

Site visit with U.S. Ambassador to Cambodia; filming of Minilab[®] sequence; Site visit to National Health Products Quality Control Center lab

Cambodia

July 8-9, 2009; July 23-26, 2009

Trip Report

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Cooperative Agreement # HRN-A-00-00-00017-00

Sponsoring USAID Missions: USAID-Cambodia Office of Public Health

Grantee: United States Pharmacopeia Drug Quality and Information (USP DQI) Program

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Language: English

Date of Publication: October 28, 2009



This report is made possible by the generous support of the American people through the United States Agency for International Development (USAID), under Cooperative Agreement number HRN-A-00-00-00017-00. The contents are the responsibility of the U. S. Pharmacopeia Drug Quality and Information Program and do not necessarily reflect the views of the United States Government.

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

On July 9, 2009, staff from DQI, USAID Cambodia, and the Provincial Health Department met with U.S. Ambassador to Cambodia, the Honorable Carol A. Rodley, during her field visit to Pailin, Cambodia on the Thai-Cambodian border to discuss medicine quality monitoring activities.

In late July 2009, Mr. Raymond met with USAID Cambodia Office of Public Health staff at the National Health Products Quality Control Center (NHQC) – formerly known as the National Laboratory for Drug Quality Control – to discuss the current status of the laboratory and how USAID and DQI can help build capacity of the lab. Additionally, Mr. Raymond and film director Mark Hammond (in association with Living Films) filmed laboratory sequences for the Minilab[®] documentary film.

Recommended Citation

Raymond, Christopher B. 2009. *Site visit with U.S. Ambassador to Cambodia; filming of Minilab[®] sequence; Site visit to National Health Products Quality Control Center lab. Cambodia; July 8-9, 2009 and July 23-26, 2009.* Submitted to the U.S. Agency for International Development by the United States Pharmacopeia Drug Quality and Information Program. Rockville, Maryland: United States Pharmacopeia.

Key Words

Cambodia, Pailin, Minilab, National Health Products Quality Control Center, dissolution apparatus, US Ambassador, malaria, artemisinin combination therapy, counterfeit antimalarial medicines

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ACKNOWLEDGEMENTS

I would like to acknowledge the USAID-Cambodia Office of Public Health, and specifically Dr. Chantha Chak, Infectious Diseases Team Leader, for helping to coordinate the July 9, 2009 meeting with the U.S. Ambassador in Pailin, Cambodia. In addition, thanks to the helpful and accommodating staff at the Pailin Referral Hospital and Provincial Health Department for hosting the field visit to the Minilab site.

I am thankful to the staff at the National Health Products Quality Control Center (NHQC) in Phnom Penh, especially to Dr. Nam Nivanna, Director, and to Mr. Tey Sovannarith, Chief Technical Officer, for meeting with and allowing us to film in the laboratory setting. I would also like to thank Mam Boravann from the Essential Drugs Bureau for coordinating the filming.

Finally, I would like to acknowledge the continued support of Tony Boni and Veerle Coigneux at USAID/Washington; Laura Krech, Program Manager at DQI, for preparing the excellent briefing for the U.S. Ambassador; and to the DQI editors for editing this document.

ACRONYMS

ABT	Antibiotic medicines
ACT	Artemisinin-based Combination Therapy
AIDS	Acquired Immunodeficiency Syndrome
AML	Antimalarial medicines
ATB	Anti-tuberculosis medicines
CPC	Cambodian Pharmacovigilance Center
DDF	Department of Drugs and Food
EDB	Essential Drugs Bureau
GMS	Greater Mekong Subregion
GPHF	Global Pharma Health Fund
GFATM or Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
HIV	Human Immunodeficiency Virus
HPLC	High Performance Liquid Chromatography
MRA	Medicines Regulatory Authority
MOH	Ministry of Health
NHQC	National Health Products Quality Control Center
OPH	Office of Public Health
PSA	Public Service Announcement
RDM/A	Regional Development Mission for Asia
TLC	Thin Layer Chromatography
USAID	United States Agency for International Development
USP DQI	United States Pharmacopeia Drug Quality and Information program
WHO	World Health Organization

Background

With the financial support of the U.S. Agency for International Development/Regional Development Mission for Asia (USAID/RDM-A), the Drug Quality and Information (DQI) Program, implemented by the United States Pharmacopeia (USP), has been assisting countries in the Greater Mekong Subregion (GMS) – Cambodia, Laos, Thailand, and Vietnam – address the quality of essential medicines, including antimalarial (AML), antibiotic (ABT), anti-tuberculosis (ATB), and HIV/AIDS medicines, since early 2003. This assistance is a contribution to the regional effort to improve access to high quality essential medicines.

With support from the USAID Cambodia Public Health Office, USP DQI developed a series of Public Service Announcements (PSAs) aimed at basic public education about the risks of exposure to counterfeit medicines in illegal or unlicensed drug shops throughout Southeast Asia. The PSAs are slated for media broadcast in Thailand, Vietnam, Cambodia, and Laos and have been translated into each national language. USP DQI, with support from USAID Cambodia and from the Cecil and Hilda Lewis Charitable Trust, is currently developing a 20-minute fictional dramatization film which outlines the basic methods for field testing using the GPHF Minilab[®] for field screening of target medicines in collaboration with the Ministry of Health field staff, the Cambodia Pharmacovigilance Center (CPC), and other relevant agencies. This film will show how patients are affected by counterfeit medicines, and how the USP DQI-supported project on medicine quality monitoring is a key component to ensure safe medicines for the consumer in resource-limited settings such as the GMS.

Purpose of Trip

The site visit to Pailin with the U.S. Ambassador to Cambodia and staff from USAID Cambodia, the Provincial Health Department, and drug inspectors was conducted to outline basic activities related to medicine quality monitoring in the field.

The meeting with USAID Cambodia Office of Public Health staff at the National Health Products Quality Control Center (NHQC), formerly known as the National Laboratory for Drug Quality Control, was held to discuss the current status of the laboratory and how USAID can help build capacity of the lab through DQI activities. Additionally, DQI and film director Mark Hammond (in association with Living Films) filmed laboratory sequences for the Minilab[®] documentary film.

Source of Funding

This trip was supported with funds from USAID Cambodia.

Overview of Activities

July 9, 2009

USAID, DQI, and Drug Bureau staff from Pailin Province, Cambodia met with the Honorable Carol A. Rodley, U.S. Ambassador, during her field visit to the Minilab[®] site in Pailin. The Minilab[®] site is one of 12 currently active in Cambodia for medicine quality monitoring in post-marketing sampling and is supported by the USAID Cambodia Mission and co-financed through the Global Fund (GFATM). The Ambassador was briefed on the DQI-related activities in Cambodia (see [Annex 1](#)), as well as informed about the emergence of drug-resistant malaria

centering around Pailin. The relationship between substandard medicines and drug resistance was discussed as well as the prevalence of counterfeit and substandard antimalarial medicines on the Thai-Cambodia border. Additionally, the group talked about the recent ban on artesunate monotherapy and its possible future impact on malaria treatment. The Drug Bureau commented on the overall reduction in the prevalence of counterfeit medicines since medicine quality monitoring began in 2003 and stressed the effectiveness of Minilabs[®] for field testing medicines.

Finally, the Ministry of Health (MoH) and DQI staff gave a brief introduction of the actual Minilab[®], including a demonstration and explanation about how field staff determine whether a drug passes tests and what type of follow-up occurs when a drug fails, for example, being sent to the NHQC for confirmatory testing, then to the Department of Drugs and Food for action, etc. The Ambassador was supportive of these activities, yet reiterated the importance of the MoH taking ownership of the project and eventually being able to fund these activities independently, or with minimal ongoing donor support. However, given the current reality in Cambodia, it is not expected that the MoH will be able to take full responsibility on this expenditure.

Field visit participants:

- the Honorable Carol A. Rodley, United States Ambassador to Cambodia
- Dr Chantha Chak, Infectious Diseases Team Leader, USAID Cambodia OPH
- Mr. Oeurn Samuth, Officer-TLC Supervisor of the Essential Drugs Bureau, Cambodia
- Mr. Nuth Tith, Chief of Drug Bureau, Pailin Province, Cambodia
- Mr. Chan Chhang, TLC Officer, Pailin Province, Cambodia
- Mr. Ph. Kong Sakal, Chief of Drug Bureau, Pailin Province, Cambodia
- Mr. Yam Chifoan, Chief of Drug Bureau, Pailin Province, Cambodia
- Mr. Christopher B. Raymond, Project Coordinator, USP DQI, Bangkok, Thailand



Figure 1. Dr. Chak discusses malaria in Pailin with U.S. Ambassador



Figure 2. Mr. Raymond presents the U.S. Ambassador with copies of the PSAs



Figure 3. U.S. Ambassador inspects TLC plates from Minilab[®] testing



Figure 4. Staff from MoH, Essential Drugs Bureau, USAID, and DQI with U.S. Ambassador

July 24, 2009

USAID, National Health Products Quality Control Center (NHQC) senior staff, and Chris Raymond met at the new laboratory, where it is temporarily housed during construction of the permanent laboratory facility on the outskirts of Phnom Penh. USAID OPH staff met with the director and the chief technical officer of the NHQC to discuss current and future needs. After a briefing by Dr. Nivanna on the current status of testing at the lab, the USAID team and DQI were given a tour of the lab facilities.

Meeting Participants:

Dr. Nam Nivanna, Director, NHQC, MoH Cambodia
Mr. Tey Sovannarith, Deputy Chief of Technical Bureau, NHQC, MoH Cambodia
Ms. Katherine Crawford, Director, OPH, USAID/Cambodia
Mr. Jonathan Ross, Deputy Director, OPH, USAID/Cambodia
Dr. Chak Chantha, Infectious Diseases Team Leader, OPH, USAID/Cambodia
Mr. Christopher B Raymond, Project Coordinator, USP DQI, Bangkok, Thailand

Next steps and Action Items:

- DQI to purchase dissolution apparatus for the NHQC, at USAID request (completed)
- USAID will continue supporting instrumentation and training and provide support to the Interministerial Committee on Counterfeit Medicines so that it can meet frequently to determine actions that need to be taken resulting from evidence generated by the NHQC.
- DQI will submit an FY10 work plan and budget (completed)



Figure 5. USAID tour of NHQC



Figure 6. Inspecting HPLC chromatograms



Figure 7. New laboratory facilities have insufficient space

July 24-25, 2009

DQI and Living Films finalized filming scenes from the laboratory for the Minilab[®] field video. Over a two-day period, the lab staff (Mr. Sovannarith and Mr. Asany, along with Mam Boravann) were filmed conducting Minilab[®] tests as well as HPLC analyses at the NHQC. The detailed nature of filming lab sequences was challenging, especially coupled with the fact that the electricity was shut off in all of Phnom Penh during the afternoon of the 24th.

The Minilab[®] video will be used during training for health staff as well as made available to interested stakeholders and partners.

Organization/Meeting

Mr. Tey Sovannarith, Deputy Chief of Technical Bureau, NHQC, MoH Cambodia

Mr. Has Asany, Officer of Drug Bureau, Battambang Province, Cambodia

Ms. Mam Boravan, EDB Officer-USP.DQI Focal Point, Department of Drugs and Food

Mr. Mark Hammond, film director, SohoFilms/Living Films Thailand

Mr. Christopher B Raymond, Project Coordinator, USP DQI, Bangkok, Thailand



Figure 8 Mark Hammond filming calculation of retention factor of a TLC

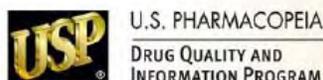


Figure 9. Lab sequences for the Minilab[®] film



Figure 10. Minilab[®] film set at the NHQC

Briefing to US Ambassador on DQI activities in Cambodia



I. STATUS OF MEDICINE QUALITY IN CAMBODIA

Access to good quality, safe, and effective essential medicines is necessary to ensure public health, but in Cambodia, as in many developing countries, good quality medicines cannot be taken for granted. According to a United States Pharmacopeia Drug Quality and Information (USP DQI) supported post-marketing surveillance program, approximately 13% of the medicines sampled in 10 provincial sentinel sites during 2003-2008 were of poor-quality (16% when considering only antimalarials). The most commonly found counterfeits are antimalarials (artesunate, quinine, chloroquine, mefloquine and tetracycline) and antibiotics (amoxicillin, ampicillin and penicillin). Furthermore, the Department of Drugs and Food (DDF) and the Pharmacists Association of Cambodia (PAC) reported that there are approximately twice as many pharmacies operating illegally in the country than legal pharmacies (1,065 are licensed). In addition to counterfeit and substandard products, it is not unusual to find unregistered medicines on pharmacy shelves or medicines past their expiration date.

The problem of poor-quality medicines has become a serious public health threat in Cambodia. The human cost of poor-quality medicines includes the extended duration of diseases (which can in turn lead to loss of work and income), disability, the increase of antimicrobial resistance, and even death.

II. USP DQI ACTIVITIES TO IMPROVE MEDICINE QUALITY THROUGH USAID SUPPORT

USP DQI has been providing technical assistance to the Ministry of Health's Department of Drugs and Food (DDF), the National Laboratory of Drug Quality Control (NLDQC) and National Priority Diseases Programs (NDPs of malaria and tuberculosis) since 2003, in an effort to strengthen the quality control/assurance systems and improve the quality of medicines in Cambodia.

USP DQI has been active in four areas in particular:

- (1) Improving detection of poor-quality medicines circulating in the Cambodian market through post-marketing surveillance¹;
- (2) Strengthening existing drug quality control and assurance systems – e.g. by providing essential equipment and training to the NLDQC.
- (3) Improving availability of, and access to, objective and up-to-date information about medicines
- (4) Raising awareness among the general public about medicine quality issues and mobilizing policy makers, regulators and health professionals.

This project uses Minilabs to carry out simple and basic testing methods that can be used to detect substandard and fake medicines. The GPHF-Minilab® manufactured by the Global Pharma Health Fund e.V. (GPHF) is a mini, mobile laboratory weighing 40kg that can test the quality of medicines in the field. Testing the quality of drugs using the GPHF-Minilab® involves a four-stage test plan that employs very simple physical and chemical-analysis techniques: visual inspection, simple tablet and capsule-disintegration test, simplified color reactions for a quick check of any drug present, thus ensuring the drug's identity and a semi-quantitative thin-layer chromatography (TLC) tests for a check of any quantities of drug present, thus ensuring the drug's identity. www.gphf.org

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Achievements related to the detection and investigation of counterfeit medicines

- Between 2003 and 2008, USP DQI has helped the DDF build up a post-marketing surveillance containing 10 sentinel sites. In total, over 1,200 samples have been collected and analyzed. The surveillance has allowed the DDF to document the presence of sub-standard and counterfeit medicines. Certain provinces (e.g. Kampong Cham, Kampong Thom, Siem Reap) have been exemplary in taking concrete action, such as circulating alerts and closing down illegal drug outlets.
- Cambodia was part of the INTERPOL investigation (Operation Jupiter) targeting counterfeit artesunate in the Greater Mekong Subregion (GMS) where 49.9% (195/361) of the samples collected were shown to be counterfeit². The packaging had fake holograms and the artesunate tablets contained little or no artesunate. The Secretary General of INTERPOL presented the findings to the Chinese government, which then carried out a criminal investigation and arrested individuals alleged to have produced and distributed the counterfeit artesunate.
- DQI was requested by INTERPOL to participate in Operation Storm, a follow-up investigation to Operation Jupiter targeting counterfeit manufacturers in the GMS who are distributing their products throughout Cambodia. INTERPOL is using the results from DQI's medicine quality monitoring program to develop enforcement strategies for police, customs and in-country INTERPOL agents.

Achievements in strengthening quality control and quality assurance systems

- USP DQI facilitated agreement on the development of a Cambodian Pharmacovigilance Center in partnership with the WHO, Cambodian MOH, DDF and pharmacovigilance experts. The Center was officially launched in June 2008. It is the first center of its kind in Cambodia and it will serve as a nexus of an adverse drug event reporting system, to be developed. A pharmacovigilance system is a cost-efficient and essential means of detecting and minimizing injury to patients and insuring against the undetected use of ineffective, *substandard or counterfeit* medicines. Furthermore, a medicines monitoring system assists in the promotion of rational drug use and the prevention of medication errors or inadvertent overdose.

Achievements in providing up-to-date information, mobilizing stakeholders, and raising public awareness about medicines quality issues

- In addition to the information provided through post-marketing surveillance, USP DQI brought together provincial and central level health staff from Cambodia and Thailand to engage in a collaborative study on anti-malarial medicine quality on the border areas using a randomised sampling protocol. The study will be finished in August 2009.

² <http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371%2Fjournal.pmed.0050032> Published Feb 12, 2008.



- DQI has made extensive use of media to raise public awareness about the dangers of counterfeit medicines. USP DQI was instrumental in the development and filming of Public Service Announcements (PSAs). Five versions were created to be culturally and linguistically appropriate – four versions for Thailand, Lao PDR, Viet Nam, Cambodia respectively as well as an English version for broadcast on regional channels and use by USAID and USP DQI. Broadcasting is currently underway in Cambodia on TVK. Furthermore, USP DQI filmed an interview with His Excellency Dr. Yim Yann, Undersecretary of State, in the Phnom Penh wholesale market to help illustrate the nature of the problems that the Ministry of Health faces to assure the quality of medicines in Cambodia and what the government has been doing to combat it. Lastly, USP DQI shot a short film in Battambang and Phnom Penh that demonstrates how the Minilab can be used out in the field to perform basic quality testing. The film will be ready for release in late 2009.

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