Global Interagency Efforts  
Stem Counterfeit Drugs in  
Greater Mekong Asia

Lessons Learned:
- Submit an early request for clearance in each country and follow up with constant communications to prevent delays in formal country clearances and in completing financial transactions.
- Starting on the first day of the project, invoke a sense of ownership among all parties to ensure unfettered collaboration.
- Reevaluate technical requirements and make sure people on the ground are well-trained and have enough equipment to do their jobs effectively.
- Check the collaborative chain for weak links. It isn’t enough for agencies, governments and law enforcement to agree to work together. The technology and mechanisms for cooperation must also be in place.
Drug-resistant strains of a variety of potentially fatal diseases are appearing globally at an alarming rate. Can the lessons learned in eradicating poor quality medicines that helped create particularly virulent and drug-resistant malaria strains in the Greater Mekong be used to prevent the rise of new strains in other diseases?

In the Southeast Asia/Western Pacific area, an estimated 10 to 35 percent of medicines are improperly made or illegally produced and sold. The area’s high burden of malaria and elevated resistance rates to treatment are in many cases directly attributable to the proliferation of poor quality medicines. Substandard medicines allow the malaria parasite to survive and then develop resistance to existing treatments. Beyond the loss of life suffered immediately though the distribution of sub-par medicines, a breeding ground for highly virulent and resistant strains develops, from which untreatable disease can eventually spread to kill thousands in many nations.

Finding and eradicating poor quality drugs in the five-country region — Cambodia, Thailand, Lao People’s Democratic Republic (Lao PDR), Vietnam, and Yunnan Province in China — has proven an exhausting exercise. Medicines are sold across all five countries in public (hospitals, health clinics, and posts), private (hospitals, clinics, and pharmacies), and informal (illegal outlets) sectors making drug collection, sampling and enforcement particularly challenging.

In an effort to combat the problem throughout the region and across its many borders, the United States Pharmacopeia Drug Quality and Information Program (USP DQI) has closely collaborated with the United States Agency for International Development (USAID)/Regional Development Mission for Asia (RDM-A), the USAID/Cambodia Mission, and the Ministries of Health of Cambodia, Thailand, Lao PDR, Vietnam, and Yunnan Province (China). Together these organizations battle the
The devastating effects of counterfeit and substandard medicines readily available in the Mekong Region.

At the requests of USAID/RDM-A, USAID/Cambodia Mission, and the Ministries of Health throughout the region, USP DQI developed a framework to support the governments in their quest to improve the quality assurance and quality control (QA/QC) of their medicines and create a comprehensive, sustainable program to build technical capacity. The process required cooperation and integral collaboration with each country's Ministry of Health (MOH), medicines regulatory authority (MRA), national medicines quality control laboratory (NMQCL), national priority disease control programs, surveillance site staffs, and, in some instances, community health care workers. USP DQI secured commitment from each through the drafting and signing of Memorandums of Understanding from the beginning in 2003 until 2007. Currently, the organizations use contract agreements that outline what USP DQI will provide and what the MRA and MOH of the respective country will carry out each fiscal year.

Through close partnerships with country MRAs, NMQCLs, and national disease control programs for malaria, tuberculosis, and HIV/AIDS, USP DQI develops yearly work plans of proposed activities. The USAID Missions make decisions on which agreed-upon activities to fund and in what amount; USP DQI oversees implementation of all activities according to an accepted time line, making regular field visits to provide guidance and monitor progress.

Counterfeit drugs are defined as those that are deliberately mislabeled to obscure source and product identity. Some of these are perfect mirrors of the drugs they copy; many more are not. Substandard drugs are defined as legally branded or labeled but the quality falls below international standards on quality, purity, strength, or packaging. Most commonly, substandard medicines have one or more of the following qualities:

- lacks an active ingredient but inactive ingredients are harmless,
- found to have poisonous or harmful ingredients,
- manufactured in poor conditions or smuggled past authorities,
- is registered but only by a weak agency,
- has passed its expiration date, or
- has been improperly stored and/or transported resulting in a tainting or reduction in strength of the active ingredient.

Since 2003 the Mekong Region monitoring program has grown from 17 to 39 sites and has broadened to include antimalarial, antiretroviral, and anti-tuberculosis medicines, as well as oseltamivir (for treatment of avian influenza) and some commonly
used antibiotics. Through information gleaned from the USP DQI monitoring program, countries have fined sellers of counterfeit medicines, closed pharmacies, confiscated products, and issued regulatory warnings and notices to alert health professionals and the public.

**From Assistance to Arrests**

In 2003 USAID asked USP DQI to provide technical assistance to the Ministries of Health of these five Southeast Asian countries. In response, USP DQI developed a framework to support the governments in improving the quality assurance and quality control of their medicines. The USP DQI also helped each government create a comprehensive, sustainable program to build technical capacity.

USP DQI began by assessing the existing quality assurance/control systems of each country, including drug registration, quality control laboratories, procurement, storage and distribution, and post-marketing surveillance efforts. It then collected data from the field on specific antimalarial drugs in order to determine the quality of medicines in the marketplace, present findings of gaps or weaknesses, and design individualized plans for improvement based on each country’s priorities. After assessments were completed, USP DQI launched the Antimalarial Medicines Quality Monitoring Program in the Mekong Sub-region. The newly designed protocol leveraged established sentinel sites.

In Cambodia, Lao PDR, Thailand, and Vietnam, USP DQI works closely with each country’s Ministry of Health; relevant government agencies, primarily the MRAs; various institutions; and national disease control programs for malaria, HIV/AIDS, and tuberculosis; national medicines quality control laboratories; World Health Organization, and INTERPOL. In Cambodia, Laos and Vietnam, USP DQI supported the creation of inter-Ministerial committees consisting of MOH, Ministry of Finance/Customs, Ministry of Interior/Police, Ministry of Trade, and prosecutors to collectively work against counterfeit drugs and illegal outlets.

The USAID Regional Development Mission for Asia and the USAID/Cambodia Mission have funded all related medicine quality monitoring activities in Cambodia, Vietnam, Lao PDR, and Thailand since the program began in 2003. Work in Yunnan Province of China was discontinued in 2005 due to political sensitivities between the U.S. and Chinese governments upon discovery of fake artemisinin samples found there.

Since monitoring began in 2003, more than 4,700 samples have been collected and tested. USP DQI has supported and encouraged collaboration among the Ministries of Health, other country Ministries, and enforcement-related agencies to act on negative results.

In one example, USP DQI contributed to “Operation Jupiter,” an international enforcement action, by supplying sentinel site data of medicines that were collected and tested as part of the Mekong Region Medicines Quality Monitoring program. INTERPOL and WHO coordinated the various partner efforts. Evidence from chemical, mineralogical, biological, and packaging analysis suggested that at least some of the counterfeit artesunate was manufactured in southeast China. This evidence prompted the Chinese Government to act quickly against the criminal traders with multiple arrests and the seizure of approximately $2.7 million worth of antimalarial products.

In another example: INTERPOL seized more than $6.65 million of counterfeit medicines for treatment of malaria, HIV, tuberculosis, and other common infections in Southeast Asia in 2008 and made 27 arrests, disrupting the region’s fake drug trade for the second time in three years. The five-month investigation, “Operation Storm,” involved almost 200 raids across Cambodia, China, Laos, Myanmar, Singapore, Thailand, and Vietnam. Under Operation Storm, police seized more than 16 million pills, including fake antibiotics for pneumonia and child-related illnesses. The USP DQI program exposed the counterfeit antibiotics and, working with country governments, provided the pertinent information to INTERPOL to initiate investigations.
As a result of these and other measurable actions, the quality assurance/quality control protocol that evolved has served as a model for activities in an additional 21 resource-limited countries. This protocol was first introduced into the Mekong region in 2003 and was presented in 2004-2005 to USAID Missions in other countries and regions and to other donors, in order to attract funding and support. The process, framework and methodology used in the Mekong Region has since been transferred — with some adjustments to fit any given country’s specific situation — to other countries in Africa and Latin America.

From Design to Results

Results from the program are encouraging. Data collected in 2004 revealed the wide availability of poor quality medicines. Most notably, up to 44 percent of samples of artesunate, an antimalarial drug, contained no active ingredient. In 2008, this figure dropped below 20 percent. Of the 358 antimalarial samples collected and tested, only 40 (11.2 percent) samples failed quality testing. Results provided incentive for medicines regulatory authorities to expand the USP DQI monitoring program.

USP DQI has designed country-specific sampling protocols plus supplied necessary laboratory equipment and reference standards for testing and trained almost 2,500 individuals to date. Additionally, it has facilitated numerous local and regional meetings to benefit communications among principals. The country governments that have requested USP DQI assistance state that their motivations are to improve health conditions in their nations, reduce the prevalence of counterfeit and substandard medicines, and restore public confidence in their ability to ensure safe, effective medicines in the marketplace.

Since sophisticated laboratory facilities are rarely available in the field, USP DQI teaches simple, practical methods for early detection of substandard and counterfeit drugs. To reach rural areas where the disease burden is generally higher, USP DQI supplies surveillance sites with portable laboratories, known as Minilabs, designed by the Global Pharma Health Fund. The Minilabs contain the necessary equipment, reagents, and secondary reference standards to test medicines for presence and content of the active ingredient and its ability to disintegrate properly.

Local analysts, usually pharmacists and community health workers from Ministries of Health are trained to perform basic tests: visual inspection, disintegration, and Thin Layer Chromatography, for example. In addition to basic tests, USP DQI has also designed a protocol and training program in sampling techniques.

The 37 active sentinel sites in the Mekong Region were selected in close collaboration with each country MOH based upon its specific national priorities. Some sites were chosen due to substantiated or anecdotal evidence on the prevalence of counterfeit medicines, especially at the border areas which are prone to illegal activity. Other sites were targeted due to the high burden of malaria or elevated resistance rates to malaria treatment, which can indicate the presence of poor quality medicines.

But this is not to say that the project has proceeded unimpeded by obstacles. Implementing medicines quality monitoring at the country level has been slow at times, primarily in the initial stages, according to USP officials. Collaborating with four separate country governments greatly magnified normally “simple” challenges, such as processing equipment and supplies through time-consuming formal country clearances, completing financial transactions, and making arrangements to the satisfaction of all parties. Differences in country quality assurance/control systems and language barriers—which could become confusing in the translation of sampling and testing protocols, for one thing—added another layer of delays.

Despite careful planning, a few unwanted surprises appeared along the way. For example, technical issues surrounding sampling procedures and testing developed in areas USP DQI had not anticipated. Some rural area sites had difficulty collecting the required quantity of samples for testing and verification and some countries lacked adequate equipment at the national laboratory to carry out verification testing. From field visits, it also became apparent that some of the trainees needed further reinforcement of basic sample collection and testing skills. To overcome these challenges, USP DQI amended the sampling protocol, reduced the number of units per sample to be collected; provided necessary lab equipment, reference materials, reference substances, and reagents;
trained sample collectors on analytical methods; and, conducted refresher training for field staff.

**Forming a Multi-Dimensional Partnership**

The relationships between many of the agencies have cemented over time and through many projects. The United States Pharmacopeia is a 185-year-old, not-for-profit public health organization whose mission is to improve the health of people around the world through public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods. USP Drug Quality and Information (USP DQI) program, a cooperative agreement between USP and the U.S. Agency for International Development (USAID), focuses on advancing the health care of people in resource-limited countries.

USP DQI has maintained a longstanding relationship with USAID regional and country Missions and takes an active role in the agency’s annual process of scheduling and budgeting activities through approved work plans. The work plan process is a collaborative effort in which all partners participate to determine priority activities. Separate work plans are proposed to each participating USAID Mission and then reviewed collectively in a regional partners’ meeting to eliminate duplicative efforts and to coordinate activities. The process is similar with any other agency funding USP DQI projects, such as the World Health Organization.

USP DQI determines in which countries activities will take place and where technical assistance is most needed. The USAID Missions make decisions on which agreed-upon activities to fund and in what amount; USP DQI oversees implementation of all activities according to an accepted time line, making regular field visits to provide guidance and monitor progress.

USP DQI’s medicines quality monitoring project in the Mekong Region is funded primarily by the USAID/Regional Development Mission for Asia and USAID/Cambodia Mission. Supplementary funding on topical aspects, for instance, testing the quality of medicines for Avian Influenza, may be provided by USAID/Global Health Bureau, Office of Health, Infectious Diseases and Nutrition. Through close partnerships with country MRAs, NMQCLs, and national disease control programs for malaria, TB,
and HIV/AIDS, USP DQI develops yearly work plans of proposed activities.

Despite the effectiveness of this extraordinary web of collaborators, relationships can and do remain delicate and occasionally lack conformity. Although all five countries experience many of the same problems, common goals and the willingness to work for common good are often lacking. Some key partners lack the financial resources for collaborative activities or the motivation to cooperate.

To bring the principals together and build alliance, USP DQI helped key partners find common ground and the trust to share data through numerous face-to-face meetings. USP DQI initiated discussions to obtain their support and encouraged their involvement as an integral part of the USP DQI project management team. This approach has invoked a sense of ownership in the program among the partners and resulted in demonstrated efforts of mutual cooperation.

Sharing information among relevant agencies within a country and between countries has been slow and ineffective, particularly among national law enforcement agencies and among medicines regional authorities, report USP staff. Consequently, when counterfeit or substandard samples are discovered in the field, weak or nonexistent information-sharing systems can further delay action. Some of the factors that contribute to the problem stem from underdeveloped human resources, fewer technology resources, and poor or restrictive regulatory procedures. In many cases, the main problem is there are no effective mechanisms for collaboration in place. USP DQI had to make the case for collaboration and then help build the bridges needed for the collaboration before the primary work could begin.

The Future
USP DQI’s future plans involve making medicine quality monitoring sustainable within each country’s own governmental construct. To that end, the plan calls for the MOH, MRA and NMQCL to gradually pick up the costs of sampling collection, testing and necessary reagents, reference standards, supplies and travel plus payroll costs for associated staff time. DQI/USAID hopes that these programs will become self-sustaining in the foreseeable future.
Meanwhile, DQI will be working with the Department of Health and other stakeholders to explore possibilities for leveraging other sources of funding such as from GFATM and WHO. DQI could help the country to develop a proposal to The Global Fund, for example, together with WHO and the Department of Health, to include key aspects of quality assurance and quality control of medicines in the proposal. These efforts too work towards eventual government sustainability and thus gradually phases out activities that donors will fund.

Beyond these measures, DQI’s future plans call for project expansion in both scope and reach:

Supporting regional or South-South collaboration and capacity building: Regional support can play an important role in strengthening national capacity and ensuring its sustainability. In this context, the DQI program plans to build sustainable capacity, where appropriate, by establishing regional centers of excellence that can serve as a technical resource in quality assurance of medicines for less developed countries in Latin America, Africa, Southeast Asia, or any other applicable region.

Participating in international initiatives to combat substandard and counterfeit medicines: DQI provides technical assistance in the form of training, facilitation of communication, and reporting field sampling and testing data to INTERPOL. A primary objective of this collaboration is to assist in providing evidence for enforcement actions taken by INTERPOL, customs, and police resulting from data generated from medicine quality monitoring programs. These actions are designed to disrupt the international trafficking of illegal, counterfeit, and unregistered drug products in countries where DQI has a presence.

Increasing community outreach to raise awareness about counterfeit and substandard medicines: In collaboration with NGOs that provide community-based services and other local players, such as pharmacists, DQI will attempt to raise public awareness through community outreach. Often, the first person patients seek for medicines and medical advice is a community pharmacist; in some countries, there is a lack of enforcement or an inability to disseminate information on poor quality medicines. In such cases, it is necessary to reach the public through alternative routes.

DQI’s plans include working with a broad spectrum of global partners and expanding collaborations (with international organizations and country partners). Some of the organizations include: WHO, USAID, the Bill & Melinda Gates Foundation, The Global Fund, INTERPOL, MeTA Alliance, PATH, and many local NGOs, among others.

By Pam Baker