The Hunt for Inferior Drugs

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Developing countries try to root out counterfeit and substandard drugs

Whether counterfeit or unintentionally substandard, poor quality medicines used to treat infectious diseases such as tuberculosis, malaria, and HIV/AIDs in developing countries may result not only in treatment failure but also in development of resistance to the few drugs available to treat them. The impact of these inferior drugs reaches beyond the health of the individual; it also leads to a loss of productivity and income due to death, disability, or extended disease duration.

In an effort to address the growing problem of poor quality medicines, the United States Pharmacopeia Drug Quality and Information (USP DQI) Program, with support from the U.S. Agency for International Development (USAID), is providing technical assistance to more than 30 developing countries. The program focuses on strengthening the capacity of medicine regulatory agencies to build quality into their processes. Strategies include increasing the ability of each country's national drug quality control laboratory to analyze medicines, providing current and unbiased information about drugs to consumers and healthcare providers, and exercising oversight of drug quality both before and after drugs hit the market.

Successes in Sub-Saharan Africa

USP DQI began working in Africa in 2003 and has so far helped establish drug monitoring programs in Benin, Ghana, Ethiopia, Liberia, Madagascar, Mali, Senegal, and Uganda.

Most efforts focus on making the transition from antimalarial drugs to artemisinin-based combination therapies (ACTs) as a first-line treatment. The countries are in varying stages of progress, depending upon the diligence of the MRA and cooperation among key players.

Madagascar is a small country with a big success story. As is common in many developing countries, the availability of substandard and counterfeit drugs in Madagascar had reached a disturbing level. In 2003, the country's Ministry of Health appealed to USAID and USP DQI for guidance. Since then, USP DQI has worked with Madagascar's newly established drug regulatory authority, l'-Agence de Médicament de Madagascar (AMM) to help improve the quality of drugs provided to its citizens. Using specially designed tools, USP DQI obtained information on the country's quality assurance/quality control systems, collected data from the field on specific drugs, and determined the quality level of drugs in the marketplace. Over the past five years, with support from the USAID/Madagascar Mission, the AMM and the national drug quality control laboratory (LCQM) have put into place much of the plan USP DQI proposed to address weaknesses that were identified in drug registration systems, quality control laboratories, procurement, storage and distribution, and post-marketing surveillance.

In collaboration with the World Health Organization (WHO), USP DQI installed specialized drug registration software and trained the AMM registration division on its use, as well as on good registration procedures. With the upgraded laboratory equipment, updated standard operating procedures, and the essential supplies USP DQI provided, the LCQM is able to perform analysis using high performance liquid chromatography and other advanced techniques. USP DQI trained the LCQM staff on the essential concepts of good laboratory practices (GLP), pharmacopeial standards, and standard operating procedures. It also taught hands-on laboratory training on pharmacopeial testing methods from basic dissolution to advanced testing for bacterial endotoxins. In Antananarivo and in five provinces throughout Madagascar, USP DQI and the AMM have established a drug quality monitoring program that collects, documents, and tests medicines from area markets, pharmacies, and community healthcare facilities.

Counterfeit drugs found in Cambodia. Data suggests that up to 44% of artesunate (a common, highly efficacious antimalarial) samples collected from selected provinces contained no active ingredient at all.

Sophisticated laboratory facilities are rarely available in the field, so 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 Minilabs, portable laboratories designed by the Global Pharma Health Fund that contain the necessary labware and reagents to test drugs for content, identification, purity, and dissolution. Local analysts are trained to perform basic tests, including visual inspection, disintegration, and thin layer chromatography. The LCQM now trains medical students from the Faculty of Medicine of Antananarivo and assigns them to sentinel sites to test the quality of drugs in the provinces. This collaboration introduces the importance of drug quality and its practical application into the university curriculum.

Within months of USP DQI training its staff, the LCQM had collected and tested a variety of drug samples for the first time in Madagascar and had discovered substandard drugs in the market. In Antananarivo, of the 46 drugs fully tested by the LCQM lab from public, private, and informal sectors, 22% were found to be substandard. Since that time, the drug quality monitoring program has analyzed more than 1,600 samples in two rounds of testing nationwide. As a result, the AMM has recalled three essential drugs from the market nationwide, closed two pharmacies, and withdrawn 16 lots of medicines.

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USP DQI has also supported the AMM in establishing a pharmacovigilance program that routinely collects data on adverse drug reactions (ADRs) from drugs that are already on

the market. USP DQI facilitated the training of all Ministry of Health staff, ensuring their support of all pharmacovigilance activities. In 2007, the program began expanding to the sentinel sites, anticipating the need to monitor ADRs that might arise from the country's rollout of ACTs for malaria.

USP DQI most recently assisted in establishing a Drug Information Center (DIC) in Antananarivo-the first in the country-which will provide drug information to healthcare providers and consumers.

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Improving Quality in Asia

The USP DQI program has also had success in Asia, another area rife with fake drugs. In the Southeast Asia/Western Pacific area, an estimated 10% to 35% of medicines are improperly made or illegally produced and sold. In 2004, USP DQI conducted a study revealing the wide availability of poor quality medicines in Mekong countries (Cambodia, Vietnam, Laos, Thailand, Myanmar, and Yunnan Province in China). The data suggest that up to 44% of artesunate (a common, highly efficacious antimalarial) samples collected from selected provinces contained no active ingredient at all.

The USAID Regional Development Mission sought help from USP DQI to turn the situation around, and the Mekong Antimalarial Drug Quality Surveillance Project was launched in Cambodia, Laos, Thailand, Vietnam, and Yunnan Province. Using established sentinel sites, USP DQI designed a protocol and trained staff in proper sampling techniques to collect and document medicines from area markets, pharmacies, and community healthcare facilities. The Mekong monitoring program has since grown from 17 to 39 sites and has expanded to collect other anti-infective medicines' for tuberculosis and HIV/AIDS, as well as some antibiotics. More importantly, the program serves as a model: Since 2005, USP DQI has established drug quality monitoring programs in 20 resource-limited countries, providing equipment, technical assistance, and training to almost 2,500 individuals.

The original Mekong program has expanded well beyond monitoring by recognizing the significance of maintaining drug quality at all levels in order to improve public health. In Vietnam and Laos, USP DQI and local partners have introduced an education program for community pharmacists, training them to provide care to people living with HIV/AIDS and supplying them with information on the safety and quality of medications. Because the community pharmacist is often the first place patients go to for drugs and medical advice, it can be a source of support for HIV/AIDS patients.

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In Cambodia, the authorities have introduced an educational campaign to raise awareness among healthcare providers and the general public about the dangers of using fake drugs. With the help of USP DQI, several articles have been published in Health Messenger magazine and Medicam Health News, and 20,000 copies of the WHO Dealers in Death CD have been distributed to healthcare providers. In addition, USAID/Cambodia Mission, USP DQI, and the Thai production company Living Films have produced public service announcements (PSAs) illustrating the possible consequences of using substandard counterfeit medicines in the treatment of illnesses common to the region, such as malaria. The PSAs, which use local actors speaking in local languages, will air in Cambodia, Laos, Thailand, and Vietnam on government and private television, in village media presentations, on Web sites, and through cellular phone downloads.

To bolster and sustain regional initiatives, USP DQI initiated the Asian Network of Excellence in Quality Assurance of Medicines (ANE/QAM), which provides specialized training to local institutions. The University of Santo Thomas Center for Drug Research, Evaluation & Studies, located in the Philippines, concentrates on bioavailability/bioequivalence analysis. In Thailand, Mahidol University Faculty of Pharmacy specializes in good manufacturing practices (GMP), while Chulalongkorn University/Pharmaceutical System Research and Intelligence (PSyRIC) focuses on quality assurance/quality control and information management. PSyRIC is building a public drug quality database to centralize results of surveillance testing in Southeast Asia and the Western Pacific Region.

Collaborating with International Organizations

USP DQI is also called upon by international organizations to provide technical assistance in quality assurance. Acting on a request from UNICEF in 2005, USP DQI was instrumental in rolling out the provision of zinc supplements for childhood diarrheal disease control. At that time, zinc was not marketed as a sole active ingredient-much less in the recommended dosage-with reliable quality or in a form conducive to easy distribution or willing consumption. USP DQI worked with French manufacturer Nutriset to increase its capacity in GMP and to become WHO pre-qualified for production of zinc supplements. USP developed monographs for zinc formulations, helped draft guidelines for the production of those formulations, and helped manufacturers to comply with GMP guidelines. USP DQI has also assisted the Bangladeshi company Square Pharmaceuticals to become WHO pre-qualified and is now working toward the same goal with Shelys Pharmaceuticals Limited in Tanzania.

Researchers at a lab in the Philippines test drug quality.

USP DQI and WHO are also collaborating on Quality of Antimalarials in Sub-Saharan Africa (QAMSA), a joint study to assess the quality of antimalarials in 10 sub-Saharan African countries. The study will provide baseline data on the extent of the problem of counterfeit and substandard products in sub-Saharan African countries and identify possible causes. USP DQI staff has trained representatives from each country on sampling procedures and basic tests, in addition to providing Minilabs and equipment to the three countries it sponsors. USP DQI continues to provide technical oversight, train additional country representatives and lab analysts, oversee sample analyses, and disseminate the data obtained to all countries involved. With the information from the QAMSA study, USP DQI and other stakeholders can propose possible strategies to address drug quality problems.

Countries with operational drug quality monitoring programs recently have begun to focus on pharmacovigilance. The same ADR reporting systems used in developed countries cannot be used in developing countries; they must be adapted to each individual setting. USP DQI sets up ADR reporting systems with a focus on new medicines used in the treatment of malaria, tuberculosis, and in the management of HIV/AIDS.

USP DQI collaborates with WHO pharmacovigilance experts to design programs based on available human and financial resources. With WHO and USAID, USP DQI has facilitated workshops on how to develop a pharmacovigilance program in Tanzania, Madagascar, and Cambodia and has provided support with implementation. The 2007 workshop for Francophone Africa, held at the National Pharmacovigilance Centre of Morocco, offered a first-of-its-kind hands-on training that examined the general aspects of pharmacovigilance, as well as issues specific to the safety of HIV/AIDS and antimalarial medicines in African countries.

Providing Continuing Support

The USP DQI Program is committed to facilitating and strengthening drug quality systems and information access for resource-limited countries. The organization will continue to strengthen the capacities of manufacturers and regulators in their efforts to ensure that quality drugs are available to those who need them most.

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