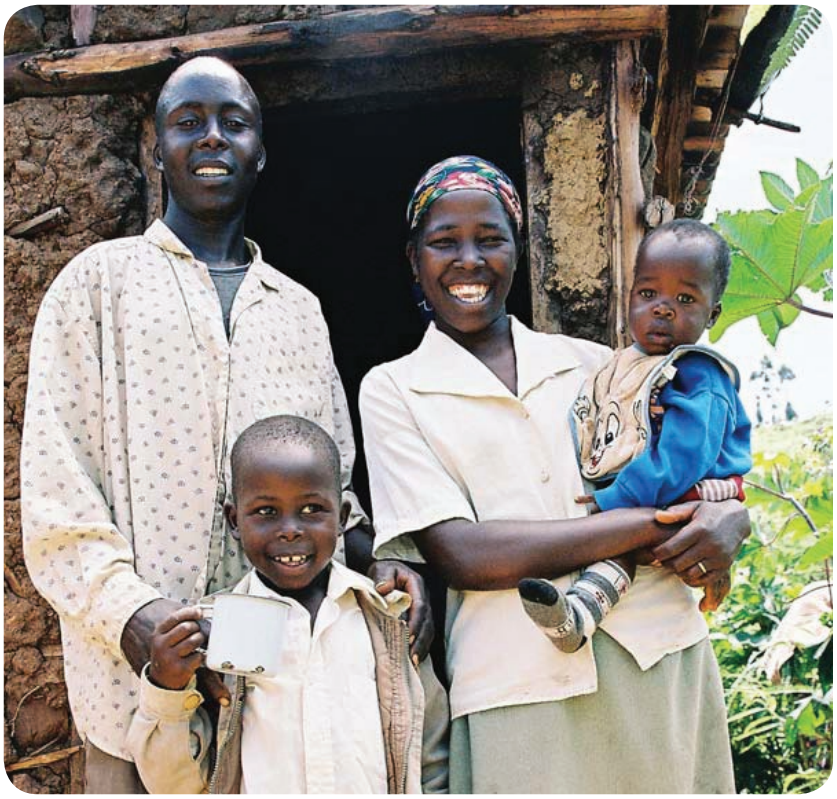
Improving Access to HIV/AIDS Drugs Abroad

Daniel Ngoshe, a father of six from Zambia, was unemployed when he found out he was HIV positive. But after starting drug treatment, his strength increased, making it easier for him to work at home and in his community. He became an adherence support worker, training others with HIV to take their medications properly so they can also live healthier lives.

Ngoshe's experience is just one of the stories of hope featured in the 2007 annual report to Congress on the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). Since it launched in 2003, PEPFAR has supported HIV/AIDS treatment for 1.1 million people, including more than 1 million in Africa. Before the plan, it is estimated that only 50,000 people in sub-Saharan Africa were receiving lifesaving antiretroviral treatment.

Antiretroviral treatment usually involves a combination of at least three drugs. This approach can dramatically reduce the number and severity of illnesses associated with HIV infection. It can also improve the duration and quality of life.



Doug Shaffer/ PEPFAR 2007 Annual Report

Through HIV counseling and testing for couples at the U.S.-supported Kericho District Hospital in Africa, Joyce and David found out they are infected with HIV. Joyce was four months pregnant with her second child at the time of diagnosis. Thanks to the clinic's program to prevent mother-to-child HIV transmission, Joyce delivered a baby boy who is HIV negative. After a year of antiretroviral treatment, David has also gained weight and feels healthy, enabling him to provide for his family.

A Unique Approval Process

To support PEPFAR's goals, the Food and Drug Administration introduced an initiative in 2004 to ensure that

FDA experts traveled to South Africa and India to discuss the guidance with drug manufacturers.

antiretroviral drugs produced by manufacturers all over the world could be rapidly reviewed, their quality assessed, and their acceptability for purchase with PEPFAR funds supported.

This was necessary because of the large amount of counterfeit and substandard pharmaceutical products available in many of the countries served by PEPFAR. The PEPFAR program sought to ensure that people receiving treatment were given quality products that would treat their diseases. A substandard product would not only be ineffective, but could possibly worsen the situation by stimulating the development of drug-resistant strains of the virus that causes HIV/AIDS.

"FDA set out to help PEPFAR make safe, effective, and lower-cost antiretroviral drugs available in the countries served by the plan," says Justina Molzon, MSPharm., J.D., Associate Director for international programs in FDA's Center for Drug Evaluation and Research. "In May 2004, we published a draft guidance encouraging manufacturers to submit applications of fixed-dose combination and co-packaged versions of previously approved antiretroviral therapies."

A fixed-dose combination has two or three drugs in a single pill. A co-packaged product contains two or three pills in a single package. "We encouraged these particular regimens for ease of use," Molzon says. "They simplify treatment, which can be a stumbling block for many people with HIV who find it difficult to maintain a regimen of several drugs."

FDA experts traveled to South Africa and India to discuss the guidance with drug manufacturers. The agency invited manufacturers to submit applications for combination and co-packaged products, even if they were not already approved and available in the United States. Additionally, FDA is helping make lower-priced generic versions of already approved and proven drugs available for purchase with PEPFAR funds, stretching resources to treat more people with HIV.

Patents protect drug companies' investments by giving them the sole right to sell the drug in the country where the patent is still in effect. FDA's assessment process helps make the drugs available in developing countries without violating the property rights of drug companies in the United States.

"For the generic antiretrovirals that can be marketed in the United States, full approval is granted," Molzon says. "But for those that cannot be marketed in the United States due to existing patent protection, a so-called "tentative" approval is granted. Tentative approval means that existing patents or exclusivity prevent the product from being sold in the United States, but that the product meets all of the scientific and quality standards for marketing in the U.S."

Only antiretroviral drugs designated with full approval or tentative approval are eligible for purchase with PEPFAR funds in developing countries. Due to the significant public health impact of these products,

About PEPFAR

- PEPFAR is the largest commitment ever by any nation for an international health initiative dedicated to a single disease.
- PEPFAR supports many countries around the world, with a special focus on 15 of the hardest hit countries in Africa, Asia, and the Caribbean.
- The five-year, $15 billion plan targets prevention, treatment, and care for people living with HIV/AIDS in the covered countries.
- The 15 focus countries: Botswana, Cote d'Ivoire, Ethiopia, Guyana, Haiti, Kenya, Mozambique, Namibia, Nigeria, Rwanda, South Africa, Tanzania, Uganda, Vietnam, and Zambia.
- On May 30, 2007, President George W. Bush announced his intention to work with Congress to reauthorize PEPFAR. The five-year $30 billion proposal would be in addition to the initial $15 billion commitment made in 2003.

For more information, visit *www.pepfar.gov*

As more drugs are approved and the choice of ARVs expands—including lower-cost, generic medications—treatment can be extended to more people.

FDA gives priority to the review of these submissions.

High Standards for Safety and Effectiveness

As part of this process, FDA maintains high standards for safety and effectiveness. The agency reviews applications to the same standards that products must meet to be marketed in the United States. Drugs designated with "tentative approval" could be on the U.S. market if it weren't for the patent protection that does not permit FDA to approve them for the U.S. market.

The process allows the manufacturers to say to those purchasing the products for the PEPFAR program outside of the United States: This product has been evaluated by FDA and was found to meet all of the scientific and quality requirements for products that are marketed in the United States.

Manufacturers can only sell to PEPFAR if there is assurance from FDA that there are not two standards--one for Americans and one for people from other countries. Under PEPFAR, the quality of products is the same.

Recent Approvals

FDA's initiative for granting full or tentative approval of antiretroviral drugs (ARVs) under PEPFAR supports the goal of purchasing the largest amount of quality products so that they can treat the largest number of people. As more drugs are approved and the choice of ARVs expands—including lower-cost, generic medications—treatment can be extended to more people.

In testimony before the House Committee on Foreign Affairs in April 2007, Ambassador Mark Dybul, the U.S. Global AIDS Coordinator, said that PEPFAR has achieved significant progress in reducing the cost of ARVs through its Supply Chain Management System (SCMS).

"We have determined that SCMS secured better purchase prices on 72% of first-line ARVs and 40% of second-line ARVs, compared with other selected benchmark pricing sources and buyers," Dybul said. "SCMS has achieved savings by purchasing generic medicines whenever possible, pooling procurement (such as consolidating multiple orders to buy in larger volumes), and establishing long-term, indefinite quantity contracts with manufacturers, thereby leveraging lower prices through bulk purchases."

For example, SCMS's purchase of the generic drugs Didanosine 200 mg and Efavirenz 200 mg resulted in cost savings of more than $46,000 (53%) and $116,000 (52%) respectively. By using generics, SCMS was able to save an estimated $1.7 million in fiscal year 2006. This is a 42% reduction of the cost of using innovator drugs.

Examples of other recent FDA approvals and tentative approvals under the program

- **Generic abacavir sulfate tablets:** In May 2006, FDA announced the tentative approval of generic abacavir sulfate tablets manufactured by Aurobindo Pharma LTD of Hyderabad, India. This is the first generic version of the already approved Ziagen Tablets, an anti-HIV medication manufactured by GlaxoSmithKline.
- **Three-ingredient fixed-dose tablet:** In June 2006, FDA issued the first tentative approval for a three-ingredient fixed-dose tablet for use as a stand-alone antiretroviral treatment for HIV-infected adults. The product, manufactured by Aurobindo Pharma LTD, contains the active ingredients in the widely used antiretroviral drugs Epivir (lamivudine), Retrovir (zidovudine) and Viramune (nevirapine). FDA

For a complete list of drugs with full or tentative approval under the program, visit FDA's PEPFAR page *www.fda.gov/oia/pepfar.htm*

To access the FDA guidance, visit *www.fda.gov/cder/guidance/6360fnl.pdf*