

Meeting with WHO Essential Medicines and Pharmaceutical Policies Department

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Trip Report

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About DQI

The Drug Quality and Information (DQI) Program, funded by the U.S. Agency for International Development (USAID) and implemented by the United States Pharmacopeia (USP), 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 DQI.

Abstract

The DQI director met with officials of the WHO prequalification program and got agreement to work closely together to support manufacturers toward prequalification of second line anti-TB medicines. He also met with Clive Ondari, the WHO contact for the Quality of Antimalarials in Sub-Saharan Africa (QAMSA) study and shared preliminary data on the quality of antimalarials in three African countries (Senegal, Madagascar and Uganda). He also met with officials in GDF, UNITAID and Global Fund to discuss current global quality assurance policies to assure pharmaceutical product quality around the world.

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I would like to extend sincere appreciation to Ms. Paloma Lerga (GDF) for coordinating my visit and for her continued diligent partnership with USP DQI to increase the number of quality assured second line anti-TB medicines.

I would like to express appreciation to the USP DQI administrative staff and editors for their assistance with logistical arrangements and for editing the trip report.

Finally, I would like to thank the USAID/Washington TB team, in particular Susan Bacheller and Irene Koek, for their continued support and leadership. I would also like to thank Anthony Boni and Veerle Coignez at USAID/Washington for their guidance and support of the USP DQI program.

ACRONYMS

CTO	Cognizant Technical Officer
Eoi	Expression of Interest
FDC	Fixed Dose Combination
GDF	Global Drug Facility
GMP	Good Manufacturing Practices
MSH/SPS	Management Sciences for Health/Strengthening Pharmaceutical Systems
PIC/S	Pharmaceutical Inspection Cooperation Scheme
QAMSA	Quality of Antimalarials in Sub-Saharan Africa study
TA	Technical Assistance
TB	Tuberculosis
TRP	Technical Review Panel
USAID	United States Agency for International Development
USP DQI	United States Pharmacopeia Drug Quality and Information
WHO	World Health Organization

Background

As the implementing mechanism for USAID to strengthen drug quality assurance systems in developing countries, DQI has provided support to the Health TB team at USAID/Washington in the following areas:

- Technical leadership in drug quality of second-line anti-TB medicines
- Support global initiatives, such as STOP TB, in particular the Global Drug Facility's (GDF) effort to provide quality assured anti-TB medicines
 - Provide technical assistance to manufacturers to facilitate the prequalification of second-line anti-TB medicines.
- Review technical literature and provide comments as guidance and recommendations to the Health TB team.
- Work with USP's Documentary Standards Division to develop monographs for first- and second-line anti-TB medicines.

To support global initiatives, DQI works closely with GDF to increase the number of prequalified second line anti-TB medicines. DQI has collaborated with the WHO prequalification team and GDF to provide TA to manufacturers in dossier preparation and Good Manufacturing Practices (GMP) to prepare them for WHO prequalification.

In the past, few anti-TB drug manufacturers expressed interest in participating in the prequalification program, probably due to a lack of understanding of the process. The quality of the dossiers that were submitted was questionable, leading to delays in prequalification.

In 2008, USP DQI collaborated with GDF to develop criteria for Expression of Interest (EoI) in WHO prequalification. Three manufacturers responded, but the dossiers submitted were of poor quality. The USAID-TB CTO (Susan Bacheller) approached USP DQI and advised getting involved earlier in the prequalification process. It was agreed that USP DQI would assist manufacturers to prepare dossiers, review the dossiers for completeness and accuracy, and conduct assessments of their facilities in order to identify gaps and make recommendations for compliance with international GMP standards. In order to provide this support it is prudent that DQI establish a good working relationship with the WHO prequalification team. It was in this regard that the trip was conducted to explore opportunities for a strategic partnership with PreQ.

A detailed description of the services provided and the scope of work with manufacturers can be found at: <http://www.usp.org/worldwide/dqi/WHOQualificationRequest.html>

Purpose of Trip

The DQI director went to Geneva to meet with:

- Officials of the WHO prequalification program to discuss ways to develop a strategic partnership to facilitate the prequalification of second line anti-TB medicines.
- Clive Ondari, the contact person at WHO for the QAMSA study, to share preliminary data for three African countries and to develop a strategy for dissemination of data.
- GDF to brief them about DQI's progress in assisting companies with dossier preparation
- Other stakeholders involved in global pharmaceutical procurement and formulating global quality assurance policies.

Source of Funding

Funding for the trip was provided by Core TB funds.

Meeting at Global Fund

Joelle Daviaud, Senior Pharmaceutical Quality Assurance Officer

Dr. Lukulay met with Dr. Daviaud to discuss the new global fund policy which went into effect July 1. The main differences between the policies include the replacement of C(i) and C(ii) with Interim Review Panel (ERP) review. The policy stipulates conditions under which a product qualifies for an ERP review. The criteria for ERP review include:

1. Less than three products exist which are either prequalified or SRA (stringent regulatory authority) approved
2. The manufacturer had applied for prequalification by WHO or SRA
3. The manufacturing plant is WHO GMP, Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S), or ICH GMP compliant

Additional new requirements for Global Fund recipient countries is that they will commit to conducting post-marketing surveillance and will test their products using laboratories that have successfully gone through a proficiency testing scheme administered by the European Directorate for the Quality of Medicines (EDQM) or WHO. A list of labs that successfully passed the laboratory proficiency test will be listed for reference by countries. Dr. Lukulay indicated that DQI will be assisting laboratories to participate in proficiency testing and will discuss the possibility of establishing a formal proficient testing scheme administered by USP and would seek recognition from Global Fund and others in the donor community.

Meeting with WHO, Prequalification

Dr. Rago, Coordinator, Quality Assurance and Safety: Essential Medicines and Medicines and Pharmaceutical Policy

Dr. Lukulay met with Dr. Rago to discuss ways that DQI could form a strategic partnership with the WHO prequalification team to facilitate the prequalification of second line anti-TB manufacturers. At the beginning of the meeting, Dr. Rago expressed concern that the mission of DQI is not very clear from that of USP and said that USP wears many hats. Dr. Lukulay explained the objective of the DQI program – to support the USAID public health agenda by promoting drug quality in developing countries. The program is fully funded by USAID but is implemented by USP. Dr. Rago thanked Dr. Lukulay for clarifying the roles and pledged to work more closely with DQI. Dr. Rago suggested that DQI experts could plan to meet with WHO PreQ assessors to discuss details of the prequalification requirements and get up-to-date information on the critical requirements. He also invited DQI to meet with PreQ during one of their training sessions. Dr. Lukulay will provide PreQ with a list of products and companies that DQI is interested in working with.

Dr. Lukulay inquired whether there was someone else that he could keep in regular contact with in case Dr. Rago is not available. Dr. Rago introduced Dr. Matthias Stahl, the manager for the

prequalification assessment team. He asked Dr. Stahl to discuss the key tenets of the assessment process and to work with DQI to support second line anti-TB drug manufacturers. Dr. Stahl explained the dynamics between his assessment team and the GMP inspectors in prequalifying a product. He explained that both the assessment team and the inspectors work closely to prequalify a product. It is only when a manufacturer passes GMP inspection and the dossier is deemed acceptable that the product becomes prequalified. Dr. Stahl invited DQI experts to attend the next dossier review session in Copenhagen on September 20 and asked for a list of topics that DQI experts would like to discuss at the meeting. He also asked for release of confidentiality information from manufactures so that WHO can share assessment information on company products with DQI. Dr. Lukulay informed him of such agreements and promised to send them upon his return. The two agreed to keep an open line of communication as they work together.

In a separate meeting, Dr Lukulay met with Dr. Clive Ondari, Coordinator of the Policy, Access and Rational Use of Medicines department, to brief him about the results of the QAMSA study for three African countries (Senegal, Uganda, and Madagascar). Dr. Lukulay indicated that the study has been completed, and DQI is ready to share the results with the countries prior to releasing them publicly. Dr Ondari thanked Dr. Lukulay for taking the initiative to share the data with him and indicated that WHO has also received the raw data from a laboratory in South Africa that was conducting the confirmatory testing for the six African countries that WHO funded for the study, but they have not yet compiled and interpreted the results. He asked Dr. Lukulay for a copy of the DQI QAMSA report when it is ready. They agreed that DQI and WHO should meet to discuss the study, including lessons learned, and to publish a joint paper.

Meeting with GDF

Ms. Meroquin Paloma Lerga, GDF Procurement Officer

Mr. Robert Matiru, the GDF Chief of Operations, was out of the office at the time of DQI's visit, so Dr. Lukulay met with Ms. Meroquin Paloma Lerga, the Procurement Officer for GDF. Dr. Lukulay briefed her about his meeting with Dr. Rago. She informed him about the recent EOI and companies that were granted tenders to supply GDF with second line anti-TB medicines. She promised to send DQI the list of companies that received the tenders and asked if DQI could work with them to help them prepare dossiers for prequalification. As a condition of the award of tender, companies would have to commit to submitting applications for prequalification in the next year. Ms. Lerga also indicated that more companies have recently indicated their agreement for WHO preQ to share their dossier information with DQI.

Meeting with UNITAID

Mr. Lorenzo Witherspoon (Procurement Officer) and Mr. Paolo Meireles (Portfolio Manager, HIV/AIDS)

UNITAID is the largest financing instrument Pre-Q. At a recent meeting in Rio de Janeiro, Mr. Witherspoon commended USAID's efforts to support DQI in assisting manufacturers with dossier preparation. Dr. Lukulay briefed them about his meeting with Dr. Rago and the PreQ team. Mr. Witherspoon and Mr. Meireles inquired if DQI could provide similar assistance to manufacturers of HIV/AIDS and pediatrics medicines. Dr. Lukulay indicated that DQI's focus is

second line anti-TB medicines, but assistance could be sought from the USP verification program.

Status Report – DQI Support to Second Line Anti-TB Drug Manufacturers

DQI GMP experts are currently working with the following manufacturers of second line anti-TB medicines to prepare dossiers for submission to the WHO prequalification team. The companies/products are at various stages of progression toward prequalification. Below is a summary of progress.

Company	Product	Country	Progress
Kilitch/Lupin	Capreomycin 1 mg Inj	India	TB 201- comments on dossier sent by WHO and DQI worked with Kilitch to address comments. API manufacturing information pending
Svizera		India	Awaiting two dossiers for second-line and one for first-line FDC for review prior to submission to PreQ
SIA Inc.		Russia	Dossier in preparation and being translated to English. DQI staff first visit in August 2009
Unilab	Levofloxacin, Ofloxacin and Amikacin	Philippines	Unilab requested help for dossier preparation and DQI first teleconference held on July 14 th 2009
Several companies	Several	Brazil	Workshop planned in September in collaboration with MSH/SPS to familiarize companies with preQ. Invitation letter and questionnaire translated into Portuguese

Next Steps

- DQI to meet with PreQ assessors in Copenhagen in September 2009 to discuss strategies for working together
- DQI to send Dr. Rago a list of companies and products that DQI is currently providing dossier preparation services
- DQI to send Clive Ondari the preliminary QAMSA report for Senegal, Uganda, and Madagascar
- DQI to send Dr. Stahl release of confidentiality letter from second line anti-TB manufacturers who have consented for WHO to share their dossier information with DQI