

# Confirmatory Testing of Antimalarial Medicines and Refresher Training in Dissolution and High Performance Liquid Chromatography

Bamako, Mali  
December 6-10, 2010

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*Trip Report*

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## **Promoting the Quality of Medicines Program**

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PROMOTING THE QUALITY OF MEDICINES

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## **About PQM**

The Promoting the Quality of Medicines (PQM) program, funded by the U.S. Agency for International Development (USAID), is the successor of the Drug Quality and Information (DQI) program implemented by the United States Pharmacopeia (USP). PQM is USAID's response to the growing challenge posed by the proliferation of counterfeit and substandard medicines. By providing technical leadership to developing countries, PQM helps build local capacity in medicine quality assurance systems, increase the supply of quality medicines to priority USAID health programs, and ensure the quality and safety of medicines globally. This document does not necessarily represent the views or opinions of USAID or the United States Government. It may be reproduced if credit is given to PQM and USP.

## **Abstract**

The PQM team assisted lab staff in conducting compendial testing of antimalarial medicines that failed screening tests at the sentinel sites. The team also provided refresher training in Dissolution and HPLC.

## **Recommended Citation**

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## **Key Words**

Antimalarial, medicine quality monitoring, Minilab<sup>®</sup>, quinine sulfate, compendia, Mali

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## **ACRONYMS**

CNAM	Centre National d'Appui pour la Lutte Contre la Maladie
CNRP	Centre National de Réf é rence de Pharmacovigilance
DQI	Drug Quality and Information Program
DPM	Direction de la Pharmacie et du Médicament
GLP	Good Laboratory Practices
HPLC	High Performance Liquid Chromatography
LNS	Laboratoire National de la Santé
MOH	Ministry of Health
MQM	Medicine Quality Monitoring
PMI	President's Malaria Initiative
PNLP	Programme National de Lutte contre le Paludisme
PQM	Promoting the Quality of Medicines Program
PV	Pharmacovigilance
QA	Quality Assurance
QC	Quality Control
TLC	Thin Layer Chromatography
USAID	United States Agency for International Development
USP	United States Pharmacopeia
WHO	World Health Organization

## **Background**

The U.S. Agency for International Development (USAID) and U.S. Pharmacopeia (USP) have been assisting the Ministry of Health (MOH) of Mali in strengthening their medicine quality assurance systems, first through the USP Drug Quality and Information (DQI) program and, currently, through the Promoting the Quality of Medicines (PQM) program. Activities focus on strengthening the capacity of the Direction de la Pharmacie et du Médicament (DPM) and Laboratoire National de la Santé (LNS) in pharmacovigilance (PV), drug registration, and medicine quality control.

In 2009, following an assessment of Mali's quality assurance (QA) and quality control (QC) systems, PQM facilitated a workshop to establish a national PV system, conducted a training workshop on drug registration and drug import verification using the World Health Organization's (WHO) SIAMED software, and provided training to the staff of the LNS medicine QC laboratory. The lab training covered good laboratory practices (GLP) and testing for antimalarial samples using high performance liquid chromatography (HPLC) and dissolution. PQM has since provided refresher training in dissolution, conducted a thorough inventory of the lab equipment and supplies, and reviewed the lab quality manual and procedures.

In 2010, in collaboration with LNS, PQM established a postmarketing surveillance program focused on monitoring the quality of antimalarials. In addition to Bamako, the program involves seven regions where antimalarial samples are collected and tested using Minilabs<sup>®</sup>.

Review of the data from the sentinel sites showed that several quinine sulfate medicines lacking the active pharmaceutical ingredient (API) were detected.

## **Purpose of Trip**

Dr. HAJJOU and Dr. DIJIBA traveled to Bamako, Mali to assist LNS staff in conducting confirmatory testing on samples that failed Minilab<sup>®</sup> tests.

## **Source of Funding**

This trip was funded by USAID/Mali through the President's Malaria Initiative (PMI).

## **Overview of Activities**

### *Briefing USAID/Mali*

Dr. HAJJOU met with Dr. SADOU at USAID/Mali and gave an overview of the activities planned for the week. He informed Dr. SADOU that several samples of quinine sulfate tablets failed screening tests at the sentinel sites. Samples that failed Thin Layer Chromatography (TLC) tests using Minilabs<sup>®</sup> were shown to lack API. Dr. Hajjou provided a preliminary list of suspected fake quinine sulfate and also shared the PQM workplan with Dr. SADOU. The two discussed the possibility of hiring a consultant who could coordinate PQM activities in Mali.

### *Preparation of the lab testing*

The PQM team met with Pr. Benoît KOUMARE, Director General of LNS, who expressed his support for the planned testing of antimalarials. Then, the team met with the lab staff and reviewed the planned pharmacopeial testing of quinine sulfate and sulfadoxine-pyrimethamine (SP) tablets. In coordination with the PQM team, the lab staff established a list of reagents and lab supplies needed for the testing,

and with the help of Mr. SEDIBE, the focal point for medicine quality monitoring (MQM) activities, the group finalized the list of samples to be tested. Nine staff members from LNS participated in the testing.

*Proceeding and results of the testing*

The lab staff were organized in small groups with specific tasks. Mrs. DARANGO, one of the analysts, coordinated the groups' work and the PQM team supervised all the testing.

Nine quinine sulfate samples that were suspected to lack API after screening at the sentinel sites and one positive control sample were selected. Although the samples were collected from different sectors (both public and private), all the samples shared the same name: Quinine Sulfate 300 mg.

*Table 1- Summary of the confirmatory testing results:*

#	Name of Product	Lot number	Results of Confirmatory Testing
1	Quinine Sulfate	12349	Absence of API
2	Quinine Sulfate	452Q16	Wrong API
3	Quinine Sulfate	97668	Absence of API
4	Quinine Sulfate	080701	Wrong API
5	Quinine Sulfate	M08093	Absence of API
6	Quinine Sulfate	305510Q	Wrong API
7	Quinine Sulfate	2803-01	Wrong API
8	Quinine Sulfate	4400Q12	Absence of API
9	Quinine Sulfate	37361	Wrong API

Based on the information provided by the sentinel site teams regarding the putative manufacturers, samples 1, 3, and 9 seemed to be different lots of the same product; likewise, samples 2 and 8. However, neither the primary nor the secondary packages were available to confirm this assumption.

To illustrate the tests conducted on quinine sulfate samples, the results obtained for sample number 9 are presented below. The sample was labeled E23 in the lab. This sample contained neither sulfate nor quinine, and TLC and HPLC analysis showed that the sample contained a wrong API.



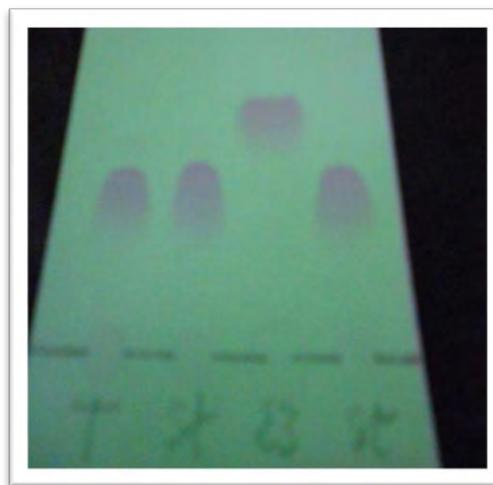
Identification test for quinine sulfate: the precipitate in the control indicates the presence of sulfate



Identification test for quinine sulfate: blue fluorescence indicates the presence of quinine

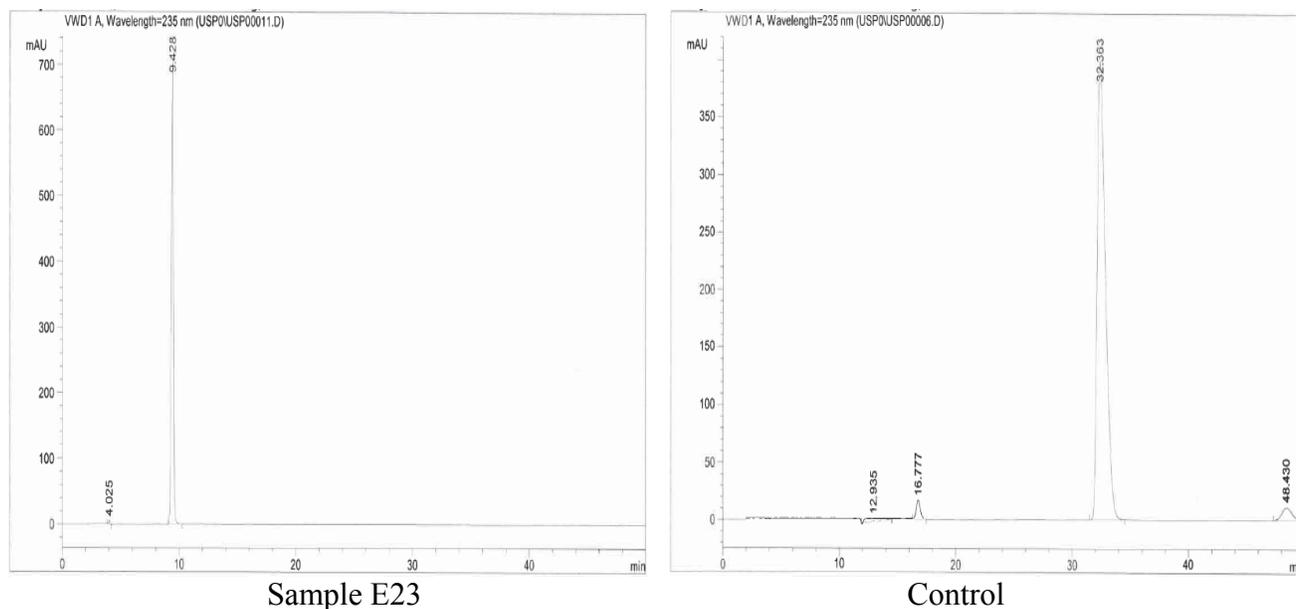


TLC: detection with UV at 366 nm



TLC: detection with UV at 254 nm

In the HPLC identification test for quinine sulfate, the retention time for quinine sulfate in the control samples was 32.36 min (right panel). The sample E23 had a wrong API. A peak in this sample eluted at 9.43 min (left panel)



The testing of two SP samples was conducted for several reasons:

- Provide refresher training in Dissolution and HPLC
- Familiarize the lab staff with the HPLC method of SP monograph. In the past, the lab staff determines the dosage of SP by using a titration method carried out manually. The HPLC method has several advantages over the titration method, including allowing the testing of multiple samples at the same time while requiring fewer reagents and less time.

Besides assisting the lab staff in analyzing antimalarial samples, confirmatory testing was an opportunity to train the staff in troubleshooting at all levels of testing. During the confirmatory testing, the lab staff encountered some difficulties in carrying out the analyses, and they learned how to plan and organize confirmatory testing involving several samples conducted by several analysts.



*Meeting with the head of the medicine regulatory authority*

Dr. HAJJOU met with Pr. Ousmane DOUMBIA at LNS, who shared a draft guideline for establishing a PV system for the country members of the West Africa Economic and Monetary Union. Pr. DOUMBIA indicated that he will also share the electronic version. Dr. HAJJOU updated him on the progress of the confirmatory testing and pointed out that the PV guidelines document should be shared with all the partners involved in PV activities in Mali (e.g. the National Pharmacovigilance Committee).

*Debriefing USAID/Mali*

Dr. HAJJOU debriefed Dr. Aboubacar SADOU on the outcome of the confirmatory testing. Dr. SADOU provided comments on the PQM workplan as well as the project of hiring a consultant to coordinate PQM activities in-country.

**Next Steps**

- LNS staff will carry out confirmatory testing on the remaining quinine sulfate samples and draft the annual report on MQM activities.

**Conclusions**

All the samples that failed basic tests were confirmed as lacking quinine sulfate API. This indicates that the tests at the sentinel sites were conducted properly for these samples and highlights the usefulness of Minilabs<sup>®</sup> in detecting counterfeit and substandard medicines. The lab staff benefited from the technical assistance the PQM team provided in conducting confirmatory testing and improving the use of Dissolution tests and HPLC methods.