tunisia for technical support
- Plan to send at least two staff members to DPM-Tunisia for advanced hands-on training

IV. Pharmacovigilance workshop

The workshop was held at Azalai Nord Sud hotel in Bamako, and 64 participants attended the workshop. Dr. Amara Cherif Traoré, technical advisor for the Minister of Health, chaired the sessions. Pr. Rachida Soulaymani, Director of the Centre Anti Poison et de Pharmacovigilance of Morocco (CAPM), and Dr. Houda Sefiani from CAPM conducted the workshop

Pr. Ababacar Maiga, Deputy Director of DPM, welcomed the participants and thanked USAID/Mali, the pharmacovigilance experts, and USP DQI. He said that because all medicines inherently possess risk factors, it is important to monitor their potential adverse reactions. Mr. Sixte Zigirumugabé, PMI Malaria Advisor/Program Coordinator at USAID/Mali, expressed his pleasure at attending at the opening of the workshop. The presence of USAID reflected the importance of pharmacovigilance. He indicated that pharmacovigilance activities, along with medicine quality monitoring, could minimize the exposure of the public to ineffective and/or substandard medicines. He emphasized that establishing an operational pharmacovigilance program would require determination and good coordination between all the stakeholders. Mr. Zigirumugabé thanked the government of Mali for supporting such a program.

Dr. Amara Traoré expressed his pleasure for chairing the workshop. On behalf of the Minister of Health, he welcomed the participants. He emphasized the importance of the workshop and the necessity to follow WHO recommendations relating to pharmacovigilance. Dr. Traore indicated that attempts to initiate pharmacovigilance activities in Mali were unsuccessful in the past and that the lack of efficiency in the distribution, collection, and analysis of adverse drug event reports was to blame. In light of the rollout of antiretrovirals and artemisinin-based combination therapies, the presence of counterfeiting, and globalization, the establishment of an operational pharmacovigilance program has become a necessity. It is time to review the whole system and work on new propositions.

The workshop proceeded with plenary presentations by Pr. Soulaymani and Dr. Sefiani and discussions. The presentations covered aspects relating to the extent of the problem of adverse drug reactions, spontaneous reporting (reporting form), causality assessments, developing a pharmacovigilance center, and pharmacovigilance as an international system. Following the presentations, four working groups were formed with the objective of making critical observations on the existing reporting form based on WHO recommendations that were presented to the participants and referring to two reporting forms (from Morocco and Togo) as examples. The terms of reference were to scrutinize the content of the forms and focus on:

- Necessary sections
- Basic criteria
- Missing elements
- Optional elements

All the groups presented and discussed their findings and observations. A small working was then formed to draft a new reporting form. The new draft was presented and discussed.

The second day started with three presentations. The first presentation dealt with the status of pharmacovigilance in Mali, and Pr. Traoré was the presenter. Dr. Touré gave the second presentation on the Ministerial Order defining the pharmacovigilance system. The third presentation was on pharmacovigilance and health programs, presented by Pr. Soulaymani.

After the presentations, six working groups were formed to discuss defining the flow of reporting and developing an action plan.

All the recommendations from the participants regarding the reporting form, the flow of reporting ADEs, and the action plan were compiled and used to draft a final document.

V. USAID Debriefing

On May 22, Dr. Hajjou met with Mr. Zigimurugabé and Mr. Wolfe at USAID/Mali and debriefed them on the implemented activities. He indicated that the lab training was an opportunity to do an additional assessment. The DQI team identified opportunities for improvement, such as the use of some instruments, safety procedures, and equipping the lab with necessary supplies. As for drug registration, Dr. Hajjou mentioned that in 2008, DPM did not use SIAMED. Consequently, the registration staff needed to enter many old data. Regarding the pharmacovigilance workshop, Dr. Hajjou indicated that he was pleased that Dr. Traoré, the technical advisor to the Minister of Health, attended the workshop and chaired the sessions. He was also pleased by the contribution of all the participants. He mentioned that more work was still ahead and indicated that a follow-up meeting was planned that same day to draft an action plan based on the outcomes of the workshop.

Dr. Hajjou presented an overview of activities that DQI was proposing based on the allocated PMI FY09 funding. He also presented an overview of activities that DQI would like USAID/Mali to consider for FY10 Malaria Operational Plan discussions.

VI. Follow-up meeting on pharmacovigilance

Participants in the meeting: Pr. Soulaymani, CAPM; Dr. Sefiani, CAPM; Dr. Diallo, DPM; Dr. Sango, DPM; Dr. Touré, DPM; Dr. Keita, CNAM; Dr. Hajjou, USP DQI

The aims of the meeting were to draft a national action plan and define the flow of information in reporting adverse drug events (ADE) based on the results of the workshop recommendations, the terms of reference, and the Ministerial Order. The reporting form was also finalized.

VII. Next Steps

- DQI will provide LNS with training in Ultraviolet-Visible spectrophotometry and quality systems
- DQI will follow up with major players in pharmacovigilance to plan next steps