

Safety first

PRODUCT QUALITY IS A TOP PRIORITY FOR SCMS

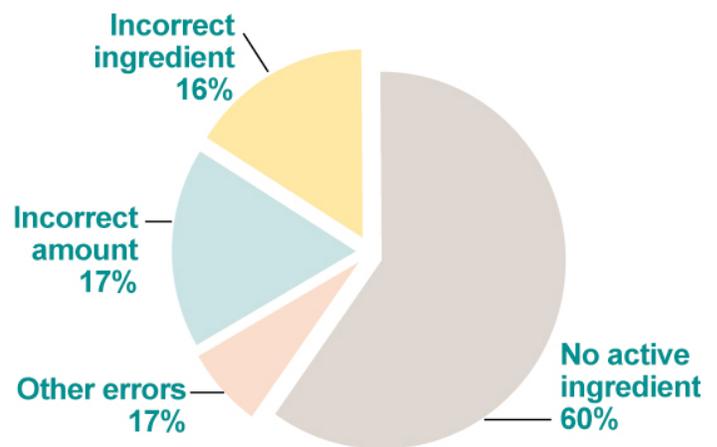
In many developing countries, street vendors selling anything from fruit to pharmaceuticals are a common sight. The medicines they sell are often of poor quality or counterfeit. At best, they may not work as intended; at worst, they can kill.

The risk to patients of substandard medicines is neither theoretical nor small. In September 2010 Reuters reported the seizure of 10 tons of counterfeit medicines in eastern Africa. (<http://www.reuters.com/article/idUSLDE67P1K1>)

Since the beginning of SCMS, our quality assurance program has been constantly innovating to ensure the commodities that we procure for people living with HIV/AIDS are of the highest quality standards.

Our quality assurance efforts initially focused on antiretroviral medicines (ARVs) due to the large volumes being procured to save the lives of those infected with HIV. Those efforts succeeded. Our quality assurance program for ARVs is the most rigorous program for developing countries and has helped to ensure that no substandard or counterfeit product has reached patients served by the US President's Emergency Plan for AIDS Relief (PEPFAR).

Over time the products requested of SCMS by PEPFAR programs have expanded beyond ARV treatment pro-



More than 300 cases of sub-standard medicines reported to the World Health Organization reveal a range of quality issues.

grams for those living with HIV/AIDS to the treatment of related diseases, testing for HIV and other conditions, and prevention of transmission of HIV and other diseases. Procuring new products leads to new challenges for quality assurance.

In this *In Brief*, you will find articles about innovative quality assurance for several product categories: two stories document innovative ways we're working to ensure the quality of medicines to treat opportunistic infections (OIs); another discusses the launch of a groundbreaking program to test the quality of diagnostic test kits; and the last explains how quality assurance is a key component of procurement of male circumcision (MC) kits for sub-Saharan Africa.

Beyond ARVs: Supplying medicines to fight opportunistic infections is the next front in the war against AIDS

Just a few years ago, many doubted that HIV/AIDS commodities could be reliably delivered in sufficient quantities to treat and care for the millions living with HIV in the world's poorest nations. The success of SCMS under PEPFAR and other major programs provides the proof that they can. The cost of ARVs has dropped from well over \$1,000 per patient each year to between \$100 and \$200, and stockouts of ARVs in SCMS-supported countries are virtually unheard of.

Although many of the challenges of procuring low-cost, quality ARVs are being addressed, supplying medicines for opportunistic infections (OIs) continues to be a frustratingly persistent challenge.

The core problem is the issue of quality. Many companies in sub-Saharan Africa and elsewhere manufacture and supply pharmaceuticals, but few meet PEPFAR's quality standards, which match those of the developed world. As a first line of defense, SCMS purchases pharmaceuticals from only those suppliers who are approved by the FDA or other stringent regulatory authority.

In addition, we can only buy and supply products that are registered and licensed for use in the country where we work. The intersection of those groups is quite small. (See illustration below.)

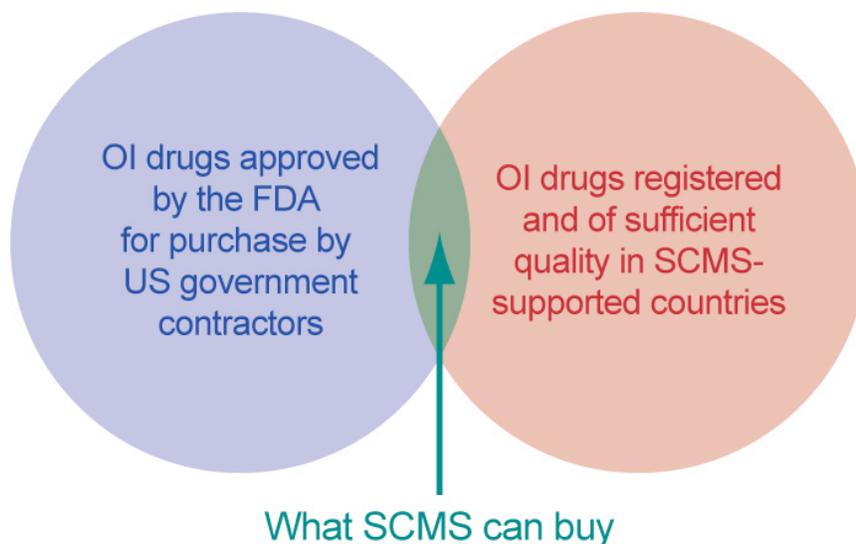
Medicines procured by SCMS are used to prevent and treat a range of opportunistic and co-infections, including:

- Herpes
- Malaria
- Pneumocystis carinii pneumonia
- Toxoplasmosis
- Tuberculosis
- Yeast infections, including thrush and candidiasis
- Other bacterial, fungal and viral infections

To address these challenges, SCMS aims to increase the number of suppliers that we can purchase from, either internationally or within PEPFAR-supported countries. To do that, we plan to leverage our position as a buyer of large quantities of medicines. Our buying power gives us a particular advantage to influence the market, encouraging suppliers to raise their quality standards so that they can have opportunities to access the orders we place for PEPFAR programs. We are pursuing two strategies simultaneously.

Identify suppliers within sub-Saharan Africa

The SCMS quality team is partnering with field office colleagues to identify and inspect local manufacturers as possible suppliers. If found to meet Good Manufacturing



SCMS's options for procuring medicines to treat opportunistic infections are relatively limited.

Practices (GMPs)*, we would then negotiate waivers with USAID to purchase from them. Our Quality Assurance team would then institute a thorough sampling and testing regimen to ensure that purchased medicines continue to meet our quality standards.

In Kenya we have inspected two manufacturers. One of those is responding positively to our feedback and will be pursuing WHO pre-qualification. In Tanzania, SCMS assessed two local pharmaceutical manufacturers for GMP compliance to participate in a new quality assurance program (see next article), and one of them was approved.

As can be expected, few suppliers will meet our quality standards the first time. The process provides them information they need to improve their processes and, at some point in the future, meet not just our quality standards but those of international stringent regulatory authorities.

Quality assurance in resource-limited settings: Innovative program launches in Tanzania

Patients needing medical attention in countries with weak drug regulatory infrastructure are at particular risk of receiving substandard or counterfeit medicines. At best, such drugs are ineffective, but at worst, they can cause serious illness and death. For example, in the fall of 2008, an allegedly counterfeit batch of paracetamol, a commonly prescribed pain medication, was suspected in the deaths of more than 30 children in Nigeria.

As a first line of defense against substandard medicines, SCMS is required to procure pharmaceuticals only from manufacturers approved by the FDA or other stringent regulatory authority. The result of this process is that most medicines we procure come from Asia, Europe or North America, where quality standards are generally higher. But the time required to procure from afar means that in urgent situations we sometimes have to go outside normal processes to meet the needs of patients.

For example, in June 2009, Tanzania experienced an impending stockout of paracetamol syrup, similar to the drug that caused alarm in Nigeria. There wasn't time, however, to procure the medicine on the international market and in keeping with importation requirements. SCMS worked with the Ministry of Health and USAID to develop a Plan B.

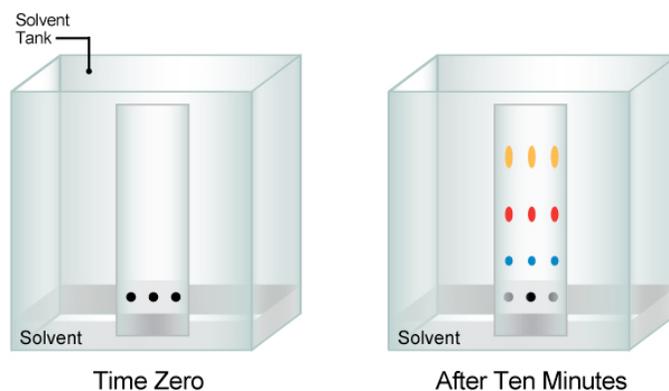
*GMPs are guidelines that outline the aspects of production and testing that can impact the quality of a product.

A local firm agreed to supply 10,000 units of the product under consignment, pending a quality assessment at the Laboratory of Pharmaceutical Analysis (LPA) at Muhimbili University of Health and Allied Sciences (MUHAS). The goal was to ensure that the medicine contained the appropriate active pharmaceutical ingredient (API). SCMS reviewed the laboratory results and obtained a waiver from USAID for Family Health International (FHI) to conduct a one-time procurement.

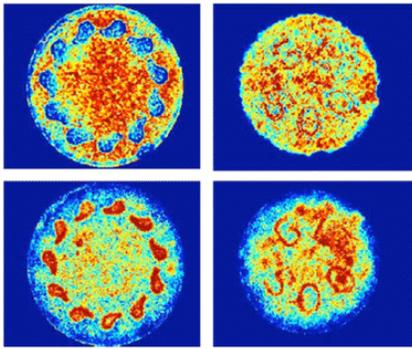
Quick thinking helped resolve an urgent situation, but the one-time waiver was a temporary fix. Potential stockouts occur fairly often in countries with limited resources and infrastructure, and having no medicine available for patients who need it is not a reasonable option. Public health programs are left with the uncomfortable inevitability of buying from local suppliers who may not meet international quality standards.

Unhappy with the current situation, officials in Tanzania began to ask for a long-term solution.

Our Quality Assurance team is working with the LPA at Muhimbili to pilot a first-of-its kind program to perform basic quality testing on pharmaceuticals. The first stage of the program involves a laboratory procedure known as high-performance thin layer chromatography (HPTLC). HPTLC assesses the APIs. As its name suggests, the procedure applies a test sample to a thin layer of material and, through capillary action over a short period of time, the active ingredients are separated for assessment and can be seen and compared to a control sample. This test indicates whether the medicine contains the right ingredients in the right amounts, and whether the pill will dissolve properly when taken.



Thin-layer chromatography reveals active pharmaceutical ingredients over a short timeframe.

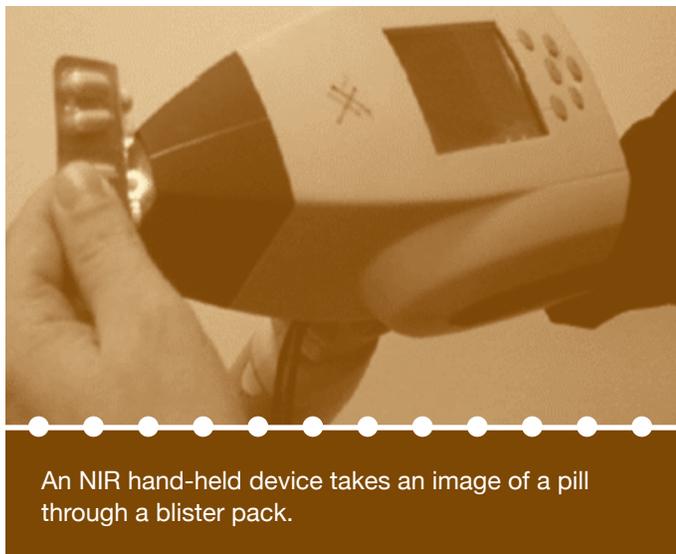


Images on the left show good-quality samples of two medicines. Images on the right show poorer blending of samples of the same two medicines.

To support country ownership of the program, our Quality Assurance team identified a laboratory in Dar es Salaam to conduct the HPTLC tests, the LPA at the MUHAS. The laboratory has proved that it can meet international testing standards. In an assessment of its program, LPA's test results compared very favorably with those of CAMAG Laboratories, a world-class facility in Muttenz, Switzerland.

Although this is a major step forward for Tanzania, HPTLC can detect no more than three or four compounds in a single sample. To augment the quality testing program, a second type of procedure, known as Near Infrared Reflectance (NIR), is currently being developed in partnership with FHI's laboratories in North Carolina.

Using the same basic technology as digital cameras, NIR employs easily transportable hand-held devices that can take a very high resolution image—a fingerprint of sorts—of a pill. By comparing the spectrum in the NIR fingerprint to an image of a pill known to be of high quality, the test will quickly identify poor-quality or counterfeit products.



An NIR hand-held device takes an image of a pill through a blister pack.

After development and testing at FHI, the hand-held devices will be sent to the SCMS office in Dar es Salaam to be used where and when they are needed. A second, more versatile instrument will be located at the LPA-MHAS for more sophisticated assessments and comparisons and is due to arrive at the laboratory in Dar es Salaam in spring 2011. The hand-held devices will then be deployed to the field to serve as the first line of defense against poor-quality medicines. The HPTLC program will then serve as a secondary test for product samples that fail NIR.

The launch of Tanzania's program is costing about \$150,000. If the program is successful, other countries could easily replicate it at a similar cost.

Neither the HPTLC nor NIR will test for everything, but at a relatively low cost they will provide a baseline of quality until further testing can be done. And that will mean all the difference to a patient who would otherwise go without a medicine they may desperately need.

Testing the tests: How reliable are diagnostic kits for HIV and other diseases?

SCMS's quality assurance program for pharmaceuticals is the most rigorous of any program providing medicines to the public sector in developing countries. Our sampling and testing program has prevented substandard ARVs and other medicines supplied through SCMS from reaching patients. Now we are turning our attention to the test kits that health care providers use to detect HIV and other conditions.

Currently, all HIV/AIDS rapid test kits (RTKs) purchased by SCMS and other PEPFAR-supported programs are validated at the US Centers for Disease Control and Prevention (CDC) before being approved for supply in PEPFAR programs; however, there is no routine surveillance to ensure the ongoing quality of the products. Also, no quality assurance programs are in place for the other kinds of test kits.

But this is not a unique situation. Worldwide, buyers of diagnostic kits—for HIV, pregnancy, syphilis and more—rely primarily on the manufacturer to ensure the quality of the test and the results it provides. In other words, those receiving a false negative or false positive result cannot reliably know if the fault lies with improper use of the test or a faulty test kit.

That is, until now.

SCMS is partnering with the University of Maryland to launch a groundbreaking program to test the test kits that we procure, providing the first quality assurance program for diagnostic tests for hepatitis, HIV, pregnancy, syphilis and tuberculosis.

The SCMS quality assurance team will collect and send samples of test kits to a laboratory in Baltimore following procedures similar to processes for pharmaceutical quality assurance:

- Routine sampling of kits collected upon delivery of shipments to our clients;
- With-cause sampling when quality issues are suspected; and
- Surveillance sampling of test kits near the point of use (i.e., clinics and hospitals)

Upon receiving the kits, technicians at the University of Maryland will then conduct tests to ensure that they are suitable for their intended use.

Routine sampling began in October 2010, and surveillance sampling will be launched soon in five countries and later expanded to include other countries where SCMS has field offices. To date, no incidents have triggered with-cause sampling.

Once the program is fully operational, it will answer a key question. Are commonly used tests for a variety of conditions as reliable as assumed.

Supporting prevention: Quality assurance is key to an innovative program that provides standardized kits for adult male circumcision

The search for a vaccine or cure for HIV/AIDS remains an elusive goal. Although 1.2 million people were brought onto treatment in 2009, two to three times that many likely contracted the virus. While the search for a vaccine and cure continues, public health providers are looking for more and effective ways to help prevent HIV transmission.

A number of studies have shown the rate of female-to-male transmission of HIV drops significantly if the male partner is circumcised. As many as 28 million men and their partners in sub-Saharan Africa could potentially benefit from the procedure. However, public health programs have been slow to adopt recommendations to implement cir-



Technicians at the University of Maryland practice protocols for testing test kits.

cumcision programs for adult men, in part because of the lack of supplies to carry out the procedure.

To facilitate the procurement of the large number of kits needed in PEPFAR-supported countries, PEPFAR partnered with WHO-UNAIDS in facilitating discussions among implementing partners on issues relating to supply chain management and in producing a comprehensive list of commodities. Participants designed three kit options to meet varying needs and, based on our track record of procuring other HIV/AIDS commodities, chose SCMS to provide the kits to interested programs.

The standard lists of commodities include scalpels and other surgical instruments, face masks, gowns, gloves, pain medication, infection prevention supplies and emergency toolkits. SCMS worked with experts from a variety of organizations to finalize the components of the three kit options, which clients can now find in the SCMS Core Formulary List. (See page 14 here: http://scms.pfscm.org/scms/docs/papers/ecatalog_january_2010.pdf)

Finding suppliers for a new product containing such a wide range of laboratory and surgical supplies was no easy task. Eventually, five potential suppliers responded to a request for proposal, submitting proposed pricing and sample kits for review.

Because circumcision is a surgical procedure, sterility is essential for all the pieces in the kit. And apparently quite a challenge. Only two suppliers passed SCMS's quality testing for sterility, and only one of those chose to participate in the launch of the program.

So far, several countries have elected to participate in the program. Zimbabwe was the first country to order male circumcision kits, totaling about 30,000. Rwanda placed an order for more than 5,000 kits, and Zambia has ordered 15,000. Kenya is currently evaluating the potential for using of disposable kits in its MC program, and Swaziland approved a fast-track plan to perform more than 200,000 MC operations within 6 to 12 months, starting around December 2010.

Although the procurement of so many kits is good news to those working to prevent the spread of HIV in east and southern Africa, having only one supplier for any commodity is a risk. No one vendor can ensure a reliable supply, particularly if presented with a number of large orders in a short time. Healthy competition also helps hold down prices while promoting good service.

Because male circumcision kits are so new, most suppliers do not yet have the core competencies to produce sterile kits. SCMS staff members are working with interested suppliers to help them find ways to complete sterilization of all kit components. We will reissue a new request for proposals and hope to soon add to the number of potential sources.

In the meantime, SCMS's procurement of male circumcision is supporting a new wave of HIV prevention efforts.

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ABOUT SCMS

The Supply Chain Management System (SCMS) was established to collaborate within country and global partners to ensure a reliable, cost-effective and secure supply of high quality medicines and health products for HIV/AIDS prevention, care and treatment. SCMS is funded as part of the President's Emergency Plan for AIDS Relief. Visit us at www.scms.pfscm.org.

The author's views expressed in this publication do not necessarily reflect the views of the US Agency for International Development or the United States government.