

Review of data from collaborative testing of antimalarial medicines

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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 LNCQM of Benin planned a collaborative testing of select antimalarial medicines. M. Hajjou met with the LNCQM director and the heads of Medicines, Microbiology, Quality Assurance, and Herbal Medicines Services of the laboratory to discuss the details of the testing results and to plan future activities. These activities were also discussed with the advisor of the Health Minister responsible for malaria activities. M. Hajjou had a courtesy meeting at the World Health Organization (WHO) office in Cotonou and also went to USAID/Benin for a brief and debrief on the activities planned and accomplished, respectively.

Key Words

Benin, Sulfadoxine-Pyrimethamine, antimalarial medicines, medicine quality, pharmacovigilance, PMI, USAID, and USP DQI

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ACRONYMS

CDC	U.S. Centers for Disease Control and Prevention
DPM	Direction des Pharmacies et du Médicament
HPLC	High Performance Liquid Chromatography
LNCQM	Laboratoire National de Control Qualité des Médicaments
NIR	Near Infra Red
NMCP	National Malaria Control Program
OMCL	Official Medicine Control Laboratory
PMI	President's Malaria Initiative
PNLP	Programme National de Lutte contre le Paludisme
PQM	Promoting the Quality of Medicines
SP	Sulfadoxine-Pyrimethamine
USAID	United States Agency for International Development
USP DQI	United States Pharmacopeia Drug Quality and Information Program
WHO	World Health Organization

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Special thanks go to Dr. Raoul Saïzonou, National Professional Officer – Neglected Tropical Diseases at the WHO office in Cotonou, for his kindness and support during the visit.

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Background

With the support of the President's Malaria Initiative (PMI), the United States Pharmacopeia Drug Quality and Information (USP DQI) Program has been providing technical assistance to the Official Medicine Control Laboratory (Laboratoire National de Control de Qualité de Medicament or "LNCQM") of Benin since 2008.

USP DQI provided LNCQM with reference materials and equipment, and the two groups planned to conduct "collaborative testing" of select antimalarial medicines. Collaborative testing includes, but is not limited to, performing the same tests on the same samples obtained from the same batch/lot. The resulting data is analyzed using the same pharmacopeial methods and then the two groups compare the results. In this instance, the objective of the collaborative testing is to assess LNCQM's abilities in carrying out such analytical tests.

The samples tested included the following fixed-dose combinations:

- Lumefantrine-Artemether
- Artesunate-Amodiaquine
- Sulfadoxine-Pyrimethamine (SP)

In July 2009, DQI received the samples from LNCQM. After testing, DQI generated a comprehensive project report to be discussed with the lab staff in Benin.

Purpose of Trip

Dr. Hajjou traveled to Cotonou, Benin to review in detail the data from the collaborative testing and discuss future activities.

Source of Funding

This trip was supported through the USAID Bureau for Global Health, Office of Health, Infectious Diseases and Nutrition, President's Malaria Initiative (PMI)/Benin.

Overview of Activities

Meeting at USAID/Benin

Dr. Hajjou met with Mr. Pascal Zinzindohoue, Team Leader of Family Health; Dr. Abdou Salam Gueye, CDC/PMI Resident Advisor; and Mr. Simplicite Takoubo from the Family Health Team. Dr. Hajjou gave an overview of the planned activities and indicated that his visit was initially planned for the week of September 7-11, 2009. Dr. Baba-Moussa, Director of the LNCQM, requested postponing the visit because his laboratory staff was not available that week. Therefore, the visit was moved to the week of October 21-25, 2009.

The group discussed a few issues affecting the implementation of DQI activities in Benin, mentioning that the gap analysis was not easy to do with the laboratory. The National Malaria Program (Programme National de Lutte contre le Paludisme, or "PNLP") had requested LNCQM to test antimalarial medicines, but LNCQM did not test the samples, reportedly due to non-payment of such services by PNL. In the future, DQI could coordinate testing by providing the resources needed to have the samples tested by the lab.

The group agreed that Benin needs a medicine quality monitoring program to monitor the quality of antimalarial medicines available in the market, especially in light of the fact that the sample of Sulfadoxine-Pyrimethamine (SP) failed the dissolution test. Such a program would make use of Minilabs[®] in the regions and would involve the LNCQM, PNL, and the Direction des Pharmacies et du Médicament (DPM). However, the 2009 funding obligated for 2010 activities in Benin will not be sufficient to establish a medicine quality monitoring program.

Review of the data from the collaborative study

After the meeting with the USAID team, Dr. Hajjou contacted Dr. Baba-Moussa, LNCQM lab director, to confirm the meeting scheduled on that day. Dr. Baba-Moussa informed Dr. Hajjou that they could not meet as planned and that he could not dedicate two days for the review of the data from the collaborative testing, as requested before the visit. He called later in the day to schedule a meeting for Thursday afternoon, September 24, 2009. Because of the large amount of work needed to review and discuss the data, Dr. Hajjou requested a meeting with the lab staff. Dr. Baba-Moussa said that his staff would not be available because they had to install new equipment and receive training. Dr. Hajjou informed USAID about these conversations.

On September 24, Dr. Hajjou met with Dr. Baba-Moussa, who gave a tour of the laboratory and showed the new equipment the LNCQM had recently acquired. After the tour, Dr. Baba-Moussa convened a meeting to which he invited the heads of the Analytical Testing, Microbiology, Herbal Medicines, and Quality Assurance divisions to discuss the results of the collaborative testing.

Dr. Hajjou inquired about the testing of the samples and learned that the laboratory did not carry out any testing. Similar inquiries made before the visit were left unanswered. The lab director indicated that the High Performance Liquid Chromatography (HPLC) equipment was out of service which prevented the lab from conducting the testing. Dr. Hajjou questioned the usefulness of discussing the DQI data in the absence of any data from LNCQM and pointed out that the objective of the collaborative testing was to evaluate the lab's capabilities in conducting pharmacopeial testing by comparing LNCQM and DQI data. The DQI report had a fair amount of data and technical information that would have required time to review and discuss with the lab staff.

Because of the limited time dedicated to the meeting, Dr. Hajjou decided to present the process that DQI staff followed to test the samples at USP laboratories instead of presenting the results of the testing. He described all the components of the project plan and emphasized the importance of good planning before starting any laboratory testing. Dr. Hajjou briefly showed some of the DQI results but focused the presentation on the tools that DQI used to generate the data. He described the example of the dissolution calculation spreadsheet and showed the spreadsheet used in HPLC. LNCQM could use these and other tools that DQI can provide to the lab to facilitate calculation and generation of data. Dr. Baba-Moussa expressed his interest in having his lab follow the same process and asked whether DQI could provide LNCQM with a procedure that described the entire process. Dr. Hajjou said that DQI could provide such a procedure but pointed out that the lab staff would find it challenging to implement it without minimal training. Such training would include other components, such as Good Laboratory Practices that are

essential for generating sound quality control results. Furthermore, through monitoring and evaluation, DQI would make sure that the trainees were able to apply the expertise they acquired in the training. The ability of the lab staff to carry out adequate pharmacopeial testing would ensure that the lab had the capacity to perform pre- and post-marketing monitoring of medicine quality. Dr. Baba-Moussa agreed and suggested planning training and subsequent evaluation for his laboratory staff. He reiterated his interest in establishing a medicine quality monitoring program that would make use of Minilabs[®]. Dr. Hajjou pointed out that the funding for DQI activities will not be sufficient to establish such a program, and Dr. Baba-Moussa mentioned that the lab might be able to procure the Minilabs[®] with its own funds. They also discussed the testing of antimalarial medicines that PNLP requested. Dr. Baba-Moussa insisted that PNLP needed to pay for the testing.

It is noteworthy that the SP sample used in the collaborative testing failed the dissolution test.

Courtesy Meeting at WHO Office

Dr. Hajjou met with Dr. Leodegal Bazira, the interim WHO representative, and Dr. Raoul Saïzonou, National Professional Officer – Neglected Tropical Diseases, at the WHO office in Cotonou. Dr. Hajjou gave an overview of DQI activities in general and described the technical assistance provided to LNCQM in particular. He informed Dr. Saïzonou about the collaborative testing that DQI conducted with LNCQM and the medicines that were used in the testing. The discussion focused on the importance of monitoring the quality of medicines at every level of the distribution chain and the crucial role of LNCQM in carrying out this task.

Dr. Hajjou inquired about the status of pharmacovigilance in Benin. Dr. Saïzonou said that Dr. Dina Gbenou, who focuses on pharmacovigilance activities, was out of the office.

Dr. Bazira and Dr. Saïzonou assured Dr. Hajjou of their support for the work DQI was providing in Benin. Dr. Hajjou reiterated that DQI is eager to collaborate with WHO-Benin in all medicine quality related activities.

Meeting at the Ministry of Health

Dr. Hajjou met with Dr. Chérifatou Bello Adjibabi, Technical Advisor to the Minister of Health and Pharmacist Advisor to PNLP. Dr. Hajjou gave an overview of the collaborative testing and mentioned the SP sample that failed the dissolution test. Dr. Adjibabi verified the lot number of the sample and compared it to SP that PNLP was providing to the public, but the sample was not provided by the malaria control program.

Dr. Adjibabi expressed her concern about the quality of medicines in Benin and indicated that PNLP is contemplating procuring a portable Near Infrared (NIR) device to control the quality of antimalarial medicines in the regions. Dr. Hajjou discussed the application of such a device as well as portable Raman devices available on the market, stressing the fact that these devices are excellent tools for detecting counterfeit medicines, but that their application in detecting substandard medicines has not been proven. Dr. Adjibabi asked if she could receive any useful information on these devices and also indicated that she is interested in acquiring Minilabs[®] for PNLP to test antimalarial medicines in the regions. Dr. Hajjou emphasized the importance of involving LNCQM in any quality monitoring activity and underlined the fact that Minilabs[®] are

a tool only for screening the quality of medicines; confirmatory testing in a qualified laboratory is needed.

Dr. Adjibabi indicated that pharmacovigilance activities are at a stand still. The program has not been established. Because of this situation, she is gathering information on possible adverse drug events herself. Dr. Hajjou pointed out that pharmacovigilance needs to be structured and requires staff dedicated solely to this activity.

Debriefing USAID Mission

Dr. Hajjou met with Mr. Pascal Zinzindhoue and Dr. Abou Salam Gueye and debriefed them on the outcome of his meeting with the LNCQM director and his staff. He informed them of the following:

- LNCQM did not perform any testing on the samples.
- The presentation of DQI results from the collaborative testing was focused on the process of testing.
- The lab acquired new equipment, but the staff has not used them yet.
- The director of the lab expressed interest in having DQI train his staff
- The director of the lab reiterated his interest in establishing a medicine quality monitoring program.

Mr. Zinzindhoue stressed the fact that PMI wants to ensure that medicines brought into the country through the program are of good quality, and that is why support is being given to the LNCQM. USAID/Benin plans to follow up with Dr. Baba-Moussa to determine the next steps.

Next steps

- Based on the outcome of the discussions between USAID/Benin and the LNCQM, DQI's successor program – Promoting the Quality of Medicines (PQM) – will coordinate with the lab to plan future activities, which could include training for the lab staff and follow-up evaluations, establishing a MQM program, and coordinating the testing of PNL samples by LNCQM.