



UNAIDS

JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS

**REPORT OF THE MEETING
ON THE EVALUATION
OF THE UNAIDS HIV DRUG ACCESS INITIATIVE**

(Geneva, 30-31 May 2000)

1. The UNAIDS Drug Access Initiative at a Glance

Launched in November, 1997, the UNAIDS HIV Drug Access Initiative (DAI) was designed to develop innovative, effective models to improve access to drugs to treat HIV and opportunistic infections. The countries participating in the initial phase of the Initiative are Chile, Côte d'Ivoire, Uganda, and Vietnam.

The Initiative seeks to address the many challenges of developing world's access to HIV-related drugs, such as lack of medical infrastructure, drug distribution channels, professional training, and patient support, by creating an environment of collaboration between pharmaceutical companies, health care providers, governments, donors, non-governmental organizations, and people living with HIV/AIDS.

The Initiative is a pilot project. In the initial phase, which lasts two to three years, the project is implemented in a small number of countries. In the second phase, the lessons learned in the pilot phase will be adapted and applied more widely.

Implementation of the Initiative in each country involves the establishment of a National Advisory Board made up of local government and NGO representatives, medical experts, and a representative of UNAIDS. Originally, drugs were supposed to be purchased at a subsidized rate by a non-profit company established in each participating country. However, it rapidly appeared that this was not necessary in all countries. The project has been amended accordingly (see details below). The project is managed in each country by a Project Management Team. Funding for the programme management, which builds on existing infrastructure and projects in the participating countries, is provided by UNAIDS, cosponsors and other donors. The CDC and the ANRS committed financial support for project evaluation.

Pharmaceutical partners in the DAI include Glaxo Wellcome plc, F. Hoffmann-La Roche, Virco, NV, Bristol-Myers Squibb, Organon Teknika, Merck and Co., and Dupont Pharma.

2. How the Initiative works?

The necessary initial phase of the Initiative has been designed to set up the necessary infrastructure and systems to increase access to HIV related drugs on a small but sustainable scale, with the objective of expanding once workable models are developed. The participating countries have been selected according to:

- political and social stability
- political commitment to respond to the HIV/AIDS epidemic
- political commitment to care and support of people with HIV infection
- active national AIDS programme
- well-established public health platform
- facility to implement and evaluate the pilot phase and collect clear and unbiased results
- geographical distribution of countries
- high HIV prevalence or high HIV incidence
- existing health care infrastructure in relatively low-income economy.

Many countries fulfill these criteria. However, during the pilot phase, UNAIDS found it important to limit the size of the project to 4 countries in order to ensure its adequate follow up.

On joining the Initiative, each country has been required to develop National HIV treatment guidelines that included guidance on the use of all drugs, also antiretrovirals, anticipated to be used in the Initiative.

In the countries involved in the DAI, the National HIV treatment guidelines have been issued by the Ministry of Health based on the recommendations of an Advisory Board established in the context of this Initiative. The Advisory Board is under the authority of the Minister of Health. Its functions are:

- to propose guidelines on the clinical management of HIV infection
- to propose a list of HIV-related drugs adapted to the local context
- to estimate the needs for HIV-related drugs
- to recommend minimum requirements health care facilities should satisfy to qualify for participation in the initiative. At least for 2 levels of health care settings were to be selected: (1) *first-level centres* where basic drugs would be available and (2) *referral centres* where sophisticated drugs such as antiretrovirals would be provided
- to make recommendations on the selection of the centres
- to recommend objective clinical and other selection criteria for a profile of patients who will participate in the pilot project
- to recommend over time an action plan for improvement of the health care infrastructure in order to make the HIV/AIDS drugs more widely accessible in the country.

The Advisory Boards include representatives of the Ministries of Health, and other relevant Ministries such as Planning and Finance, a representative of UNAIDS nominated by the UN Theme Group on HIV/AIDS, the National AIDS Programme Manager as well as representatives of relevant AIDS authorities in the country, representatives of NGOs involved in HIV/AIDS care, representatives of PLWAs, and clinicians and public health persons from the academic sector who are knowledgeable in HIV/AIDS epidemic and clinical management of HIV infection.

The availability of the following were taken into consideration when accrediting centers to deal with HIV/AIDS drugs:

- well trained doctors and other health workers
- good clinical facilities for diagnosis and management
- standard laboratory facilities
- social support
- drug dispensing facilities

Each participating health care centre, whether first level or referral level, was given a single procurement number which authorizes the centre to purchase the type of drugs according to its level of qualification. The products are supplied to the centres from a central distribution point.

The drugs are dispensed against a medical prescription issued by one of the centers' physicians. As part of the Initiative's activities, all centers keep accurate prescription and dispensing records. Stock management programmes have been provided and standardized by UNAIDS. The programmes feature anonymous data on patient number, CD4 cell count, viral load, clinical staging, prescriber's code and drugs names.

The pharmaceutical companies deliver the products either through the national medical store or a non-profit company. These subsequently distribute the drugs to the health care centres.

Information and training strategies were developed by the coordinator of the initiative for the Ministry of Health and the National AIDS Programme, in accordance with the recommendations of the Advisory Board. These strategies target doctors and other health workers as well as patients and communities. Community organizations play an active role in dissemination of relevant information. The training programmes target clinical management as well as psycho-social support of patients living with HIV. Some of the participating companies also participate and contribute to the training and education programmes.

3. What are the mechanisms implemented by the DAI for price reduction on HIV/AIDS drugs?

Three mechanisms have been used to reduce the price of HIV/AIDS drugs:

- friendly negotiations with the proprietary pharmaceutical companies
- open competition including generic medicines
- cancellation of import taxes in drugs.

Establishing contact with pharmaceutical companies has been a significant focus of UNAIDS activities to support the first phase of the HIV Drug Access Initiative. Starting in July of 1996, UNAIDS had been in contact with most of the major multinational producers/suppliers of HIV related drugs, viral load tests, and CD4 diagnostics. Most of the companies joined the Initiative as collaborators and significant price reductions followed from their participation. However, after the initial price reductions, to late 1999, no further substantial price reductions were obtained. Consequently, alternative supplies of antiretrovirals were considered. Independently of the Advisory Board, the National Medical Store of Côte d'Ivoire, the Pharmacie de la Santé Publique, opened its tender for antiretrovirals to generic manufacturers of AZT and d4T, which led to further price reductions. In March 2000, UNAIDS facilitated discussions between the DAI and Brazilian manufacturers of antiretrovirals.

More recently, five companies (Boehringer Ingelheim, Bristol-Myers Squibb, Glaxo Wellcome, Merck & Co., Inc., and F. Hoffmann - La Roche) began constructive discussions with UNAIDS, WHO, the World Bank, the United Nations Children's Fund (UNICEF), and the United Nations Population Fund (UNFPA), to explore practical and specific ways of working together more closely to accelerate access to HIV/AIDS-related care and treatment in developing countries. This endeavor raised the expectation that the cost of antiretrovirals would be reduced quickly, and generated substantial interest.

With regard to cancellation of import taxes on drugs, it does not apply to Cote d'Ivoire, Uganda, or Vietnam since there are no import taxes on drugs in these countries. In Chile, where the import taxes on goods are 21%, the Initiative uses procurement via UNDP to avoid having to pay this tax.

4. Financing Issues of the Drug Access Initiative

International sources of funding

Financing for the pilot phase comes from a variety of sources. For the start-up phase, the UNAIDS Secretariat has spent US\$ 1.3 million for the set-up and management of the Initiative in 1998-1999. Of this, US\$ 800,000 have been spent in the countries themselves. The participating pharmaceutical companies have also provided financial support through various means; in addition to reduced drug costs, the companies have supported the nonprofit companies, drug donations, and cash to support salaries and operational costs. The United States Centers for Disease Control (CDC) and the French government's Agence Nationale de Recherches sur le SIDA (ANRS) have provided financial support for the evaluation of the project. Lastly, the International Therapeutic Solidarity Fund provides support for a limited number of treatments in Côte d'Ivoire and will likely also do so in Vietnam.

Government Funding

The use of Government funds in the DAI varies from country to country. In Uganda, Government covers the costs of support systems. In Côte d'Ivoire, the government provides subsidized access to the drugs and support system for antiretroviral therapy for selected patients. In Chile the government funds the full cost of antiretroviral therapy for all patients in the public health facilities. In Vietnam the government funds the ARV treatment of about 70 people, most of them health care staff that were infected through professional exposure.

Private funding

Despite the current price reduction on a number of antiretroviral molecules, the costs of antiretroviral treatments is still beyond the reach of most governments. Given the paucity of international donor funds to fund antiretrovirals, the DAI relies on private sources of funds in countries where government funding cannot cover the entire cost of these drugs, including:

- 1. Households:** In Africa and many low-income countries, households are the primary source of funding for care, including that of antiretrovirals. For example, in Côte d'Ivoire, a survey of AIDS related expenditures in households of average income in Abidjan shows that households would be able to pay as much as 50,000 FCFA per month and per household (approximately US\$100). The compliance study in Uganda has also documented the significant contributions of the extended family to enable PLWAs to cover the costs of continued antiretroviral treatment. The key problems with household financing are the issues of affordability and equity; in Côte d'Ivoire, the average AIDS related expenditures per month mentioned above is more than twice the GNP per capita.

2. **Private employers:** in Côte d'Ivoire, Uganda and Chile, some private employers have expressed interest to study the advantage of providing antiretrovirals to their employees if it reduces the number of sick days and the costs of health care related to opportunistic infections and death. In Cote d'Ivoire, Compagnie Ivoirienne d'Electricite is now offering antiretrovirals to all employees living with HIV/AIDS. To encourage other companies to do so and to scale up the coverage of more employees within the existing interested companies, economic data on the cost-benefit of such interventions is needed. The Drug Access Initiative provides an opportunity to conduct this evaluation in real life.
3. **Insurance companies:** In the four countries of the DAI, health insurance companies do not yet cover AIDS care expenditures. However, at present, the opportunistic infections are not declared as such by the physicians and these companies end up paying for opportunistic infections anyway. The DAI now needs to start discussions on insurance coverage of antiretroviral therapy.

5. Status of implementation activities in the countries

Uganda

Uganda has a population of 21 million and 1 million are estimated to be HIV infected.

The project started in August 1998 after an advisory board and a nonprofit company for the procurement and distribution of the drugs had been set up. Five clinics in Kampala now prescribe antiretroviral therapy and 6 mid-level centres outside Kampala have been assessed for the provision of more sophisticated treatments for opportunistic infections and AIDS-related cancers. A total of 183 physicians and health care workers have attended clinical training sessions on the use of antiretrovirals, and many medical officers have participated in a comprehensive training programme on HIV/AIDS. The Initiative favours the development of HIV/AIDS drug policies. To date, there exist guidelines/policy documents on antiretroviral therapy, drug importation, and financing. National guidelines on the use of cotrimoxazole prophylaxis were adopted in March 2000. Within the Initiative, a medical information system allows to monitor adherence, drug resistance, and quantity and quality of drugs used. The Initiative is perceived as a real partnership between the government, the pharmaceutical companies, the health care providers, non-governmental organizations, people living with HIV/AIDS, and UNAIDS.

To date 900 PLWAs are on antiretrovirals within the Initiative and the number is increasing. For instance, 166 new people have been enrolled from January to March 2000.

Côte d'Ivoire

Côte d'Ivoire has a population of nearly 13 million and an HIV-infected population of over 800,000.

The project started in June 1998, after an advisory board and a non-profit company were create. The non-profit company rapidly appeared as redundant for Côte d'Ivoire where the National Medical Stores (Pharmacie de Santé Publique) took over its role. Eight referral centres currently prescribe HIV/AIDS drugs within the Initiative. The Initiative promoted national

recommendations of cotrimoxazole prophylaxis among PLWAs, which were adopted in March 2000. More than 190 physicians, other health care workers, and social workers have been trained in three large 5-day workshops. The sessions included training on the use of antiretrovirals, drugs for opportunistic infections and psychosocial counselling. One million USD per year were budgeted by the government as a national solidarity fund, to help the poorest patients to meet the cost of treatment. Even though this subsidy mechanism was criticized for being slow and insufficiently transparent, this allowed to subsidize 300 people on ARVs, for their treatment, most of them active participants of PLWA groups. The “Fonds de Solidarité Thérapeutique International” has also provided US\$1.3 million for two years to provide long-term antiretroviral treatment to HIV pregnant women who are symptomatic or at the stage of immune depression, and recently decided to contribute to the funding of people switching from double therapy to triple therapy.

Approximately 650 patients were receiving antiretrovirals and 2000 were receiving cotrimoxazole prophylaxis through the Initiative.

Chile

Of the 15 million inhabitants in Chile, 16000 are deemed to live with HIV/AIDS.

The activities within the Initiative started in January 2000, after the advisory board had been appointed in July 1998. Chile currently has satisfactory drug purchasing and inventory controls, making a non-profit drug purchasing company unnecessary. The procurement of drugs in Chile is performed through an arrangement with UNDP, which reduced the cost of the drugs by over 25%. The money saved is used to provide universal coverage for the management of opportunistic infections and improvement of the coverage for antiretroviral therapy. An emphasis has been put in the psychosocial component of the Initiative, which is the weaker component. Chile differs from the other countries in that it is stronger economically, and has an extensive and relatively strong healthcare infrastructure in place.

To date, 60% of PLWAs registered in the government social security system with the indication of antiretroviral therapy are given antiretrovirals free of charge (n= 2500). Nearly half of these patients receive double therapy and the other half, triple therapy. The objective of the Initiative by the end of 2000 is to increase significantly the percentage of PLWAs receiving triple therapy.

Vietnam

The total population in Vietnam is 80 millions people. The number of HIV infected people is estimated to be 88,000.

The Initiative officially started in March 2000, the advisory board having been appointed 2 years before. Seven referral centres have been selected for the provision of antiretroviral therapy to patients, including two in Hanoi, two in Ho Chi Minh City, one in Quang Ninh, one in Khanh Hoa and one in Can Tho. To date the Initiative provides Nevirapine to reduce mother-to-child transmission of HIV. However, the Initiative promoted national recommendations of cotrimoxazole prophylaxis among PLWAs which were accepted as national recommendations in April 2000. Several training sessions were also organized through the Initiative. The sessions

included training on the use of antiretrovirals and drugs for opportunistic infections.

The government currently provides antiretroviral treatments for free for 70 PLWAs, mainly HIV-infected health workers.

7. Evaluation highlights

The mid-term evaluation of the Initiative has been conducted in Cote d'Ivoire and Uganda. In Chile, the evaluation is underway. No partner has been formally identified for Vietnam yet.

Characteristic of patients at enrollment

Patients access antiretrovirals within the DAI at an advanced stage of their disease. In Uganda, for example, 74% have WHO stage 3 or 4, and 80% CD4+ cell counts less than 200/mm³. Nearly 70% had a viral load >100 000 at the start of their treatment.

In Uganda where treatments are not subsidized by the government, there is a balanced gender distribution and a relatively high socio-economic status among PLWAs accessing antiretroviral therapy. In Côte d'Ivoire, the same was observed among those who pay the full cost of their treatment. However, among those receiving subsidies from the government a high percentage have no professional activity.

Treatment regimens

The Initial treatment regimen is dual therapy for half of the treatment prescribed. However, there is now a trend for increasing use of triple therapy as a first line treatment within the Initiative. This became the official treatment recommendation in Côte d'Ivoire in October 1999. Follow-up information indicated that antiretroviral regimens are frequently changed (15%). The main reasons for these changes are toxicity, virologic non-response, clinical disease progression, and financial affordability.

Compliance

A qualitative study performed in Uganda shows a good compliance of PLWAs on antiretroviral therapy. Lost to follow up occurs early, this probably reflecting a self-selection. The same tendency is observed in Côte d'Ivoire, where, according to a conservative estimate >60% are retained in the treatment programme after one year.

Survival

In the worst case scenario where people lost to follow up are considered as deceased, the survival rate at 18 months among PLWAs receiving antiretrovirals is approximately 55%. This survival rate probably reflects the advanced stages of illness at the start of the treatment. Indeed, the factors associated with death within the Initiative are low CD4 counts, high viral load, low hemoglobin, older age, and dual therapy. In Côte d'Ivoire, there was no statistically significant difference in mortality between those receiving double therapy as compared to those receiving triple therapy. However, the follow up period is short, and hence firm conclusions are premature. This tendency has not been observed in Uganda.

Immunologic and virological response to therapy and pattern of resistance

There is evidence of a substantive immunologic and virological response to antiretrovirals: Many patients maintain CD4+ cell counts above baseline and viral load below baseline even after one year of treatment.

Resistance testing indicates the emergence of resistance to drugs according to a pattern similar to that observed in Europe and the USA.

Access to antiretrovirals

The main reported barrier in both countries is the cost of the drugs. A few limited stock outs occurred in Côte d'Ivoire when the slow disbursement of government subsidies precluded ordering the drug in a timely manner. The intermediary structure (Medical Access) has proved useful in Uganda. According to the meeting evaluation, the open competition recently introduced in Côte d'Ivoire had a clear effect in reducing the prices of the drugs.

8. Lessons learnt

What has been accomplished so far?

First, with the DAI demonstrated that rational use of antiretrovirals is feasible in developing countries within an institutional framework that may be accommodated according to the specificity of the countries. Partly because of the Initiative, most of the antiretrovirals currently available in western countries are now available in the countries involved in the Initiative. This is an important step forward since, only 2 years ago, those living with HIV/AIDS who could afford the antiretrovirals had to travel in the western countries in order to get them.

The Initiative set an example for other developing countries to move forward with access to antiretrovirals. Senegal, Morocco, Malawi, and Rwanda, for example, developed their own initiatives.

The DAI clearly increased capacity in the area of care and support for PLWAs in the four countries. There is an increased knowledge of the use of antiretrovirals by the health care workers as well as a successful transfer of know-how for a comprehensive follow up of those PLWAs on antiretroviral therapy. This has been possible through the training sessions organized within the DAI, and the development of local guidelines. The accreditation system contributed to the success of the transfer of know-how. One may also note the improvement in the distribution of drugs, in the stock management of drugs, and a decrease in the relative importance of informal supply mechanisms of antiretroviral drugs. In Côte d'Ivoire, for example, reportedly the 'free' or 'black' market of antiretrovirals no longer exists.

The Initiative served as an entry point for wider access to HIV/AIDS care. The accreditation system contributed to the improvement of the management of opportunistic infections (prevention and treatment). This has a direct positive effect for all patients.

In the fields of price reduction of drugs, the Initiative has been a continuing learning experience. This has led to the use of a mixed model of price reduction, combining negotiations and competition, that appeared to yield positive results in at least 1 country. A comparison of price reductions achieved in Côte d’Ivoire (practicing open competition for some nucleosides since April 2000) and in Uganda (not practicing open competition) to an extent shows the effects of competition within that drug class (see table below).

Drug	Defined Daily Dose	Price of daily dose in US dollars (year 2000)			
		Brazil **	Uganda #	Cote d’Ivoire #	USA ^α
3TC (Lamuvudine) 150 mg	300 mg	1.66	3.28	2.95	8.70
ddC(Zalcitabine) 0.75 mg	2.25 mg	.024	4.17	3.75	8.80
Didanosine 100 mg	400 mg	2.04	5.26	3.48	7.25
Efavirenz 200 mg	600 mg	6.96	NA	6.41	13.13
Indinavir 400 mg	2400 mg	10.32	12.79	9.07	14.93
Nelfinavir 250 mg	750 mg	4.14	4.45	4.39	6.47
Nevirapine 200 mg	400 mg	5.04	NA	NA	8.48
Saquinavir 200 mg	1200 mg	6.24	7.37	5.52	6.50
Stavudine 40 mg	80 mg	0.56	6.19	4.1	9.07
ZDV/3TC 300/150 mg	600/300 mg	1.44	7.34	NA	18.78
Zidovudine 100 mg	600 mg	1.08	4.34	2.43	10.12

**Prices from Brazilian government tender, 2000.

End user prices in the Drug Access Initiative

^α End user prices in USA (from globalRx.com)

The Initiative also generated a networking effect. This is reflected in the links that currently exist between the countries, and within the countries, between the program the health care workers involved in the initiative and the evaluation team.

Finally, the Initiative shows the complexity of the financial aspects related to access to HIV/AIDS drugs.

What should be reinforced or done differently?

If we had to start again the Initiative, we would:

a. Strengthen the “hook” effect of antiretrovirals to promote wider access to a comprehensive care package.

Until mid 1999, the Initiative focused almost exclusively on making antiretrovirals

available, and has insufficiently emphasized, also during its accreditation process, performance in voluntary counseling and testing, psychosocial support, management of opportunistic infections and palliative care. Antiretrovirals should be used more as an entry point for wider access to a comprehensive care and support package. A more comprehensive accreditation process and a support system to upgrade services in the centers could be used to support this

Specific efforts are also needed to:

- expand the efforts for HIV testing and counseling
- expand the awareness of the Initiative among AIDS patients (information should be expanded to family and community and not just to individuals)
- expand the geographic access to treatment and monitoring by expanding the referral system in periphery and/or develop a care package for the peripheral centers
- improve the access to the Initiative earlier in the course of the disease (patient come late for the vast majority)
- investigate alternative cheaper regimens
- decrease the cost of HIV/AIDS drugs.

At the same time, it is essential that countries not detract resources from other public health programs, and from HIV prevention efforts to support treatment access. This requires more and new funds.

b. Improve the feasibility and sustainability of the monitoring of antiretroviral therapy

Within the Initiative the monitoring of the antiretroviral therapy is possible through outside support from research/evaluation teams. The cost of the biological follow up including CD4 count and viral load is 257 USD per patient per year in Côte d'Ivoire. This is not sustainable. Alternative solutions must be found. First, a special focus may be put on the reduction of the costs of CD4 count and viral load measurement through negotiations with the pharmaceutical companies. Second, one may consider changing the current testing algorithm, e.g.: eligibility by CD4 alone, decrease of the frequency of viral load measurements. In the meantime, there is most probably room for adoption of testing technologies that are less expensive, e.g. the immunophosphatase method for CD4 counting, or other alternatives.

c. Integrate the procurement and distribution of the HIV/AIDS drugs including antiretrovirals into the national pharmaceutical structures

The experience of Cote d'Ivoire and Chile are quite conclusive in this direction. However, in some countries, functional essential drug programs with good accountability may not exist. More, certain central medical stores do not accept responsibility to deal with very expensive drugs because of the possibilities of losses related to expired medicines. In such circumstances, a parallel structure may be necessary. However, a conflict of interest may arise when pharmaceutical companies are the only funding source for such a structure. Hence, there may be a need for independent financing mechanisms such as funding by a non-governmental organization.

d. Advocate for multipartite approach involving other stakeholders than the governments and international donor community for the funding of wider access to HIV/AIDS drugs in severely resource-restricted countries

There is a need to identify sources of funding other than the households, such as private companies to buy treatment for their own employees and insurance mechanisms to support the cost of treatment.

In countries where governmental subsidies are available for a limited number of PLWAs, there is clearly a need for standardized criteria and methodology for the selection of patients eligible for subsidies in order to improve the transparency of the selection systems.