The United States President's Emergency Plan for AIDS Relief

# Bringing Hope:

## Supplying Antiretroviral Drugs for HIV/AIDS Treatment


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**Report on Antiretroviral Drugs for HIV/AIDS Treatment**

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Report to Congress Mandated by H.R. 3057


Submitted by the Office of the U.S. Global AIDS Coordinator
U.S. Department of State
May 2006

The Coordinator of the United States Government Activities to Combat HIV/AIDS Globally shall make available to the public a report setting forth the amount of United States funding provided under the authorities of the United States Leadership Against HIV/AIDS, Tuberculosis, and Malaria Act of 2003, or under an amendement made to that Act, to procure antiretroviral drugs. The report shall include a detailed description of the antiretrorival drugs procured, including a) the amount expended for generic and for name brand antiretroviral drugs; b) the price paid per unit of each such drug; and c) the vendor from which such drugs were purchased.

The Emergency Plan has supported treatment for approximately 471,000 people worldwide in 2005, including this mother and child in Guyana. The family also participates in counseling and nutrition activities and receives home care visits three times a month.

"Before the Emergency Plan for AIDS Relief, only 50,000 people of the more than 4 million people in sub-Saharan Africa needing immediate AIDS treatment were getting medicine -- think about that, only 50,000 people. After two years of sustained effort, approximately 400,000 sub-Saharan Africans are receiving the treatment they need."

President George W. Bush
World AIDS Day
December 1, 2005

## Introduction

In just over 2 years, the President's Emergency Plan for AIDS Relief (PEPFAR/Emergency Plan) has moved faster than any other bilateral or multilateral initiative to support the expansion of HIV/AIDS services. PEPFAR has used a network model of care to bring life-extending antiretroviral treatment (ART) to areas that are among the world's most difficult to serve. This success is rapidly transforming the social landscape in many of the world's hardest-hit nations, and it is an achievement to celebrate. From the inception of the initiative through September 30, 2005, the Emergency Plan has partnered with host nations to support treatment for approximately 401,000 people in the 15 focus nations, and 70,000 people in the rest of the world, for a total of 471,000 people worldwide. In Fiscal Year (FY) 2005, $421 million in funding supported treatment in the fifteen focus countries. In FY 2006, the planned funding is significantly increased - $663 million for ART [of which $279 million is planned for antiretroviral drugs (ARVs)].

Comprehensive treatment is a complicated endeavor, and the needs of host countries, as defined by their national strategies, differ. There are a number of significant components of quality ART, including: general clinical support for patients, such as non-antiretroviral medications and laboratory tests; training and support for health care personnel; physical infrastructure, including clinics, counseling rooms, laboratories, and distribution and logistics systems; monitoring and reporting systems; and other relevant components of treatment, including the ARVs themselves. Funding in FY 2005 and 2006 illustrates that the procurement of ARVs constitutes only a portion of all PEPFAR support for treatment activities.

Figure A: Antiretroviral Treatment and ARV Procurement Support

| | FY05 | Planned FY06[1] |
|---|---|---|
| **Total ART Support** | $421 million | $633 million |
| **Share of ART Support for ARV Procurement** | $191 million | $279 million |

[1]These funding levels are current estimates for FY06.

Strong leadership and dedicated personnel are essential to the successful delivery of ART. The Emergency Plan is working to provide such training through innovative methods. In FY 2005, PEPFAR supported training or retraining for approximately 36,500 ART service providers in the focus countries. These efforts range from lecture format to bedside mentoring, and include on-the-job training and other strategies to support those trained in remaining at their posts.

Antiretroviral treatment supported by PEPFAR has enabled Ruth Nkuya to continue to work and care for her family in Malawi.

Strengthening sites for quality ART provision is critical: this includes addressing deficits in infrastructure, laboratory capacity, and procurement and distribution of ARVs and other commodities. The Emergency Plan supported approximately 800 ART service sites in the focus countries in FY 2005, and the new Partnership for Supply Chain Management (PFSCM), described in Section II, was designed to help meet the procurement and distribution challenges for ARVs and other commodities needed for quality treatment. PEPFAR support for laboratory capacity – including equipment, training, and quality control – is also helping nations improve their ability to monitor individuals' response to care and treatment and make better informed clinical judgments.

Although they are often overlooked, the costs of clinical monitoring are an important part of Emergency Plan support. Establishing whether an individual is infected with HIV and determining their eligibility for ART is essential, and clinical monitoring remains critical for patients who begin ART. Ongoing contact with the health care system, including monitoring by a well-trained health care provider and laboratory monitoring, is important for the well-being of a patient. Laboratory support is also needed because ARVs have specific toxicities and it is important to understand whether an individual can tolerate therapy. Initial laboratory tests help clinicians determine the baseline function of the immune system, the liver, and bone marrow. The tests also serve to establish a baseline that can be used to measure improvement or deterioration in status. People living with HIV/AIDS (PLWHA) suffer from a number of opportunistic infections and laboratory support also plays a key role in ensuring proper diagnosis and prompt treatment for illnesses such as TB or cryptococcal meningitis.

Successful ART programs rely on community involvement to support patient adherence. ART requires a high degree of adherence to taking ARVs as prescribed. Patients who take less than 95% of their medications run a serious risk of developing resistance and failing therapy. Additionally, there is the very real danger of patients transmitting these resistant viruses to others. Involving the community is thus an essential component of successful Emergency Plan supported programs, and the costs of community support programs are an important part of delivering ART.

## Challenges to Establishing and Maintaining an Adequate Supply Chain for Antiretroviral Drugs (ARVs)

Providing support for prevention, care and treatment programs requires a serious commitment to supply chain management. In this context, supply chain management represents the procurement, distribution and delivery of essential drugs and supplies. Scaling up from an estimated total of 50,000 people on ARVs in all of sub-Saharan Africa prior to the Emergency Plan's initiation to almost 500,000 people supported currently by PEPFAR poses significant challenges, particularly in the area of ARV supply chain management. Weak supply chain infrastructure and a lack of human capacity to ensure that essential products reach ART points of service are considerable hurdles. Environmental conditions are challenging and ensuring that ARVs arrive in usable condition requires considerable efforts. In FY 2005 the surge in demand for ARVs stretched global supply chains to the limit and in some instances produced delays in delivery. This has required ongoing dialogue between the U.S. Government (USG) and pharmaceutical manufacturers to work to ensure sufficient and timely supply.

Drug quality has also been a significant challenge, and the Department of Health and Human Services/Food and

Drug Administration (HHS/FDA) and other regulatory bodies have worked to review and approve products to meet the global demand. A lack of formulations for pediatric regimens appropriate for resource-limited regions of the world has posed a significant barrier to reaching the millions of children impacted by HIV/AIDS. In addition, although not as problematic as might have been expected, there remains a need to prevent the diversion of donated ARVs to the private or black markets.

The Emergency Plan, by working closely with host governments and multilateral organizations, has developed a number of approaches to address the significant challenges involved in a large-scale increase in ART. The following sections provide additional details on some of these efforts and the context for Emergency Plan efforts to reduce ARV-associated costs to allow for further expansion of ART services.

## Supply Chain Management Capacity

In concert with its partners, the USG is supporting host nations to build the necessary infrastructure to meet the challenges of building a reliable supply chain for ARVs. The Emergency Plan and its partners have worked with partners on the ground, including indigenous community- and faith-based organizations, to strengthen their procurement systems. Efforts have included detailing of procurement experts to Ministries of Health, training in-country partners regarding supply chain management, and helping to ensure the physical infrastructure necessary to maintain a regular supply of quality commodities.

As part of this effort, the PFSCM, established in FY 2005, has begun to strengthen systems to deliver an uninterrupted supply of high-quality, low-cost products that will flow through a transparent, accountable system. PFSCM supports the purchase of ARVs, as well as non-ARV drugs that are needed for HIV/AIDS patients, including medications for opportunistic infections, sexually transmitted infections (STIs) and tuberculosis, and some antimalarial drugs. PFSCM also supports the purchase of quality laboratory materials, such as rapid test kits, and supplies like gowns, gloves, injection equipment, cleaning and sterilization items.

Participation in PFSCM is voluntary and services can be selectively utilized depending on the needs of the country and program. In those countries where existing supply chains are working well, PFSCM is available as an option to "fill in the gaps" and monitor key steps in the supply chain process. Among the menu of services PFSCM offers are commodity quantification, procurement, and shipping and delivery to points of service. PFSCM helps deliver essential lifesaving medicines to the front lines of Emergency Plan joint efforts with host nations. PFSCM ensures a healthy, robust lifeline of continuous drugs and supplies that are safe, secure, reliable and sustainable, and will offer the possibility of cost efficiencies. It also allows reliable forecasting of need to ensure adequate production.

Use of the PFSCM is encouraged in order to promote efficiency through centralized procurement. PFSCM can also provide technical assistance to strengthen existing local or national supply chain management systems even if no commodities are being procured through PFSCM. Although the PFSCM is a U.S. Agency for International Development (USAID)-managed contract, it is intended to support commodities procurement for all USG projects (i.e., projects managed by any USG Agency).

Under the President's Emergency Plan, PFSCM is not charged to build parallel systems, but to be additive and complementary to existing supply chain efforts in the field. It is intended to fill in the gaps where supply chain services are needed the most. Its portfolio includes:

- Developing and maintaining a competitive and transparent procurement system, including forecasting future need and leveraging volume purchasing to achieve significant reductions in the current costs of commodities;
- Establishing a quality assurance plan to manage documentation and ensure quality of commodities;
- Providing freight forwarding and warehousing services to facilitate consolidation and shipping from manufacturers worldwide;
- Establishing in-country support teams to provide the highly complex technical assistance needed to improve existing programs; and
- Developing Management Information Systems (MIS) to track the commodities provided through this agreement by estimating needs by recipient programs, financial accounts by country and funding source, production and warehouse stock levels, and the status of all shipments in-transit.

Each PFSCM partner offers unique capabilities that will ensure that high-quality ARVs, HIV tests, and other supplies for treating HIV/AIDS are available to the

people – patients, clinicians, laboratory technicians, and others -- who need them.

## Drug Approvals and Regulations

The Emergency Plan remains committed to funding the purchase of the lowest-cost ARVs from any source, regardless of origin, whether copies, generic, or branded, as long as those ARVs are proven safe, effective, and of high quality, and their purchase is consistent with international law.

To meet the need for rapid identification of ARVs proven to be safe, effective, and of high quality, HHS/FDA introduced in May 2004 an expedited review and inspection process whereby ARVs from anywhere in the world, produced by any manufacturer, could be rapidly assessed by HHS/FDA and, if approved or tentatively approved, made eligible for purchase under PEPFAR. (Tentative approval means that the product meets all of HHS/FDA's safety, efficacy and manufacturing quality standards, but that patent or market exclusivity prevents HHS/FDA from issuing a full approval for marketing in the United States. Because the distinction is not significant for this report, the report uses the term "approved" to refer to drugs that have received either full or tentative approval.)

ARVs approved through the expedited process are determined to meet standards equal to those established for the U.S., ensuring that no ARV drug purchased for use in PEPFAR programs abroad falls below standards for those drugs available to U.S. families. Through December 2005, 15 new generic formulations received approval from HHS/FDA under the expedited review process established in May 2004, including four pediatric formulations. By late 2005, at least four focus countries had begun to import HHS/FDA-approved generics, and FY 2006 data to date indicates this group will continue to expand. As a side benefit, the process developed for PEPFAR has also expedited availability of some generic versions of ARVs for which U.S. patent protection has expired.

Most host nations, however, require additional marketing authorization application review that can delay or prevent implementing partners from using ARVs that have been found safe and effective by HHS/FDA. To promote exchange of information regarding technical approaches to the regulatory process, HHS/FDA conducted a workshop for host governments' counterpart agencies on this issue in September 2005. HHS/FDA is engaging in additional outreach efforts to inform drug regulatory officials about its review process, and to keep them informed about the current list of such ARVs. This collaboration will improve mutual understanding of the regulatory processes and hasten the in-country approval process.

The USG has also worked with multilateral partners. HHS/FDA has signed a confidentiality agreement with the WHO Prequalification Unit to hasten the inclusion on the prequalification list at WHO of generic ARVs approved by HHS/FDA, and such ARVs have begun to be added to the drug list maintained by the WHO prequalification project based solely on the HHS/FDA assessment. The Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) now recognizes HHS/FDA approval as approval by a "stringent regulatory authority," which means Global Fund resources may go to purchase HHS/FDA- approved generic antiretroviral drugs.

U.S. Embassies have been provided with cables regarding the above issues and have been requested to work with the host governments to facilitate the local registration process for these drugs as appropriate. As part of its activities, the Emergency Plan has asked PFSCM to provide technical assistance to USG and host country authorities to build capacity and to facilitate the review and approval process as appropriate.

## Quality of ARVs

In the area of treatment, it is particularly essential that programs maintain the highest quality. Because treatment is complex, quality treatment has many elements. ARVs are one of these critical elements. The quality, safety and efficacy of formulations must be ensured, and ARVs and other needed commodities must travel to treatment sites via a secure and reliable supply chain.

The effects of poor quality treatment go beyond simple waste of scarce resources. Poor quality treatment means increased risk of morbidity and mortality for individual patients. Just as importantly, it can lead to widespread development of toxicity and transmission of viruses resistant to current treatment. The Emergency Plan is thus devoting intensive resources to strengthen the systems necessary to ensure that the treatment offered to HIV-positive people in the developing world is of high quality.

Low-quality or inappropriately prescribed ARVs can do more harm than good in the fight against HIV/AIDS. Drug interactions often alter the preferred first-line therapy, as in the case of those treated for HIV and TB simultaneously, many of whom cannot use their nations' preferred first-line regimens. Drug resistance and toxicity are already increasing in nations as ART becomes widely available, making it increasingly crucial that a broad formulary be available.

## Antiretroviral Drug Procurement

This report details the procurement of antiretroviral drugs in the Emergency Plan's fifteen focus countries in FY 2005, as well as some preliminary trend data for procurement in FY 2006. It is important to note that data after September 30, 2005 is limited, and is only used to demonstrate initial FY 2006 activity in the purchasing of ARVs. Complete data on ARV procurement in FY 2006 will be included in the Emergency Plan 2006 Annual Report.

### Report Methodology

The Congressional report language requested "a detailed description of the anti-retroviral drugs procured, including a) the amount expended for generic and for name brand anti-retroviral drugs b) the price paid per unit of each such drug; and c) the vendor from which such drugs were purchased." Based on this request, a survey instrument was designed by PFSCM to obtain the required data. Data collection was facilitated by the creation of a spreadsheet form, complete with validation tables, for respondents to use.

PFSCM e-mailed the request and survey tool to the four central programs, in addition to four US-based and 30 in-country partners. These initial communications were followed with more detailed correspondence as the responses were received and technical assistance was offered to compile the data. Responses accounted for $128 million of the total $191 million funded in FY 2005 (note that some responses included FY 2006 planned funding). The assembled data was migrated into a database format to facilitate the analysis of the data. During this stage the data was "cleaned"; for example, typographical and numerical errors were corrected and blank fields amended to be consistent with other provided data. Inconsistencies and other queries were raised with the survey respondents as necessary.

An adherence counselor at the Binh Thanh Out-Patient Clinic in Vietnam shows a PLWHA how to fill a pill box to support adherence of ARV.

Analysis focused on the following characteristics by country: generic versus branded product, manufacturers, prices paid, and trends from FY 2004 to FY 2005 (and for partial data received for FY 2006). Aggregated cost information was derived for each of these characteristics and cross-tabulations of the data in order to respond to the Congressional request.

In addition, the results of the survey were used to (1) estimate the "savings" achieved by the procurement of product from generic manufacturers, using the mean price for the actual procurements of ARVs from originator manufacturers, and (2) estimate the annual cost of treatment with generic and with branded products.

### Results

*Proportional costs of ARVs versus other aspects of treatment*

Because there are so many elements of quality ART, the cost of ARV drugs is only one component of the average cost per person per year for the complete ART package. Drugs remain a significant component of cost, to be sure, but are no longer the fundamental obstacle to treatment that they once were. This reality highlights the importance of all the components required to provide quality ART.

A recent publication emphasizes that the cost of ARVs is one among many costs of supporting ART for PLWHA.[1] In Haiti, the estimated cost of ART was $1600 per year, with ARVs accounting for 35 to 45% of the total. The $1000 per patient per year costs of ART included personnel ($450), laboratory monitoring ($300), medications other

1 Severe P, Leger P, Charles M, Noel F, Bonhomme G, Bois G, George E, Kenel-Pierre S, Wright PF, Gulick R, Johnson WD Jr, Pape JW, Fitzgerald DW. Antiretroviral therapy in a thousand patients with AIDS in Haiti. N Engl J Med. 2005;353(22):2325-34.

than antiretroviral drugs ($75), data monitoring ($75), and miscellaneous costs ($100).

ARV costs can be significantly reduced with the use of HHS/FDA-approved generics. However, most of the HHS/FDA-approved generics that are currently used are part of first-line regimens. Second line regimens are vital for patients who are unable to use first-line regimens due to failure or resistance. As more people are placed on chronic ART, the demand for second-line therapy will increase as resistance and other side effects emerge. Although the exact proportion varies, an estimated 10% of patients fail or become resistant each year. Many countries rely on the USG to meet this growing demand for second-line therapy as part of their Emergency Plan support. Second-line regimens are more complicated and often employ far more costly medications. Additionally, patients may require a number of different costly combinations before finding an effective regimen. Although second-line regimens that utilize less-costly HHS/FDA-approved generics should be available in the future, in the interim it is likely that the costs for these life-saving regimens will not significantly decrease. In fact, the costs are likely to remain stable or increase as the current most popular first-line regimen, Stavudine/Lamivudine/Nevirapine, increasingly falls out of favor. Although difficult to predict, it is probable that current regimens will be replaced with more costly medications such as Tenofovir, Emtricitabine, and Efavirenz. Some further reductions in ARV costs are probable, but resistance and failure among an increasing number of people on life-saving ART will mean that the Emergency Plan costs for ARVs will remain considerable.

### *Generic Drugs and Diversification in Procurement*

The Emergency Plan is a performance- and target-driven initiative. Every dollar that can be saved can be used to support additional prevention, care and treatment services. In order to reduce costs and place more people on ART, PEPFAR focuses on reducing the costs of delivering ART. Reducing the costs of ARVs is an essential component of reducing overall costs. One way to reduce these costs is to rationalize the procurement of ARVs to take advantage of bulk purchasing agreements and reduce waste through a more finely tuned system for delivering product to point-of-service end users. As Figure B indicates, in every case generic prices present an opportunity for cost savings; in some cases, the branded price per pack of a drug is up to 11 times the cost of the approved generic version.

Figure B: Branded versus FDA-Approved Generic Anti-retroviral Mean Pack Prices, FY04 and FY05

NOTE: Country data collected via PFSCM survey.

| **Brand Name - Generic Name** Note: Generics have an asterik | **Mean Pack Price US$** | |
|---|---|---|
| | | |
| **Stocrin-- Efavirenz*** | **FY04** | **FY05** |
| Stocrin 600mg (30 TAB) | 32.50 | 32.76 |
| Efavirenz 600mg (30 TAB)* | n/a | 23.30 |
| | | |
| **Retrovir-- Zidovudine*** | **FY04** | **FY05** |
| Retrovir 300mg | 21.67 | 34.78 |
| Zidovudine 300mg* | n/a | 14.48 |
| | | |
| **Zerit-- Stavudine** | **FY04** | **FY05** |
| Zerit 15mg (60 CAP) | 4.88 | 9.22 |
| Stavudine 15mg (60 CAP)* | n/a | 5.18 |
| Zerit 1mg/ml | 10.73 | 8.71 |
| Stavudine 1mg/ml* | n/a | 7.15 |
| Zerit 20mg (60 CAP) | 6.36 | 5.99 |
| Stavudine 20mg (60 CAP)* | n/a | 5.64 |
| Zerit 30mg (60 CAP) | 6.48 | 6.20 |
| Stavudine 30mg (60 CAP)* | n/a | 3.83 |
| Zerit 40mg | 6.60 | 6.14 |
| Stavudine 40mg* | n/a | 4.32 |
| | | |
| **Viramune-- Nevirapine*** | **FY04** | **FY05** |
| Viramune 10mg/ml | 24.81 | 24.30 |
| Nevirapine 10mg/ml* | n/a | 7.50 |
| Viramune 200mg | 50.23 | 59.86 |
| Nevirapine 200mg* | n/a | 5.79 |
| Viramune 50mg/5ml | 26.19 | 34.79 |
| Nevirapine 50mg/5ml* | n/a | 7.50 |
| | | |
| **Epivir-- Lamivudine** | **FY04** | **FY05** |
| Epivir 150mg | 7.22 | 13.56 |
| Lamivudine 150mg* | n/a | 4.93 |
| Epivir 10mg/ml | 7.34 | 9.12 |
| Lamivudine 10mg/ml* | n/a | 5.35 |
| | | |
| **Combivir-- Zidovudine/ Lamivudine*** | **FY04** | **FY05** |
| Combivir 300/150mg | 24.87 | 24.23 |
| Zidovudine/Lamivudine 300/150mg* | n/a | $17.51 |

This data shows the mean cost per pack and illustrates the significant cost-savings that PEPFAR is achieving by using HHS/FDA-approved generics. The cost-savings ranges from 5% to 90%. As additional manufacturers receive HHS/FDA approval, market forces can be expected to further reduce costs.

As can be seen in Figure C, the costs of the standard first-line regimens can also be significantly reduced through the use of HHS/FDA-approved generics. As this cost savings is applied to growing numbers of patients, the cost savings will become even more significant.

Similarly, cost savings can be seen in the purchase of ARVs at the country level when extrapolating the amounts spent on generic drugs versus branded drugs, as seen in Figure D. Examining ARV costs by country reveals that programs are maximizing their purchasing ability by importing HHS/FDA-approved generic ARVs, and the savings offer the potential to further expand support for vital services for people living with HIV/AIDS (PLWHA) and orphans and vulnerable children (OVCs).

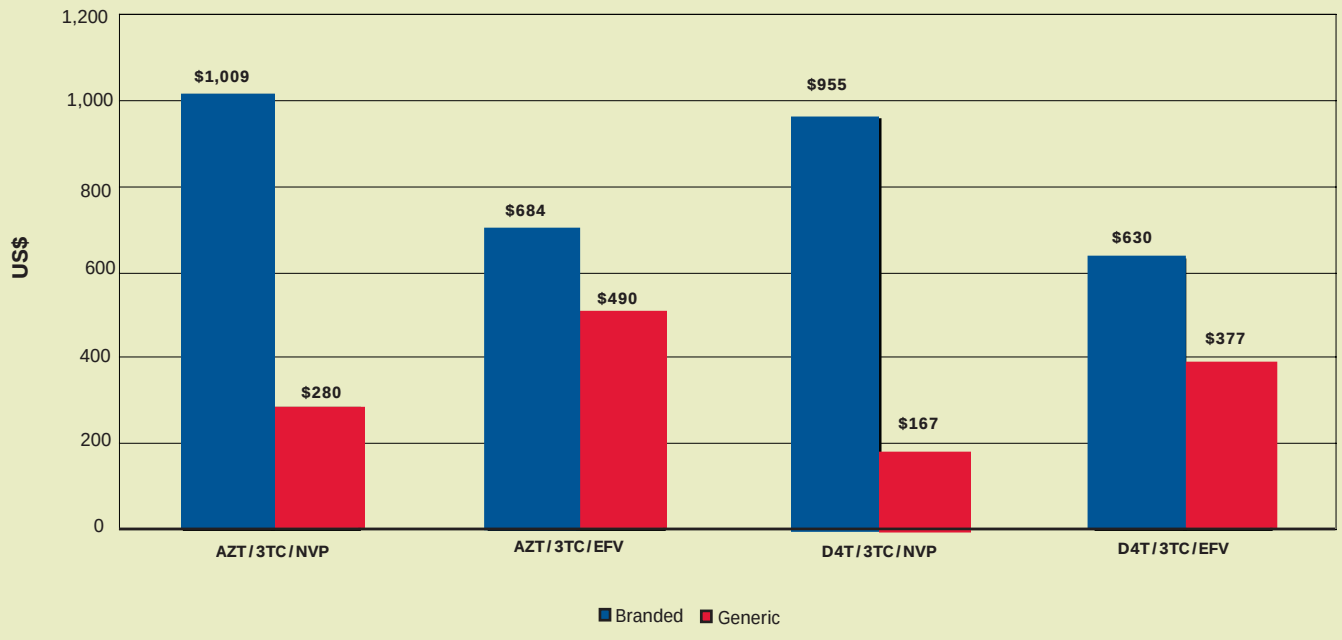
The Emergency Plan has been successful in its initial scale-up of drug procurement in the fifteen focus countries.

Sponsored by an Emergency Plan partner, the Djibouti Armed Forces deliver laboratory equipment, including a CD4 counter, to assist with antiretroviral treatment.

All countries reported substantial increases in their drug purchasing from FY 2004 to FY 2005. Even countries such as Kenya, Nigeria and Zambia, with significant funds allocated to drug purchases in FY 2004, more than tripled their funds spent on drug procurement in FY 2005.

Figure C: Comparison of Average Annual Treatment Costs Based on Branded and Generic Costs, FY05

NOTE: Country data collected via PFSCM survey.



## Figure D Country-Level Antiretroviral Savings, Comparable Branded versus FDA-Approved Generic by Country, FY05

NOTE: Country data collected via PFSCM survey.

| Country | Branded Drug Product (FDA-Approved Generic Drug Product) | Dosage | Mean Country-Level ARV Expenditures Using FDA-Approved Generic ARVs | Mean Country-Level ARV Expenditures Using Branded ARVs | Savings ($) |
|---|---|---|---|---|---|
| **Botswana** | Combivir (Zidovudine/Lamivudine) | 300/150 mg | 1,850,000 | 2,423,000 | **573,000** |
| **Cote d'Ivoire** | None | | | | |
| **Ethiopia** | None | | | | |
| **Guyana** | Epivir (Lamivudine) | 150 mg | 1,630 | 4,421 | |
| | Viramune (Nevirapine) | 200 mg | 1,792 | 15,324 | |
| | Zerit (Stavudine) | 30 mg | 165 | 291 | |
| | Zerit (Stavudine) | 40 mg | 48 | 74 | |
| | | **Total** | 3,635 | 20,110 | **16,476** |
| **Haiti** | Stocrin (Evafirenz) | 600 mg | 958,181 | 1,223,783 | |
| | Zerit (Stavudine) | 40 mg | 5,028 | 7,718 | |
| | Viramune (Nevirapine) | 200 mg | 176,981 | 1,817,170 | |
| | Combivir (Zidovudine/Lamivudine) | 300/150 mg | 1,194,721 | 1,673,300 | |
| | | **Total** | 2,334,911 | 4,721,971 | **2,387,060** |
| **Kenya** | Zerit (Stavudine) | 15 mg | 3,924 | 7,247 | |
| | Zerit (Stavudine) | 20 mg | 4,535 | 4,816 | |
| | Zerit (Stavudine) | 30 mg | 50,593 | 73,211 | |
| | Zerit (Stavudine) | 40 mg | 46,530 | 63,488 | |
| | | **Total** | 105,582 | 148,762 | **43,181** |
| **Mozambique** | Retrovir (Zidovudine ) | 300 mg | 22,505 | 57,378 | |
| | Combivir (Zidovudine/Lamivudine) | 300/150 mg | 208,396 | 282,238 | |
| | | **Total** | 230,900 | 339,616 | **108,716** |
| **Namibia** | Zerit (Stavudine) | 1 mg/ml | 12,162 | 13,065 | **903** |
| **Nigeria** | Zerit (Stavudine) | 30 mg | 31,497 | 55,794 | |
| | Zerit (Stavudine) | 40 mg | 64,000 | 98,240 | |
| | Epivir (Lamivudine) | 150 mg | 129,600 | 366,120 | |
| | Viramune (Nevirapine) | 200 mg | 229,600 | 2,454,260 | |
| | Combivir/Viramune (Lamivudine/Zidovudine/Nevirapine) | 150/300/200 mg | 2,992,790 | 9,935,402 | |
| | Retrovir (Zidovudine ) | 300 mg | 1,088,750 | 2,260,700 | |
| | | **Total** | 4,536,237 | 15,183,581 | **10,634,279** |
| **Rwanda** | None | | | | |
| **South Africa** | None | | | | |
| **Tanzania** | None | | | | |
| **Uganda** | Epivir (Lamivudine) | 150 mg | 65,000 | 17,628 | |
| | Viramune (Nevirapine) | 200 mg | 30,000 | 359,160 | |
| | Retrovir (Zidovudine ) | 300 mg | 42,804 | 125,208 | |
| | Zerit (Stavudine) | 30 mg | 42,000 | 7,440 | |
| | Zerit (Stavudine) | 40 mg | 31,200 | 47,892 | |
| | Zerit (Stavudine) | 1 mg/ml | 29,760 | 41,808 | |
| | Combivir (Zidovudine/Lamivudine) | 300/150 mg | 135,330 | 188,994 | |
| | Viramune (Nevirapine) | 50 mg/5ml | 45,000 | 208,704 | |
| | | **Total** | 421,094 | 996,834 | **575,740** |
| **Vietnam** | None | | | | |
| **Zambia** | Combivir (Zidovudine/Lamivudine) | 300/150 mg | 2,018,339 | 2,826,841 | |
| | Stocrin (Evafirenz) | 600 mg | 351,939 | 550,335 | |
| | Epivir (Lamivudine) | 10 mg/ml | 648,051 | 1,104,715 | |
| | Viramune (Nevirapine) | 200 mg | 549,489 | 5,980,443 | |
| | Viramune (Nevirapine) | 10 mg/ml | 285,000 | 923,400 | |
| | Retrovir (Zidovudine ) | 300 mg | 360,005 | 927,478 | |
| | | **Total** | 4,212,822 | 12,313,203 | **8,100,381** |
| | | | | | |
| | | **Overall Totals** | **13,707,342** | **36,160,142** | **22,439,735** |

## Figure E: ARV Procurement by Country Funding

NOTE: Country data collected via PFSCM survey.

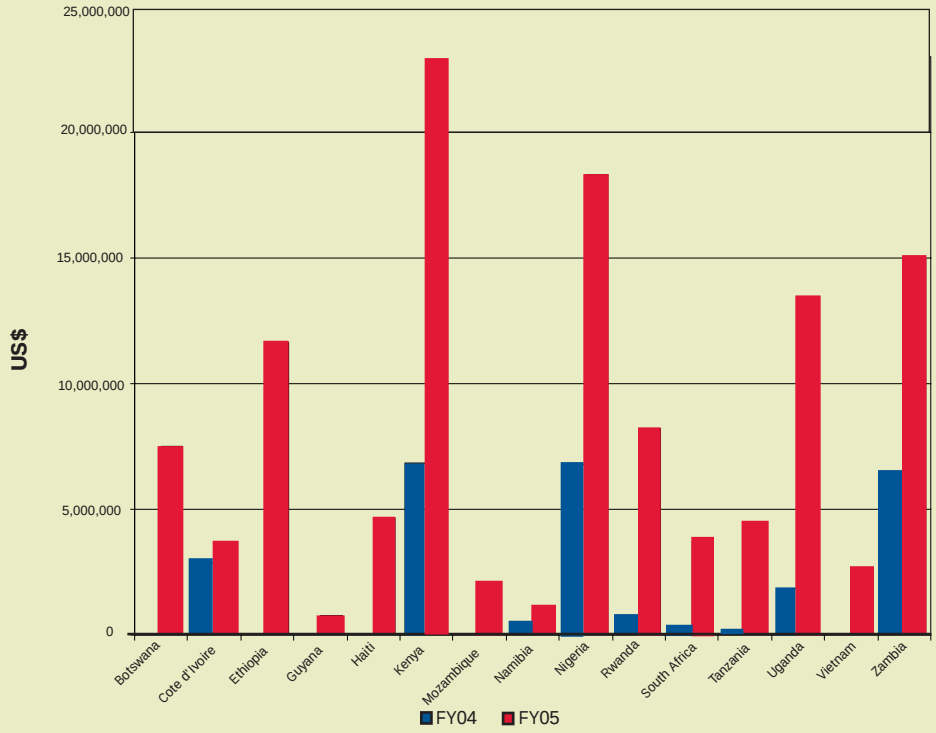



Figure E shows the dramatic increase in the purchase of ARVs as PEPFAR has increased its support for ART. Of these funds, an increasing amount is being spent on the procurement of HHS/FDA-approved generic drugs, totaling $13.7 million in FY 2005. 9 of the 15 focus countries dedicated some portion of their drug purchasing funds to the purchase of generic drugs (see Figure F for complete spending on generics by country). These figures illustrate the dramatic increase in the purchase of HHS/FDA-approved generics. Figure G reflects the rapid utilization of HHS/FDA-approved generics after their approval in mid FY 2005.

Countries have begun the transition from branded-only purchasing strategies to incorporating more generic regimens in their procurements. Given the recent HHS/FDA approvals of 15 generic ARVs, the Emergency Plan anticipates that countries will continue to scale up generic ARV procurements planned for FY 2006.

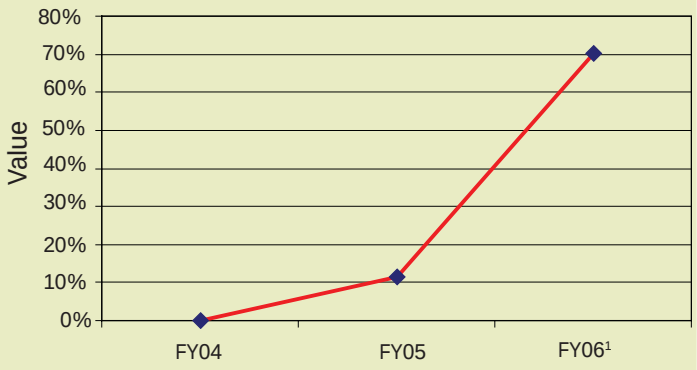
## Figure F: Total Antiretroviral Procurement by Branded and Generic, FY05

NOTE: Country data collected via PFSCM survey.

| Country | FY05 Branded ($) | FY05 Generic ($) |
|---|---|---|
| Botswana | 5,648,614 | 1,850,000 |
| Cote d'Ivoire | 3,659,463 | --- |
| Ethiopia | 11,639,711 | --- |
| Guyana | 741,079 | 3,635 |
| Haiti | 2,280,879 | 2,334,911 |
| Kenya | 22,873,492 | 105,582 |
| Mozambique | 1,853,660 | 230,900 |
| Namibia | 1,122,409 | 12,162 |
| Nigeria | 13,763,247 | 4,536,237 |
| Rwanda | 8,213,076 | --- |
| South Africa | 3,731,836 | --- |
| Tanzania | 4,427,795 | --- |
| Uganda | 12,918,721 | 421,094 |
| Vietnam | 2,508,066 | --- |
| Zambia | 10,711,381 | 4,212,822 |

## Figure G: FDA-Approved Generic Producs as Percentage of Total Procurement, FY04-FY06

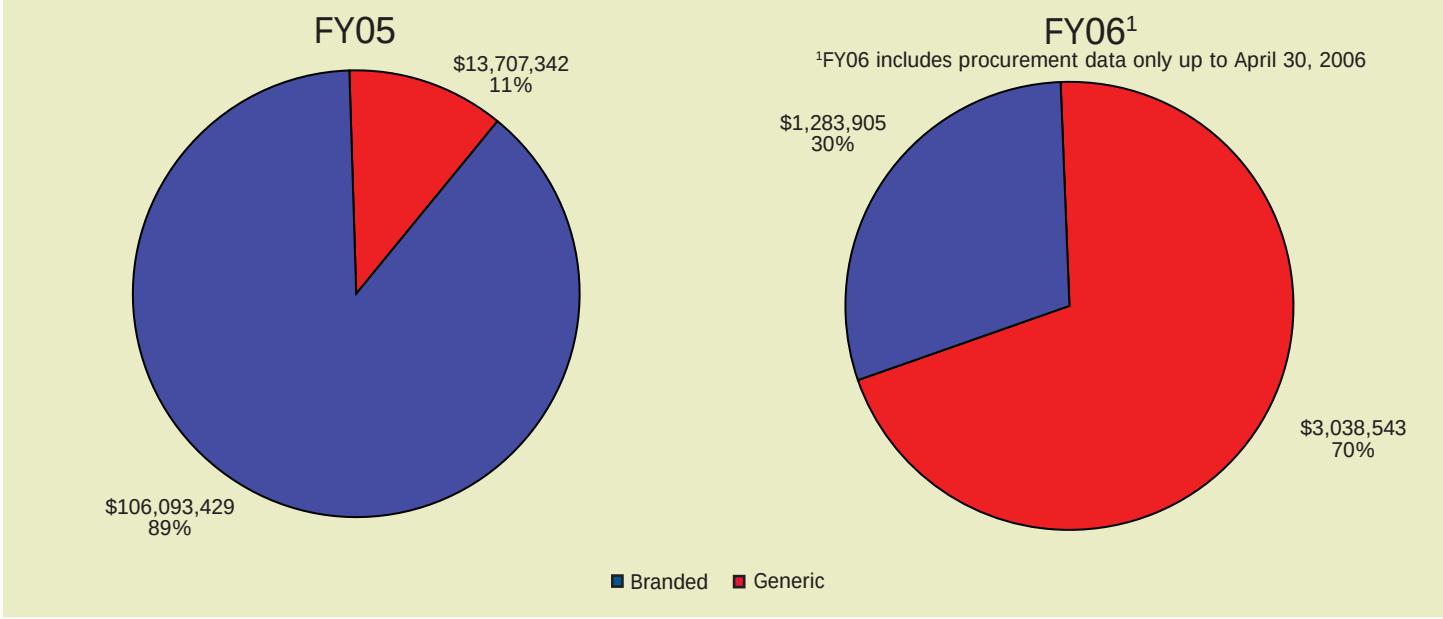
NOTE: Country data collected via PFSCM survey.




[1]FY06 data represents a limited sample of four respondents (total value $4,322,448)

## Figures H1 and H2: Amount and Percentage of FDA-Approved Generic and Branded Procurement in FY05 and FY06

NOTE: Country data collected via PFSCM survey.




Figures H1 and H2 demonstrate the comparative increase in generic ARV purchases between FY 2005 and FY 2006. With only several months of FY 2006 data, procurements of generic ARVs already make up a significant proportion of overall ARV purchases. As HHS/FDA-approved generics are registered for purchase according to each country's own national regulatory policies, all of the focus countries can then begin to procure HHS/FDA-approved generic drugs.

Though data for FY 2006 is incomplete, procurement activity to date shows a promising trend toward an increasing percentage of procurements being generic ARVs. The Emergency Plan expects that the percentage of generic products will level off as FY 2006 procurement continues, but it is notable that countries have made a commitment to purchasing HHS/FDA-approved generic ARVs for their programs at the onset of this fiscal year.

Some focus countries have led the charge in incorporating more generic ARVs into their overall drug procurements. Nigeria, Zambia and Haiti each allocated substantial funding amounts to the purchase of generic ARVs in FY 2005, and have begun FY 2006 with the majority of ARV procurement being for generic ARVs. These graphs show the marked increase in importation of HHS/FDA-approved generics in Haiti, Nigeria and Zambia. Although it is early in FY 2006 and the annual percentage may be smaller than reflected here, we anticipate that the proportion will be significantly increased over FY 2005.

## Figure I1 and I2: Selected PEPFAR Focus Country ARV Procurement by Branded/FDA-Approved Generic Product, FY05 and FY06

NOTE: Country data collected via PFSCM survey.

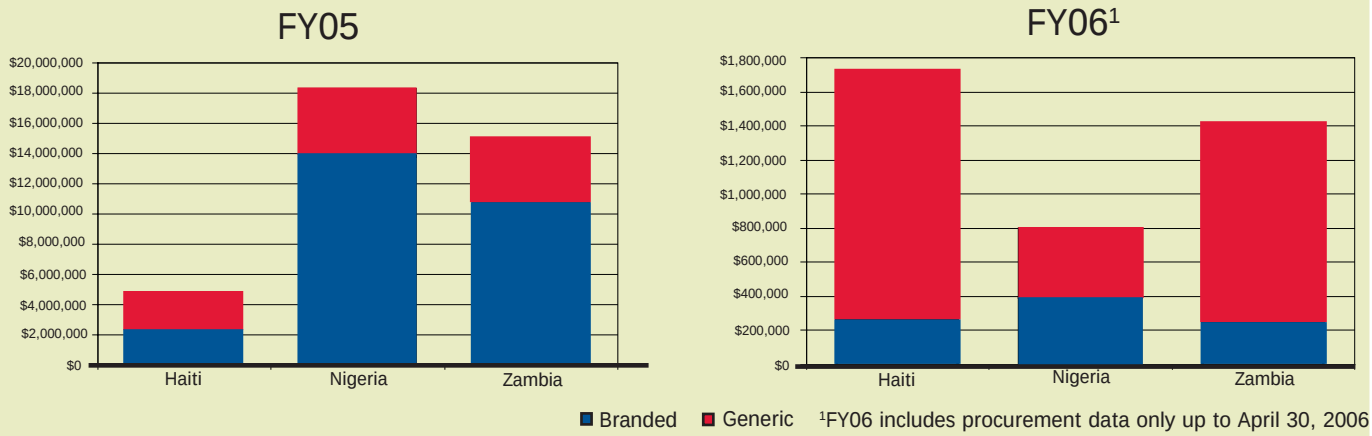


Figure J: PEPFAR Partner Antiretroviral Procurements by Country and Manufacturer, FY05

NOTE: Country data collected via PFSCM survey.

| COUNTRY | Abbott | Aspen* | Aurobindo* | BMS[1] | Boehringer | Gilead | Glaxo[2] | Hoffmann[3] | Merck | Patheon | Pfizer | Ranbaxy* | Roxane* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Botswana | X | X | | X | X | X | X | X | | | | | |
| Cote d'Ivoire | X | | | X | X | | X | X | X | | | | |
| Ethiopia | X | | | X | X | | X | X | X | X | | | X |
| Guyana | X | | X | X | X | X | X | X | X | X | X | | |
| Haiti | X | | X | X | X | | X | X | X | X | | X | X |
| Kenya | X | | | X | X | X | X | X | X | X | | | X |
| Mozambique | X | | X | X | | | X | X | X | | | | |
| Namibia | X | | X | | X | X | X | | X | | | | |
| Nigeria | X | X | X | X | X | X | X | X | X | X | | X | |
| Rwanda | | | | X | | X | X | | X | X | X | | |
| South Africa | X | | | X | X | X | X | X | X | X | | | X |
| Tanzania | X | | | X | X | | X | X | X | | | | |
| Uganda | X | | X | X | X | X | X | X | X | X | X | X | |
| Vietnam | | | | X | X | X | X | X | X | X | | | X |
| Zambia | X | | X | X | X | | X | | X | | | | |

[1]Bristol Myers Squibb
[2]GlaxoSmithKline
[3]Hoffmann-La Roche
*Generic Manufacturer

The data collected shows that countries have diversified the procurement of ARVs, purchasing from numerous manufacturers (including generic manufacturers) as seen in Figure J.

## Future Directions and Approaches

### Moving toward different regimens

The most common regimen, D4T/3TC/EFV, is increasingly falling out of favor due to toxicities associated with D4T. As treatment standards shift, the Emergency Plan will increasingly support alternative first line regimens, some of which have lower costs (see AZT/3TC/EFV cost comparison in Figure C on page 7). These sorts of shifts will also positively impact the Emergency Plan bottom line for ARVs. Additionally, PEPFAR is working with HHS/FDA and manufacturers to ensure that the fast track approval process continues to quickly review and approve the appropriate high-quality ARVs. Despite the strides described above toward use of HHS/FDA-approved generics, Emergency Plan-supported programs will need to continue to purchase brand products to be used as second-line therapy. As the virus evolves, support for second-line regimens will remain a vital part of our support for people living with HIV/AIDS, and some of these products can be expected to become available in generic form through the HHS/FDA approval process.

### Sustainability

A challenge to the hope that ART scale-up brings is the possibility that treatment will become unavailable in the future. When managed with ART, HIV is a chronic condition, and patients who begin therapy must maintain it for the rest of their lives. If people on ART lose their access to medications, they will die.

While helping host nations rapidly scale up high-quality treatment today, the Emergency Plan is also supporting them in building the capacity and instituting the systems to expand treatment in the future. The Emergency Plan has been working with governments to promote the "network model," which seeks to allocate highly trained health workers – such as physicians with specialized training – to referral centers where their level of training is essential, while allowing non-physicians trained in ART to administer treatment at field sites. The soaring demand for ART in resource-poor nations requires a flexible health workforce, and PEPFAR supports policy initiatives to permit such flexibility. The geographic dispersal of PLWHA, with many in remote rural areas, provides a key

challenge in making ART available to those who need it. PEPFAR efforts to reach rural populations include innovative models, as well as expansion of the network model and outreach to community- and faith-based providers. The Emergency Plan also focuses support on helping host nations develop critical network systems. PEPFAR partners with these nations, supporting them as they harness the resources of their own societies to build capacity to treat their people for the long term.

Quality and sustainability in HIV/AIDS treatment begin with people – but under-resourced nations typically lack the trained health workforces to meet their desperate needs. The Emergency Plan supports national strategies with innovative approaches to training and retention; broadened policies regarding who can administer HIV/AIDS services; and the use of volunteers and twinning relationships to rapidly build the army of local service providers required to combat this disease.

## Children and ART

The Emergency Plan features a firm and continued commitment to pediatric AIDS treatment. Of those receiving ART at downstream sites for whom partners reported age in FY 2005, approximately 7 percent were children. This number is likely understated, as many partners are still developing systems – with PEPFAR support – to report adult or child status in all data. Because ARV doses are dependent on weight and other biologic factors that may differ for adults and children, pediatric ARV formulations are necessary, and the Emergency Plan is working to ensure their availability. As discussed earlier, the USG has created an expedited review process for generic versions of ARVs, including pediatric formulations, and such products are being submitted for review and approval, providing additional sources of high-quality, inexpensive products. As of January 2006, four generic pediatric formulations had won approval or tentative approval from HHS/FDA and were thus available for use in Emergency Plan programs.

Although PEPFAR is supporting rapid expansion of care and treatment for children, making ARV formulations more widely available for young children who need treatment remains a high priority. Building on recent successes in this area, the USG continues to work with other partners on this difficult issue in 2006. Ensuring availability of ARVs that are appropriate for children to take and easy for providers to dispense will also improve adherence to what will be a lifetime of treatment.

Due to coordinated procurement of ARVs, this patient and others in Rwanda are receiving treatment in a cost-effective manner, allowing resources to go farther.

In early 2006, the USG, through the Emergency Plan, announced an unprecedented public-private partnership to promote scientific and technical discussions on solutions for pediatric HIV treatment, formulations and access. This partnership encourages innovator and generic pharmaceutical companies, multilateral organizations such as UNAIDS and UNICEF, and agencies across the USG to bring together a wide range of expertise, seeking to maximize the utility of currently available pediatric formulations and to accelerate children's access to treatment. This partnership will complement other efforts of the President's Emergency Plan to support programs that expand treatment for adults and children, such as support for health care capacity-building and expedited regulatory review of drugs through HHS/FDA. The partnership will offer children and parents hope for a better day – the hope of families staying together, leading healthy lives, and living positively with HIV/AIDS.

## Ongoing Monitoring and Evaluation of Treatment Services

In most of the resource-limited countries served by the Emergency Plan, achieving the Plan's vision of a high quality, sustainable HIV/AIDS response requires implementing and strengthening essential systems, including clinical quality assurance systems; health care networks, including infrastructure; and commodity procurement, distribution, and management systems. One critical area of PEPFAR work with host nations is development of surveillance and monitoring and evaluation (M&E) capacity, including training of host

government staff to carry out surveillance activities, analyze data, and report results to key stakeholders.

The Emergency Plan is working to support the implementation of effective M&E systems across USG implementing partners in support of national monitoring and evaluation systems. This is supporting in-country teams and implementing partners to monitor and improve delivery of services and, in particular, adherence to therapy. In Uganda, for example, PEPFAR has implemented a comprehensive M&E system across some of its treatment partners, allowing the partners and USG to have a snapshot of partner-level data on key quality-specific indicators such as the retention of patients on ART and adherence to preventive care guidelines (such as the use of cotrimoxazole). This approach has yielded valuable information for both PEPFAR and its partners, and the USG is now planning to expand it to other partners in Uganda. Other innovative M&E programs are being developed in focus countries for use in them and beyond.

## Conclusion

PEPFAR has rapidly scaled up funding for quality ART while also supporting the reduction of purchasing costs of HHS/FDA-approved generic ARVs. The Emergency Plan is continuing to work to ensure that people living with HIV/AIDS receive the life-saving treatment they need. PEPFAR will continue to coordinate with host nations and other partners to provide the full spectrum of antiretroviral drugs and treatment services. These goals have been, and will continue to be, a central focus of the Emergency Plan, because all HIV-infected children, women, and men deserve quality treatment.