

# DQI Meetings with Key Partners in Hanoi and Site Visits to Quang Tri Province and Ho Chi Minh City, Vietnam

February 6-17 2009

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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 and USP.

## **Abstract**

DQI staff met with the Vietnam Ministry of Health's National Institute of Malariology, Parasitology, and Entomology (NIMPE) in Hanoi, and conducted supervisory site visits in Quang Tri province and Ho Chi Minh City to collect infectious disease medicines for Minilab<sup>®</sup> screening. Additionally in Hanoi, DQI staff met with key partners including Supply Chain Management System (SCMS), USAID, World Health Organization (WHO), NIMPE, and Drug Administration of Vietnam (DAV) to discuss the medicine quality monitoring in nine sentinel sites and the status of oseltamivir phosphate products stockpiled in Vietnam.

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## **Key Words**

Vietnam, Quang Tri, Ho Chi Minh City, site visits, medicine quality monitoring, avian influenza, oseltamivir phosphate, stockpile, medicines quality monitoring, NIMPE, DAV, SCMS.

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## ACRONYMS

AI	Avian Influenza
ARV	Antiretroviral
ASEAN	Association of Southeast Asian Nations
CDC	U.S. Centers for Disease Control and Prevention
DAV	Drug Administration of Vietnam
FDA	Food and Drug Administration
FDC	Fixed Dose Combinations
GFATM or Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
GMP	Good Manufacturing Practices
GPHF	Global Pharma Health Fund
MQM	Medicines Quality Monitoring
MOH	Ministry of Health
NIMPE	National Institute of Malariology, Parasitology, and Entomology
NIDQC	National Institute of Drug Quality Control
OI	Opportunistic Infection (related to HIV/AIDS)
PEPFAR	President's Emergency Plan for AIDS Relief
QA	Quality Assurance
QC	Quality Control
RDM/A	USAID Regional Development Mission for Asia
SCMS	Supply Chain Management System
TA	Technical Assistance
USAID	United States Agency for International Development
USP DQI	United States Pharmacopeia Drug Quality and Information program
WHO	World Health Organization
WPRO	WHO Western Pacific Regional Office

## **Background**

DQI has been active in monitoring the quality of antimalarial medicines in Vietnam since 2003; the program is implemented in-country by NIMPE, the NIDQC laboratory, and DAV. The program has also received support from the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM) and will again in 2009.

In 2007, a week-long training workshop was conducted by DQI to expand medicines quality monitoring to include anti-retroviral (ARV), anti-tuberculosis, antiviral (oseltamivir), and selected antibiotic medicines. Routine surveillance of the quality of anti-infective medicines in Vietnam is currently being implemented in nine provincial sites (Binh Dinh, Binh Phuoc, Daklak, Ha Giang, Ho Chi Minh City, Kontum, Dien Bien, Thanh Hoa, Quang Tri) throughout the country, which are each supplied with Global Pharma Health Fund (GPHF) E.V. Minilabs<sup>®</sup> for initial screening of post-market pharmaceutical products. DQI provides the necessary commodities, training, reference materials, and ongoing support for the provincial sites and for verification testing at the national laboratory (NIDQC) and coordinates appropriate data dissemination to the regulatory authority (DAV) for enforcement actions.

In addition to routine monitoring of the quality of infectious disease medicines in Vietnam, DQI is pioneering a regional strategy to establish monitoring of stockpiled and circulated oseltamivir phosphate, which is the principal antiviral medicine used to reduce mortality and morbidity resulting from avian influenza (AI) infection, caused by H5N1 virus. As part of regional pandemic preparedness for AI, oseltamivir is often stored in stockpiles at both country and regional centers. In some cases, sub-optimal storage conditions may contribute to a reduction in the quality of the product regardless of expiration date. Additionally, limited capacity for ongoing vigilance of stockpiled or circulated products may result in products being kept beyond expiration dates. The shelf life according to Roche, the manufacturer of Tamiflu<sup>®</sup> is five years. DQI is piloting studies to investigate the quality of oseltamivir products using basic screening and compendial testing. Since Vietnam is highly concerned about avian influenza (the country has had occasional AI transmission to humans), it is imperative that a routine protocol for sampling and ensuring good quality oseltamivir is established there. Working with the WHO-Vietnam office as point of contact and in collaboration with the USAID-Vietnam Mission, DQI will begin implementing the sampling protocol developed for the region.

## **Purpose of Trip**

- Meet with NIMPE, WHO, SCMS, and USAID in Hanoi to discuss joint activities.
- Offer technical assistance (TA) to the Government of Vietnam to determine the quality of stockpiled oseltamivir and learn more about the status of oseltamivir manufacturing, distribution, and quality testing in Vietnam.
- Visit sentinel sites in the provinces of Quang Tri and Ho Chi Minh City to provide needed TA to the staff regarding collecting and testing medicines as part of the medicines quality monitoring program (MQM) and learn what actions are being taken and by whom when circulated medicines are found to be counterfeit or substandard.

## **Source of Funding**

This trip was supported with funds from the USAID Regional Development Mission for Asia (Mekong Malaria and Tuberculosis funding streams).

## **Overview of Activities**

**Feb 6, 2009**

*Meeting with SCMS*

Participants:

Dr. David Kuhl, SCMS; Ms. Laura Krech, DQI; Mr. Christopher Raymond, DQI

Dr. Kuhl mentioned that the Centers for Disease Control (CDC) will be purchasing medicines for opportunistic infections (OI) on the local market in Vietnam. Since DQI is already collecting and testing some of the OI medicines that the CDC plans on purchasing, DQI could propose testing/monitoring these medicines for the CDC. DQI tried to contact the CDC country coordinator and the CDC HIV/AIDS treatment coordinator from the Global AIDS Program, but they were on mission and unavailable.

Dr. Kuhl agreed that DQI should try to sample/test from clinics throughout the supply and distribution chain, not only for OI medicines but also for antiretrovirals (ARVs). At this point, the President's Emergency Plan for AIDS Relief (PEPFAR)-procured ARV medicines are randomly selected and sent by SCMS to Northwest University in South Africa for confirmatory testing. DQI will follow up with the SCMS country director, CDC, and USAID to further clarify this point, and provide any requested technical assistance. A one-time pilot study to check the quality could provide relevant and useful information for stakeholders. If results demonstrate that there are no problems with ARV quality throughout the supply chain, then a general assumption can be made that, at this point in time, adequate quality ARVs are being procured.

The Central Pharmaceutical Companies (Vietnamese state-run pharmaceutical companies; they only import and repackage in conjunction with the National Pharmaceutical Companies) collect the ARVs purchased under PEPFAR Food and Drug Administration (FDA) acquisition rules and distribute them. All agencies receiving PEPFAR monies are required to buy products that are FDA-certified (as listed in the "Orange Book"). No FDA-certified products are currently manufactured in Vietnam. The warehouse is in Ho Chi Minh City (HCMC), and, according to the SCMS, storage seems to be acceptable; there could be some issues in terms of the distribution that may necessitate further investigation.

Dr. Kuhl will send DQI a list of the OIs purchased locally. Approximately 95% of PEPFAR ARVs are purchased from India, and PEPFAR medicines are distributed in approximately 20 provinces of Vietnam. PEPFAR, the Vietnam Administration for HIV/AIDS Control (the General Department of Preventive Medicine and HIV/AIDS Control within the Ministry of Health), and the Global Fund combined are only covering about 20% of those HIV-positive patients who are in need of receiving ARV therapy.

*Meeting with USAID Vietnam Mission*

Participants:

Ms. Ellen Lynch, Senior HIV/AIDS Technical Advisor, Office Public Health, USAID/Vietnam;  
Mr. Tim Meinke, Avian Influenza Technical Advisor, Office Public Health, USAID/Vietnam;  
Ms. Laura Krech, DQI; Mr. Christopher Raymond, DQI

The DQI team debriefed USAID on activities in Vietnam and the goals of this trip and discussed future funding. In order to solicit funding from Vietnam Mission, DQI should first send a solid concept paper and follow up the next time DQI is in Hanoi. The USAID Vietnam Mission was recently established and, at this point, they are still considering which projects and organizations they will fund under their public health portfolio.

Ms. Lynch informed the DQI team that the FDA has an office in Vietnam, and any GMP assessments of manufacturers will be done by them. They have already done assessments of manufacturers that produce ARVs locally.

At this point, USAID has not expressed interest in DQI providing TA to local companies to produce methadone as part of the HIV/AIDS program, since they are currently importing it from the U.S. at relatively low cost. Ms. Lynch prefers the FDA to be spearheading this process.

**Feb 9, 2009**

*Meeting at NIMPE with DAV, NIDQC, and NIMPE*

Dr. Nguyen Mah Hung, Director, NIMPE; Dr. Tran Quoc Tuy, Vice Director, NIMPE; Dr. Nguyen Van Vien, DAV; Dr. Bui Thi Hoa, Vice Director, NIDQC; Dr. Throng Van Nhu, NIMPE; Mr. Trinh Ngoc Hai, NIMPE; Dr. Nicole Smith, WHO Vietnam; Ms. Laura Krech, DQI; Mr. Christopher Raymond, DQI

The objectives of this meeting were to: (1) Offer TA to Vietnam to determine the quality of stockpiled oseltamivir and to learn more about the status of oseltamivir manufacturing, distribution, and quality testing in Vietnam; (2) Learn what actions are being taken, and by whom, when circulated medicines are found to be counterfeit or substandard; and (3) Discuss updates of Global Fund 7 and determine how some of the funds will be used for MQM.

NIMPE, DAV, and NIDQC did not answer questions regarding the existence and location of the Japan-ASEAN oseltamivir stockpile that was pre-deployed to Vietnam from Singapore. According to WHO, it arrived in August, and the MOH is in charge of it. Mr. Raymond will follow-up with his contact at ASEAN who knows more about this.

NIDQC stated that there were 4 Vietnamese manufacturers who participated in a pilot program to test production capacity in-country by importing raw material for oseltamivir from Hetero (India) and creating the finished product for the national program. NIDQC checked the quality of material at import using in-house methods since the official USP Monograph for oseltamivir had not been officially published in the USP-NF. This program started in 2005, and appears to have ended, although it was not clear when this project was completed.

Dr. Smith asked what the Ministry of Health (MOH) is doing to recall expired oseltamivir drugs deployed to provinces. The NIMPE director said that oseltamivir is stockpiled at the central (national) level only.

Dr. Smith requested that the NIDQC test WHO stockpiles for quality. There is a formal process for requesting samples to be tested at the NIDQC. Tamiflu®, the oseltamivir dosage form manufactured by Roche, is used in stockpiles; however, little information was forthcoming

regarding details of the national stockpiles. DQI needs to send a signed letter from our director to the Vice-Minister of Health, Mr. Cao Minh Quang, requesting permission to talk to the person in charge of Tamiflu® at the DAV.

Global Fund Round 7 will be in effect from 2009-2013. The money has been disbursed to MOH, and NIMPE will get \$18,000 USD per year for five years to monitor malaria medicines in nine provinces. These funds will be used together with DQI monies.

In terms of enforcement updates, the DAV will have more information in March 2009. DQI is waiting on the full certificates of analysis from the latest round of sampling and testing to understand which products failed quality testing and why, and what subsequent enforcement actions were taken.

NIDQC sends the quality results to the DAV, and DAV sends notices to the provinces to take quick action and investigation. The DAV also sends out alerts through a pharmaceutical journal, which is also accessible on a MOH website.

Dr. Hoa from the NIDQC said that 32 samples from the last two rounds were of poor quality; one of those was counterfeit. Most of the poor quality samples seemed to be as a result of storage problems, not necessarily GMP issues. Mr. Hai will provide DQI with the certificates of analysis from the last two rounds.

#### *Visit to the NIDQC*

##### Participants:

Dr. Bui Thi Hoa, Vice Director of NIDQC; Ms. Nguyen Thanh Binh, Deputy Head of Planning Department, NIDQC; Ms. Laura Krech, DQI; Mr. Christopher Raymond, DQI

The NIDQC is an impressive institute that obtained ISO 17025 accreditation for all laboratories and equipment procedures in 2001; their status was renewed in 2005. They received Good Laboratory Practices (GLP) status in 2004 from the Government of Vietnam, and in 2008, they achieved WHO pre-qualification status. The NIDQC produces over 200 reference standards and the Vietnamese Pharmacopeia and participates in the ASEAN reference standards harmonization with the other ASEAN nations. DQI will alert our partners (including USAID, SCMS, and CDC) about NIDQC's status so they can use the lab for testing samples.



DQI staff toured NIDQC's facilities

*Meeting with DAV staff*

Participants:

Mr. Christopher Raymond, DQI; Mr. Thanh Nguyen Tu, Officer, Drug Registration, DAV

A brief, informal meeting with some of the staff from DAV was held to ‘field test’ the translation and content of the recently produced public service announcements (PSAs) in Vietnamese. After multiple viewings and careful interpretation of the Vietnamese voiceovers, the DAV staff felt that all three of the PSAs were appropriate and accurately translated from the original English scripts. The content was culturally appropriate, and the voiceover actor was a well-recognized talent from Vietnam.

**February 11-13, 2009**

*Field Visits to Quang Tri Province*

Participants:

Ms. Laura Krech, DQI

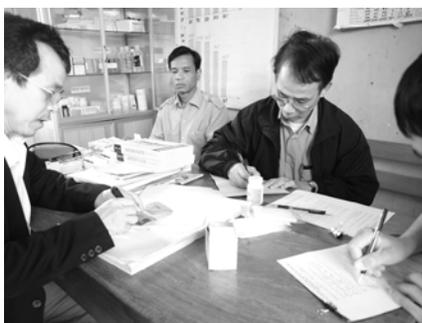
Mr. Christopher Raymond, DQI

Mr. Trinh Ngoc Hai, NIMPE

Mr. Le Minh Dao, NIMPE

Dr. Nguyen Vun Quang, Director of Drug Quality for Quang Tri province,

The team, with local staff from Quang Tri province (in Central Vietnam near the border with Laos), sampled medicines from public clinics and private pharmacies in the towns of Huong Hoa (Khe Sahn) and Lao Bao. Most of the public clinics only had antimalarials and antibiotics, while the district hospitals of Huong Hoa and Da Krong had many classes of medicines. To prevent stock-outs, samples were not taken from clinics where there were low quantities of medicines. At a private pharmacy visited in Huong Hoa, expired vitamins and TB medicines were observed.



Mr. Dao and Mr. Hai from NIMPE collecting samples in Quang Tri province

The Minilab<sup>®</sup> is located in the city of Dong Ha at the ‘So y Te’ (District Health Office) of Quang Tri province. The testing room is clean and well ventilated. Mr. Hai and Mr. Dao normally organize 6 to 7 staff from the district health office to perform all the basic tests together so the work is done quite efficiently. For example, they work together to test all artesunate samples and, once complete, move on to the next medicine product. The team found some suspicious looking artesunate that was labeled as “Guilin” (in Chinese characters) that passed disintegration and TLC testing; however, the blister pack did not contain the normal hologram that Guilin uses.

Additionally, there was no information regarding the manufacturer's address on the blister pack. This particular sample was found in the Dong Ha market, but Mr. Hai was not able to obtain enough samples to send to the NIDQC for confirmatory testing. Mr. Hai will follow up to see if more of this sample can be procured at the point of purchase.



Hospital near border with Laos



Sample collection in Quang Tri province



District health staff test samples in Dong Ha

### January 16-17, 2009

*Field Visit to HCMC Sentinel Site located at NIMPE's Regional office for South Vietnam*

#### Participants:

Ms. Laura Krech, DQI; Mr. Christopher Raymond, DQI; Mr. Trinh Ngoc Hai, NIMPE; Mr. Le Minh Dao, NIMPE

The director of NIMPE's Regional Office would not permit DQI staff to accompany NIMPE staff to collect medicines from public and private sector outlets in the Cu Chi and Hooc Mon districts (outside of HCMC). The director maintained that he was not notified two weeks prior to the visit, which is required. He is a new director, as the previous director of the HCMC NIMPE unfortunately passed away. It is imperative that the new director and vice-director have a better understanding of the goals and objectives of the medicine quality monitoring program. Ms. Krech will draft a document that synthesizes DQI activities to date in Vietnam and have it translated into Vietnamese. In addition, Mr. Hai pledged to give the director adequate notice prior to DQI visits in the future to gain his approval to participate in sample collection.



NIMPE staff performing Basic Testing



DQI and NIMPE Staff in HCMC



Traffic in HCMC

The director did, however, welcome the DQI team to participate and watch the analyses of the samples collected in the lab the following day. As in the previous sentinel site visited, a group of laboratory staff was gathered to test the samples together by type of medicine, thereby making the testing process very efficient. The medicines tested were artesunate, erythromycin, amoxicillin, TB medicines (FDC and single dose preparations), co-trimoxazole, and cephalexin. The lab was air-conditioned and in good condition for testing and waste disposal.

*Overall comments from the two site visits:*

In order to facilitate better communication between DQI and NIMPE staff, it will be prudent to have an interpreter on the next visit to accompany the DQI team. Improved communication can help DQI understand and report on the important actions taken by the DAV against counterfeit and substandard medicines. Audits will be performed on expenditures for sentinel site visits and related activities. Specific sites will be selected and detailed information will be requested to adequately track how program funds are being spent. This is customary with all countries DQI works with in the region. DQI will request NIMPE to submit information from two sites that were visited during the last round of sampling and testing in 2008.

### **Next Steps**

- Order more GPHF pipette bulbs for all sites (completed March 1, 2009)
- Draft a new Memorandum of Agreement between the Government of Vietnam, Ministry of Health, and DQI as the current one expires in July 2009
- Include Global Fund commitment for malaria medicine quality monitoring
- Obtain the certificates of analysis from the past two sampling and testing rounds from Mr. Hai (NIMPE) or Dr. Hoa (NIDQC)
- Send a new USP-NF to the DAV and NIDQC after receiving the certificates of analysis
- Draft a formal letter of request to MoH Vietnam to provide technical assistance on quality testing of oseltamivir
- Obtain information on oseltamivir production, storage, and distribution
- Follow up with ASEAN contacts regarding their deployment of oseltamivir to Vietnam
- Send requested USP reference standards to the NIDQC
- Audit two sentinel sites' expenditures using information received from NIMPE
- Create a 1-2 page brief on DQI activities in Vietnam as requested for NIMPE (Ho Chi Minh City), USAID, SCMS, and the CDC
- Send USAID the results of ARV quality testing in Vietnam over the past five years

### Vietnam Sentinel Site Map

