Pre-publication Draft





Surmounting Challenges : Procurement of Antiretroviral Medicines in Low- and Middle-Income Countries

The Experience of Médecins Sans Frontières

World Health Organization

CAMPAIGN FOR ACCESS TO ESSENTIAL MEDICINES

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Contents

Patients and staff celebrating the 2nd anniversary of MSF's ARV programme in Khayelitsha, a township near Cape Town, South Africa, in May 2003.

1. Executive Summary

MSF has been offering ARV treatment to patients in Yaounde, Cameroon, since January 2001.

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Background

As the price of antiretrovirals (ARVs) in low- and middle-income countries has fallen in recent years, governments, international agencies and non-governmental organizations (NGOs) have been able to start developing treatment programmes for people living with HIV/AIDS (PLWHA). Procurement strategies are a key element in this global scaling-up process. As Médecins Sans Frontières[1] (MSF) was one of the first NGOs providing ARV therapy, the World Health Organization (WHO) requested that MSF document its procurement experiences in 10 countries where it has ARV treatment programmes, so that others could benefit from what has been learnt.

The importance of assisting ARV treatment programmes to procure low-cost, quality ARVs cannot be underestimated. In sub-Saharan Africa, the region hardest-hit by the HIV virus, only one percent of the four million people in need currently receives ARV therapy. While other medicines can cure the opportunistic infections caused by HIV or provide relief from symptoms, these are ultimately only temporary measures. Conversely, ARVs decrease the level of the virus in the body, reduce morbidity, prolong and improve quality of life, and prevent most opportunistic infections.

MSF's experience shows that for numerous reasons ARV procurement is often more challenging than that of other types of essential medicines. Products are expensive and stock management is crucial to avoid disruption of treatment. Treatment protocols are diverse, and procurement systems have to respond quickly to evolving treatment regimens. Also, the limited amount of publicly available information, including the lack of quality reference standards, makes assessing the quality of generic ARVs more difficult than that of most other essential medicines - even though quality generic ARVs are being produced.

Method

Data collection for this report is based on MSF's purchasing experience over the past two years in 10 countries. Potential ARV sources, patent and registration status, prices, and distribution options have been analysed and systematically documented in each of the 10 countries - Cambodia, Cameroon, Guatemala, Honduras, Kenya, Malawi, Mozambique, South Africa, Thailand and Ukraine.

Before presenting the detailed country case studies, the report looks in some detail at ARV selection, pricing and procurement issues in general, as part of the medicines management cycle. Five issues of particular importance are highlighted: sources (quality); registration; prices; patents; and continuous availability of medicines.

Main findings

An important finding from the country case studies is that procurement works best when there is a national HIV/AIDS strategy that includes ARV treatment, and that is supported by government commitment and political will. Sufficient funding is crucial to implement national action plans.

Another major finding is that there is no single or ideal approach to ARV procurement. There are several effective strategies that can result in the supply of affordable, quality

[1] MSF is an independent, international medical relief organization that aids victims of armed conflict, epidemics, natural and man-made disasters, and others who lack health care due to geographic remoteness or ethnic marginalization. MSF has been caring for people living with HIV/AIDS since the early 1990s.

ARVs. Often a combination of these procurement strategies worked well for MSF country programmes. From MSF's perspective, the most effective and easiest systems are either one or a combination of: strong public procurement agency (Cameroon); local drug production (Thailand); and/or dynamic private sector distributors (Malawi).

It was also found that the following factors affected efficient procurement systems at country level: limited numbers of registered ARV products (generic and originator); unclear patent status of ARV medicines; lack of generic policies; limited information available about internationally publicized prices; and countries' eligibility for differential prices offered by pharmaceutical companies. The ability to use generics has been one critical factor for procurement success, to allow competition and guarantee a continuous supply of ARVs.

Main recommendations

The report's main recommendations on ARV procurement highlight that for

Ministries of health/national AIDS programme/policy-makers – it is important to have national HIV/AIDS treatment guidelines and ARVs included in the national list of essential medicines. Taxes, duties and mark-ups on ARVs should be lowered or abolished by governments to avoid significant price increases that make products unaffordable. Systematically collected information on patents, and international and local prices of medicines will increase price transparency and will facilitate price negotiations and improve procurement.

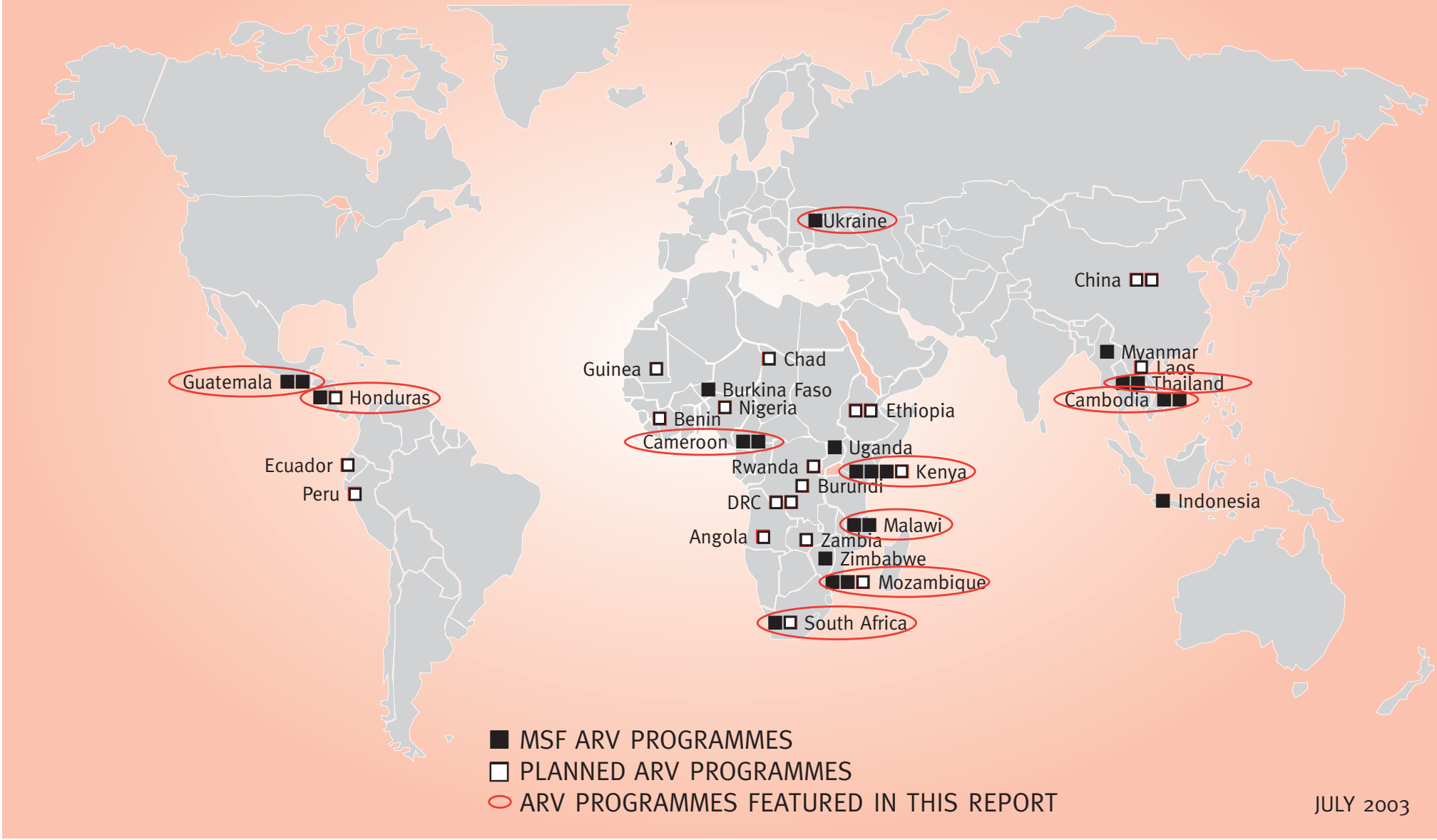
Governments of Least Developed Countries (LDCs) – have no need to grant and enforce patents on pharmaceuticals until 2016, as stipulated in the Doha Declaration on TRIPS and Public Health, 2001. Also they can exercise their right to access low-cost medicines (compulsory licences or parallel importation), as provided for in the World Trade Organization (WTO) Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement.

ARV procurers – the most important task is to obtain appropriate ARV products and formulations of assured quality at the lowest price possible. Some of the key issues for successful procurement are: forecasting ARV needs accurately, having up-to-date price information and quality assessment (WHO's pre-qualification project) obtaining ARVs that are registered by the national drug regulatory authority (NDRA), introducing generic competition, knowing of reliable suppliers and distributors (international and national) and having guaranteed funding (e.g. from the Global Fund to Fight AIDS, Tuberculosis and Malaria).

Manufacturers – manufacturers worldwide should develop fixed-dose combinations (FDCs) and paediatric formulations, as well as more user-friendly and affordable diagnostics. They should also be committed to developing and participating in a differential pricing mechanism, in WHO's pre-qualification project and in maintaining stocks at country level.

United Nations and international agencies – a differential pricing system for newer medicines should be further explored at international level. Regional, as well as national, ARV procurement initiatives should be supported. If requested, UN and international agencies should stock ARV supplies on a country's behalf.

MSF ARV PROGRAMMES



2. Introduction

Until recently, few PLWHA in developing countries could access ARV treatment. This is beginning to change as drug prices have come down, allowing governments to take the first steps towards larger-scale treatment programmes.

At WHO's request MSF has documented its experiences in procuring ARV medicines in 10 countries, in the hope that this will benefit others. This report also shares observations about how government and market dynamics impact drug availability in poor countries.

Apart from the price of medicines, there are many real and perceived barriers to expanding ARV treatment to large numbers of people in the developing world. Among those most often referred to are lack of political will, lack of trained staff and other elements of health care infrastructure, and the complexity of treatment protocols and laboratory monitoring. However, these barriers are not absolute. The question is no longer, "do we scale up treatment?" but "how?". Procurement strategies are a key element of scaling up, which is why this report focuses on how to procure ARVs effectively.

2.1 Purpose

This report aims to inform and help ARV treatment programmes procure low-cost, quality ARVs effectively and efficiently. It is particularly geared toward ministries of health, national programme managers, national pharmaceutical authorities, public and private health providers, international, national and regional drug procurement agencies, NGOs, charity organizations, and any other organizations or individuals engaged in procuring ARVs in resource-poor settings.

Based on MSF's experience over the past two years, the report outlines the major parameters that ARV procurement agents need to consider. Ten country case reports illustrate how challenges were, and continue to be, overcome in specific contexts.

Those looking for a ready-made step-by-step guide may be disappointed, though: as the country cases show, there is no single or ideal approach to ARV procurement. Rather there are several effective strategies that result in the supply of affordable, quality ARVs. These need to be adapted as the international, regional and national environment evolves.

2.2 Why procurement matters

The need to get effective medical treatment to people living with HIV/AIDS (PLWHA) in developing countries has never been more urgent, and will only grow in the coming years. In December 2002, UNAIDS estimated that 42 million people are now infected with the virus[2], five to six million of whom are in immediate need of ARV therapy. However, only about 300,000 people in the developing world are currently on ARVs, and Brazil alone accounts for about half of this number.[3] In sub-Saharan Africa, the region of the world that is both the poorest and hardest-hit by HIV/AIDS, only one percent of the four million people in need are currently receiving ARV therapy.

Two trends have contributed to expanding access to treatment in recent years: the rapid

Coverage of ARV therapy in developing countries, December 2002 (adults by region)[4]

Region	No of people on ART	Estimated need	Coverage
Sub-Saharan Africa	50,000	4,100,000	1%
Asia	43,000	1,000,000	4%
North Africa, Middle East	3,000	9,000	29%
Eastern Europe, Central Asia	7,000	80,000	9%
Latin America, Caribbean	196,000	370,000	53%
Total	300,000	5,500,000	5% av.

ART = Antiretroviral therapy

2 UNAIDS/WHO: AIDS Epidemic Update. 2002: http://www.unaids.org/EN/resources/epidemiology.asp
3 & 4 International HIV Treatment Access Coalition. A Commitment to Action for Expanded Access to HIV/AIDS Treatment. December 2002. http://www.who.int/hiv/pub/prev_care/pub23/en/

Why Antiretrovirals?

Antiretrovirals (ARVs) stop or inhibit the progression of a virus such as HIV. While other drugs can cure the opportunistic infections caused by HIV or provide relief from painful symptoms, these are ultimately only temporary measures — ARVs are necessary to decrease the level of the virus in the body. Along with prevention, voluntary counselling and testing, psychosocial support and reducing pain and suffering, ARV treatment is an essential element of a comprehensive approach to addressing the AIDS epidemic. ARV therapy prolongs and improves the quality of a person's life, improves productivity and reduces stigma. The fact that treatment is available encourages other people in the community to seek testing. Pilot projects have demonstrated that ARV therapy can be successfully and responsibly delivered even in very resource-poor settings

fall in the prices of some first-line ARV treatments over the past few years, and the increase in political attention, commitment and funding for anti-AIDS efforts worldwide. WHO has confirmed a target of providing three million people with ARV therapy by the end of 2005, known as the "3 by 5" target.[5] This requires sustained international support from wealthy countries.

Yet, despite these encouraging developments, there is still a complex chain of activities that must take place before ARVs get from the producer to the patient. Skillful medicine procurement is one of the most critical steps in the medicine management cycle because it can extend tight health budgets and enable resource-constrained actors to reach more patients.

2.3 Medicine management cycle

MSF has observed that developing country governments and other organizations that provide care to PLWHAs can maximize their efforts by purchasing quality ARVs at the best prices. However, ARV procurement is often more challenging than that for other types of essential medicines. The procurement agency must familiarize itself with and take into account many medicine management issues before it can purchase and deliver drugs to the patient.

Medicine management involves four main elements: selection, procurement, distribution, and use (see Figure 1). It is a real cycle, as each element is based on the previous element and is followed by the next.
At the centre of the cycle, there is a core of management support systems, such as organization, financial mechanism, information and human resources management, keeping the cycle moving. The entire cycle is supported by a policy and legal framework that emphasizes the political commitment to essential medicines supply. (Managing drug supply, 2nd edition, 1997).

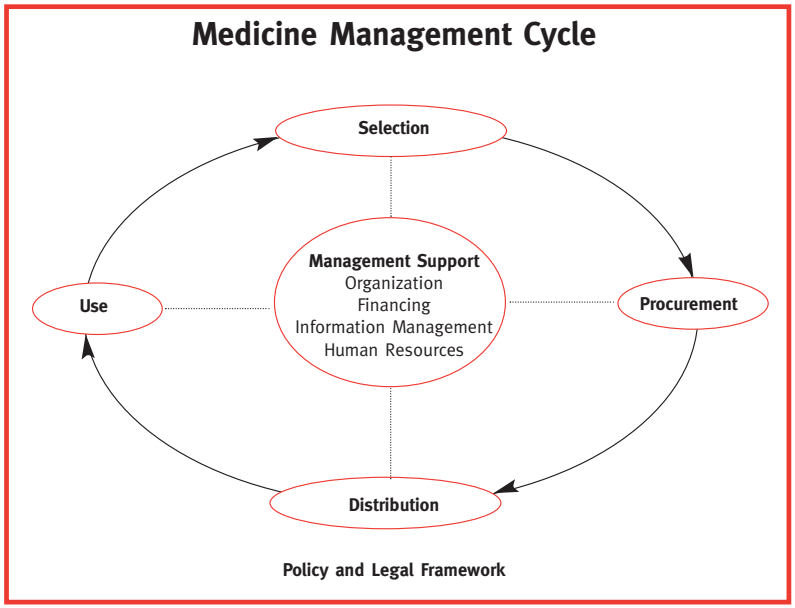


Figure 1 *Medicine management cycle*

2.4 MSF and ARV procurement

In response to the AIDS epidemic, MSF has provided prevention services, voluntary counselling and testing, psychosocial support, palliative care and safe blood transfusions since the early 1990s. Treatment for opportunistic infections in Latin America, South-East Asia and Africa has also been given. In addition MSF has been using ARVs for post-exposure prophylaxis for health workers and rape victims, and the prevention of mother-to-child transmission (PMTCT).

By the end of the 1990s, MSF had decided to start providing ARV therapy as part of the continuum of care. The first ARV project began with just a handful of patients in Thailand in late 2000. By June 2003, more than 5,000 people had received ARVs in MSF projects in Burkina Faso,

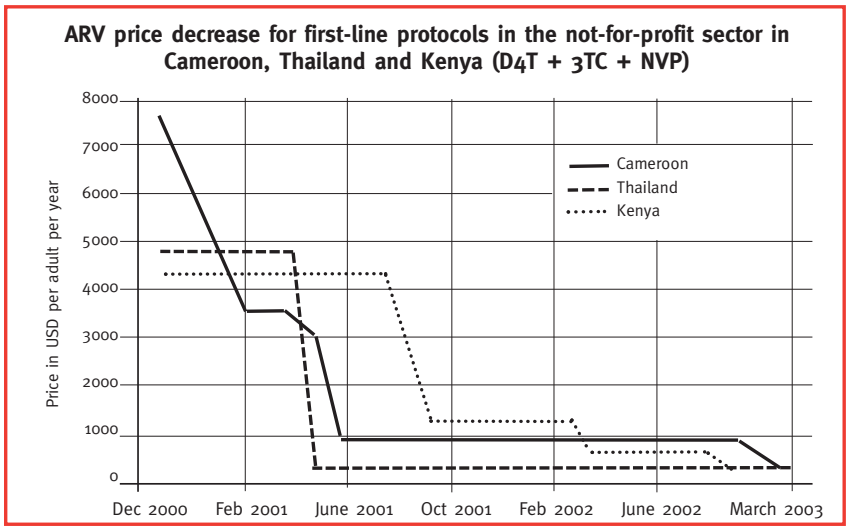
5 Fifty-sixth World Health Assembly Resolution WHA56.30/2003, Global Health-Sector Strategy for HIV/AIDS: http://www.who.int/gb/EB_WHA/PDF/WHA56/ea56r30.pdf

Cambodia, Cameroon, Guatemala, Honduras, Indonesia, Kenya, Malawi, Mozambique, Myanmar (Burma), South Africa, Thailand, Uganda and Ukraine. By the end of 2003, MSF expects to be treating approximately 10,000 people, opening new projects in Angola, Benin, Burundi, Cambodia, Chad, China, the Democratic Republic of Congo, Ethiopia, Guatemala, Guinea, Honduras, Kenya, Laos, Nigeria, Rwanda, Peru, Zambia and Zimbabwe. In most countries, MSF provides ARVs free of charge to its patients.

MSF's projects aim to make life-prolonging AIDS treatments available to individuals in need, and also to provide experience that informs and is replicable for building individual and national treatment programmes. MSF uses projects both to assess and demonstrate the feasibility of ARV therapy in a range of resource-poor settings, with some projects operating out of slums, others via mobile HIV clinics and others within district or provincial hospitals. One overarching principle is to work closely with national authorities to adapt treatment programmes to local settings.

This experience not only covers a broad geographic area but has also spanned a range of countries with a variety of development and per capita income levels, health system infrastructures and patent systems. While these projects can only reach a small fraction of those in need, MSF hopes that its operational research will have broader impacts in the longer-term.

Figure 2. *The figure demonstrates the reduction of prices offered to MSF and other not-for-profit treatment providers over the past three years in three countries.*



2.5 Prices of ARVs

In 2000, when MSF first began using ARVs in its HIV/AIDS programmes, most ARVs were neither available nor affordable in developing countries. In industrialized countries, a triple-combination of ARVs generally costs US$10,000 to US$15,000 per patient per year (ppy), and the medicines were only available as patented products from originator companies. In addition, there were no alternative generic sources of ARVs whose quality had been assessed, nor were ARV supply channels set up in developing countries. As a result, only a small number of patients in the developing world had access to ARVs, usually through the private sector, donations or participation in clinical trials.

Since 2000, the international prices of some first-line ARVs have tumbled, due to a combination of sustained public pressure, discount offers from originator companies, competition from generic companies, vocal criticism of the TRIPS regime, and in general, the growing political attention paid to the AIDS epidemic. Several major events have played a key role, beginning with the local manufacture of ZDV (AZT) by the Brazilian government in the early 1990s. In 1996, a presidential decree led to universal free access to HIV medicines including ARVs, which made it possible to guarantee HIV-positive Brazilians access to treatment. Brazil's triple-combination at less than US$3000 ppy demonstrated that lower prices were possible, and that developing countries could have an alternative to originator products. Public pressure on the pharmaceutical companies built up over the next few years, and in May 2000, five originator firms announced a new partnership, Accelerating Access to HIV/AIDS Care, Treatment and Support (also known as the Accelerating Access Initiative (AAI)). This is a private/public partnership with the United Nations to offer discounted ARVs to developing countries. It was the first time that these firms had initiated differential pricing policies for ARVs.

In February 2001, the Indian generics firm Cipla shattered the price barrier when it publicly announced that it would sell a triple combination for US$350 ppy, demonstrating how low prices could fall. In MSF's experience, the ability to use generics has been critical for a number of reasons: even with differential pricing, originator medicines were often much more expensive than generics; generic production was necessary to introduce competition to the market; and the right of developing countries to use generic pharmaceuticals was at the core of a wider debate about the tension between intellectual property rights and public health (see box on p. 13).

3. From producer to patient

The following sections describe how MSF handles the selection, procurement and distribution of ARVs to its patients. It should be noted that the high cost of diagnostic tests and monitoring tools – vital components of any ARV programme – continues to be a concern for MSF and others providing ARV treatment, but the issue is outside of the scope of the present report. (MSF is preparing a new publication on diagnostics and monitoring, which is due for publication in 2004.)

3.1 Selection of ARVs

"Selection involves reviewing the prevalent health problems, identifying treatment of choice, choosing individual medicines and dosage forms and deciding which medicines will be available at each level of the health care system."

(Managing Drug Supply, 2nd edition, 1997)

The first step in all treatment programmes is the development of treatment protocols. In countries that have already defined a national treatment protocol, MSF follows country recommendations. However, in many of the countries where MSF works, there were no government-issued treatment guidelines when MSF's programmes began, nor were ARVs included in national essential medicines lists (EMLs). MSF often worked closely with the authorities in each country to establish ARV treatment protocols for its own programmes. These sometimes triggered the development of national treatment guidelines. MSF's early treatment protocols were identical to those used in wealthy countries but they have since evolved to include more FDCs of ARVs, which decrease patients' pill load considerably. For example, nearly all MSF programmes began by using the two-drug FDC ZDV/3TC (zidovudine/lamivudine) with efavirenz (EFV) or nevirapine (NVP). However, after MSF validated the quality of generic three-in-one pills (3TC/d4T/NVP), many of the programmes switched to this regimen[6], reducing the intake of pills from 4 or 5 to 2 per day.

Proven safety and efficacy are necessary prerequisites for a drug to be included in treatment protocols. Once this pre-condition is met, MSF weighs the following three criteria together, before deciding on the best treatment protocol for a new ARV treatment project:

Inclusion in national or international standard treatment guidelines and/or EMLs

MSF checks to see if a drug is included in existing national standard treatment guidelines and/or national essential medicines lists (EML), as well as international treatment guidelines, such as the WHO/UNAIDS standard treatment guidelines[7] and the WHO Model EML.[8]

Ease of use in resource-poor settings

i. **Minimum required monitoring of side-effects:** If possible, MSF uses medicines that have side-effects that can be clinically detected and monitored rather than those requiring lab testing.
ii. **Minimum drug interactions:** For example, MSF tries to avoid drugs that might interfere with tuberculosis (TB) drugs.
iii. **Minimum frequency of dosing:** To facilitate patient adherence, MSF favours two- and three-drug FDCs and/or once-a-day formulations that require fewer pills per day.
iv. **Minimum dietary restrictions:** Medicines that do not have dietary restrictions are easier for patients to take.
v. **Minimum storage requirements:** For example, medicines that do not require refrigeration are more practical for resource-poor settings.

Cost

Ideally, unit prices should not influence the choice of medicines but the total treatment costs should be balanced against the medicine's safety and efficacy. In cost comparisons between medicines, the cost of the total treatment, and not only the unit cost of a medicine, should be considered. Cost comparisons should be made among alternative treatments within the same therapeutic group.

Particularly in resource-poor settings, the price of treatment does play a role. Thus, when prices were at the US$10,000-15,000 ppy level, MSF (along with many others) was forced to include price considerations as one of its criteria in the medicine selection process. Efforts to lower drug prices have borne fruit (see 2.5. "Prices of ARVs"). Today, the hierarchy of decision-making can refocus

6 This drug combination is not available as an FDC in developed countries because it contains patented originator products from different companies.
7 Scaling up antiretroviral therapy in resource-limited settings. Guidelines for a public health approach. WHO, June 2002.
8 WHO Model List of Essential Medicines, 13th list, April 2003. In 2000, when MSF first started to provide ARV therapy in its HIV programmes, few ARVs were included in the EML. Twelve ARVs are on the 13th EML published in 2003.

Paediatric formulations: the continuing challenge

Paediatric formulations of ARV regimens present a persistent challenge. In general there are very few of them because of the relatively small market in wealthy countries. The ones that do exist often have technical limitations that make them difficult to dispense. Caregivers of children with AIDS have to deal with the consequences of the unpleasant taste of drugs, the difficulty of preparing oral powders, the problem of transporting and storing large volumes of syrups/suspensions, and the task of making complex calculations to determine dosages. In addition, originator and generic companies often do not register paediatric formulations in developing countries, which further limits their availability. To improve accessibility of ARVs for children, more research and development into adapted paediatric formulations is urgently needed.

on the most medically appropriate and convenient drugs as a first-line therapy. However, it is vital that prices of ARVs drop further, to an estimated US$50-100 ppy, so that more people in developing countries can access this treatment.

3.2 Procurement of ARVs

"Procurement includes quantifying drug requirements, selecting procurement methods, managing tenders, establishing contract terms, assuring drug quality, obtaining best prices, and ensuring adherence to contract terms."
(Managing Drug Supply, 2nd edition, 1997)

3.2.1 Quantifying ARV requirements

In MSF projects, drug need is quantified by considering the initial protocols chosen, the anticipated number of monthly patient admissions and the projected need to change protocols. These forecasts are challenging for new projects because some of the elements, such as whether and when a patient's treatment should be changed, are unpredictable. Building buffer stocks helps to avoid medicine shortages and treatment interruptions.

3.2.2 MSF's procurement system

This section provides some background on MSF's general procurement policy.

Over the course of its 30 years, MSF has developed its own drug procurement system to supply its various projects worldwide. Traditionally, MSF has purchased mostly generic drugs from multiple international sources, centralizing procurement in Europe (Belgium, France and The Netherlands). This centralized system has enabled quick emergency responses especially in situations where medical infrastructure is weak or non-existent. Part of this centralized procurement system is a quality assurance (QA) mechanism under which any products are assessed, and to which field projects report any quality-related problems. MSF's procurement system was traditionally supplemented by in-country procurement when there were limits on importation.

The AIDS epidemic presented MSF with a significant new challenge, and forced the organization to find in-country procurement solutions. When MSF first began using ARVs in its projects, the WHO pre-qualification project did not exist and ARVs were on patent in some of the countries where MSF worked, as well as in supply centre countries. Initially, these medicines were extremely expensive compared to others used in MSF projects.[9]

These challenges led MSF to promote ARV procurement at country level in order to access lower-priced drugs for its own programmes, as well as others (MEDS in Kenya, CENAME in Cameroon; see the country cases for details) in the countries where it works.

3.2.3 Key elements to consider in ARV procurement at country level

Procurement is a complex and dynamic process. MSF constantly monitors and weighs together changes in relevant details, such as price, quality and the terms of offers, in order to arrive at the best procurement decisions.

Five issues are of particular importance: **sources (quality), registration, prices, availability and patents**. Each of these elements is explained in Figure 3 and text overleaf.

Useful tools for drug selection

(See full references and web citations in the annotated bibliography in Annex 1):

- WHO Model List of Essential Medicines, 13th list April 2003.
- WHO Model Formulary. WHO, 2002.
- Scaling up antiretroviral therapy in resource-limited settings: Guidelines for a public health approach. WHO, 2002.
- Managing drug supply, 2nd edition. Management Sciences for Health, in collaboration with WHO, 1997.

9 Previously, MSF had mostly handled procurement of generic drugs that were no longer on patent in most parts of the world.

Figure 3: Key elements to consider in ARV procurement at country level

The steps presented in the table are interlinked and are usually taken simultaneously, not one after the other.

A. Identification of possible sources: (see e.g. "Sources and prices of selected drugs and diagnostics for people living with HIV/AIDS" and other guidelines listed in Annex II): For an assessment of the quality of the sources, refer to the National Drug Regulatory Authority (NDRA), the WHO pre-qualification project and your organization's quality assessment.

B. Registration:

Is the product registered by the National Drug Regulatory Authority (NDRA)?

If yes:
The product can be purchased in the country and you can proceed with procurement.

If no:
a) Apply to the NDRA for special authorization to import non-registered products; and
b) Contact the manufacturers to ask them to apply for registration.

C. Price:

Is the product available at the best price?

Compare prices offered locally with the international offers taking into account duties, charges or mark-ups. There is often a difference. You need to find out about all the conditions attached to the offers (see p. 9 for more details).

You may need to negotiate with the distributor and the company headquarters to get the best price through the distributor. If this is not possible, you will have to import the drugs.

If you have two sources of the same drug, encourage competition between the two suppliers to obtain the lowest price.

D. Availability:

Find out from the Ministry of Health or company headquarters whether there is a local distributor in the country. (Official list of licensed distributors.)

If yes:
Analyse the services offered by the local distributor (prices, storage and distribution practices) and proceed with procurement.

If no:
Work with the company headquarters to identify a potential local distributor, or import the drug from a regional distributor, or from the company headquarters.

E. Patents:

If you want to purchase generic drugs, find out from the local Patent Office, the Ministry of Trade and/or WIPO whether the originator product is patented in the country (or region, e.g. OAPI countries) before you import. Note that LDCs do not have to grant patents on pharmaceuticals until 2016 (see page 13).

a) If the originator product is under patent in the country, you/the government can:
   1) Explore the use of compulsory licence or governmental use in order to import or use locally manufactured drugs.
   2) Purchase originator drugs requesting differential prices.
   3) Import the generic drugs. Some originator companies have announced they will not file a lawsuit against developing countries infringing patents.
   4) Challenge the validity of the patent – it may have been granted on the wrong grounds.

b) If the originator product is not patented in the country: there is no barrier to importing the generic medicines.

Your procurement strategy is the combined result of assessing the various elements mentioned here. In the ideal situation, a central procurement agency deals with all the issues covered in this table.

*Launched in March 2001, **WHO's pre-qualification project**, a voluntary scheme open to all relevant manufacturers, assesses the quality of generic and originator AIDS-related products, and periodically publishes a list of pre-qualified products, manufacturers and their production sites.*[10] *The first list of pre-qualified sources of ARVs, including several generic manufacturers, was published in March 2002. It provided countries with another reliable tool to guide them in purchasing quality ARVs from lower-cost generic and research-based producers. The list will be expanded as more producers join the scheme and are subject to dossier review and site inspection. In addition, the WHO project aims to create unified standards for inspecting manufacturing sites, evaluating information on product quality specifications, and creating a single, harmonized quality system and assessment. This project has facilitated the introduction of quality generic ARVs. WHO is also in the process of developing monographs for ARVs.*

*Decisions about which drugs or sources to use are about striking a balance between risks and benefits. With thousands of patients waiting for treatment in **Brazil** in the late 1990s, each month of delay meant more lives lost. The Brazilian authorities considered that the benefits in lives saved outweighed the relatively limited quality risks, and proceeded with distribution. They registered products which met national quality criteria but would not necessarily have met the WHO pre-qualification standards. It should be noted however, that such decisions can only be taken by NDRAs of individual countries.*

A. Sources (quality): The limited information available in the public domain, including the lack of reference quality standards (pharmacopoeia monographs), makes the quality assessment of generic ARVs more difficult than that of most other essential medicines. However, quality generic ARVs are being produced (see box on WHO pre-qualification).

MSF considers three main sources of quality assurance in deciding which drugs to use in its projects:

(1) national drug regulatory authorities (NDRAs),
(2) the WHO pre-qualification project and
(3) MSF's internal qualification system.

MSF relies on the assessment of NDRAs, which are ultimately responsible for drug quality, and its projects only use drugs that have been authorized by relevant national authorities. Secondly, MSF refers to the WHO list of pre-qualified drugs (see box).

However, to supply its projects, MSF may consider products and producers that are not yet included on the WHO list of pre-qualified products. For example, MSF treatment protocols use fixed-dose ARVs that are not yet pre-qualified by WHO, such as d4T/3TC/NVP. Decisions like this are based on MSF's own internal assessments, the third source of quality assurance used by MSF. These entail MSF pharmacists and external experts conducting a qualification process based on an assessment of both product dossiers and manufacturing sites[11] on an ongoing basis. MSF does not grant blanket qualification for all the drugs that a given manufacturer produces; rather, each drug must be individually qualified. For example, MSF will not simply qualify Company A, but rather may qualify Company A's Drug X, but not its Drug Y.

B. Registration status: Registration is granted by a country's NDRA for a given medicine from a given manufacturer, after the medicine has been evaluated on the basis of its efficacy, safety and quality. Once a drug has been registered, it can be marketed in the country. The NDRA is ultimately responsible for approving the use of any drug in its country. However, if MSF found a selected product was not registered, it asked for temporary authorization to import and use the drug and urged the company to apply for registration. Special drug-by-drug, import-by-import authorization requires extra time and administrative work. A more efficient and sustainable solution — and indeed the ultimate goal — is for the manufacturer to obtain registration for its product in the country.

Finally, it should be emphasized that *registration* of a drug is quite distinct from a *patent* on a drug, although it is a common mistake to confuse or equate the two. If a manufacturer's drug — whether generic or innovator — is deemed safe, efficacious and of quality, then an NDRA may choose to register it, whether or not there is a patent on the molecule in the country. Similarly, a patent office may grant a patent on the drug, even if the originator firm has not registered that

10 Pilot Procurement, Quality and Sourcing Project: Access to HIV/AIDS Drugs of Acceptable Quality http://www.who.int/medicines/organization/qsm/activities/pilotproc/pilotproc.shtml
11 MSF refers to WHO Good Manufacturing Practice (GMP) standards.

Differential pricing and the paradox of Middle-Income Countries

While nearly all Least Developed and sub-Saharan countries are eligible for differential pricing from originator companies, the system is far more haphazard for those developing countries not included in the LDCs category. Only Merck and Roche have publicized prices for some of these countries: Merck's prices are valid for the United Nations Development Programme's (UNDP's) Medium Human Development Countries, and Roche has discounts for Lower-Middle Income countries, as defined by the World Bank. Also, the eligibility criteria and conditions attached to the price offers make the purchase of these drugs quite complex. For example, private institutions are often excluded from the offers, and sometimes programmes have to be certified by a third-party before discounts will be granted. Middle-Income Countries may find it simpler to deal with generic companies, because all developing countries are able to access their offers.

drug in the country. In MSF's experience, governments have been hesitant to register a generic drug if there is a patent on it in the country, even if the generic version meets all the requirements for registration. (For additional information see the section below on patents).

C. Prices: When gathering price information, MSF compares local and international prices from both originator and generic manufacturers. In-country distributors often did not offer the prices or discounts publicized internationally by generic or originator companies. Frequently, in order to access the best price, MSF had to contact the companies' headquarters directly, either to arrange for better prices with the local distributor, or to import directly from headquarters.

Also, price offers often came with other requirements or conditions, such as eligibility criteria for a country or type of institution; transport and insurance costs (incoterms); and/or minimal quantities stipulated to obtain the price offer. See more on conditions of offers in box opposite.

In situations where there is more than one quality source, tenders among manufacturers are a useful tool for fostering further competition, particularly with large quantity purchases. It should be noted that buying drugs once from an originator company does not preclude the buyer from also purchasing generic versions of that same drug, or from using generic prices as a bargaining tool.

In addition to competition, negotiation with producers and distributors can also yield price reductions. The lowest prices offered internationally should always be used as a basis for negotiations with companies at national level. In some countries, MSF was able to get even better prices than those offered internationally by negotiating with the distributor. For example, while Cipla's best international price on the FDC d4T/3TC/NVP is US$304, MSF buys this drug for US$288 in Honduras and US$277 in Cameroon. Providing forecasts about future drug needs to suppliers can also bring down prices because the unpredictability of orders is a challenge for them. However, during the start-up phase of a treatment programme, it is difficult to anticipate the exact long-term needs because of unanswered questions about increasing numbers of patients, changes of protocols, and when patients will need to switch to a second-line treatment.

Increasing the volume of purchases through pooled medicine procurement, nationally, regionally or internationally helps decrease prices further. Cameroon is a recent example of a country which has managed to bring down prices of ARVs with the help of centralized procurement involving competition between generic and originator companies.

D. Availability: When no public procurement agency was supplying ARVs at country level, MSF attempted to find a local or regional private distributor for each needed drug. In many countries, distributors were not in place for most ARVs and MSF assisted manufacturers in creating new distribution channels. When ARV distribution is just beginning in a country, it is essential to give manufacturers and local agents advance warnings about needs.

E. Patent status: MSF looks for the selected drug's patent status by checking first with the national patent office. This can be time-consuming for various reasons. Some patent offices are not equipped with computers or local databases containing all patent information and some patent information may need to be translated etc. Patent searches are seldom free of charge and may be very expensive, depending on the country.

MSF also checks information in international patent databases. However, some countries, such as Guatemala and Thailand, are not included in these databases.

What is a patent?

A patent is an exclusive right granted to the inventor of a medicine to prevent others from making, marketing and using the invention. There are limitations on and exceptions to patent rights that can be used to help procurement agencies and authorities to access less expensive, generic versions of a patented product.
It is important to note that there are no international patents: they are granted on a country-to-country basis, and sometimes on a regional basis. The duration is typically 20 years from the filing of the patent application, but this term may vary. For various reasons it is common that products are patented in certain countries but not in others. There might be more than one patent on one medicine. Not all patents that have been granted are necessarily valid. For example some countries' patent law does not allow the granting of new use patents or patents on combinations of existing medicines. Yet at times such patents are granted even though the law does not allow it. In Thailand, AIDS activists challenged the validity of a BMS patent on ddI and won the case in October 2002. The judgement has been appealed by the company.

*In a landmark case in April 2001, 39 drug companies dropped their lawsuit challenging **South Africa's Medicines Act**. This case spurred an international debate on intellectual property and access to medicines, including discussions inside the WTO. Later that year, WTO Members adopted a declaration that "the TRIPS Agreement can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all". It was becoming clear that developing countries could take a number of legal measures to gain access to low-cost medicines, including generic versions of ARVs that are patent protected.*

Patent information may also be available from regional patent offices, such as the African Regional Industrial Property Organization (ARIPO), the African Organization of Intellectual Property (OAPI), or the World Intellectual Property Organization (WIPO).

Once a search has been completed and no patent has been found on the drug in the country, there is no legal barrier to importing a generic. If there is a patent on the drug in the country, it is worth verifying whether the patent is valid. Also, there may be legal procedures that would enable the use of generics, such as government use or compulsory licensing clauses in the intellectual property legislation. For more information about the patent status of specific drugs in particular countries, see the country cases in this report and "Drug patents under the spotlight – sharing practical knowledge about pharmaceutical patents", another MSF report (2003).

The 2001 World Trade Organization (WTO) Doha Declaration re-affirmed countries' rights to use provisions in the TRIPS Agreement to protect public health and promote access to medicines.

It should be noted that even LDCs that are WTO members are under no obligation to grant patents for pharmaceuticals or enforce patents that have already been granted until at least 2016. This special extension of the TRIPS transitional period for pharmaceutical products was provided in paragraph 7 of the Doha Declaration on TRIPS and Public Health. In practice this means patents should not be a barrier to purchasing or producing generic versions of medicines.

In some cases the patent holder has decided not to take action against generic versions of ARVs. For example, Roche has pledged that it will not take action against generic versions of its ARV medications where Roche holds the patent in sub-Saharan Africa and in countries on the United Nations list of LDCs.[12]

3.3 Distribution of ARVs

Although MSF projects are often within public health care structures, they frequently rely at least partially on an MSF-dedicated supply chain that manages all aspects of supply and distribution from customs clearance (when drugs are imported) to final distribution to patients. MSF does not develop or manage national drug distribution networks but rather purchases from them, sharing information and offering technical assistance as necessary.

MSF takes full responsibility for ensuring an uninterrupted drug supply to its projects and individual patients, and therefore manages a stock of drug supplies. Drug interruptions are sometimes blamed on poor patient

12 Roche's "Global Initiatives in Caring"; Commitment to access, see http://www.roche-hiv.com/Roche_Template.cfm?link= InitiativesinCaring

Useful tools for ARV procurement

(See full references in Annex 1)

- WHO pre-qualification list. Pilot Procurement, Quality and Sourcing Project: Access to HIV/AIDS drugs and diagnostics of acceptable quality, 6th Edition. WHO, May 2003. http://www.who.int/medicines/organization/qsm/activities/pilotproc/pilotproc.shtml
- Sources and prices of selected medicines and diagnostics for people living with HIV/AIDS. WHO, UNAIDS, UNICEF and MSF, 2003.
- Untangling the web of price reduction for available ARVs. MSF, 2003.
- Drug patents under the spotlight: sharing practical knowledge about pharmaceutical patents. MSF, 2003.
- NDRAs and local distributors, drug manufacturers.
- National patent office (where one exists), ministries of trade or justice. Patent information may also be available from regional patent offices, such as ARIPO or OAPI in Africa and WIPO.
- WHO/UNAIDS 2000: Patent situation of HIV/AIDS-related drugs in 80 countries.
- Managing drug supply, 2nd edition. Management Sciences for Health in collaboration with WHO, 1997.

compliance, but in developing countries, the problem is more likely to be caused by drug shortages.

Like colleagues in other organizations or in private practice, MSF teams have witnessed numerous ARV shortages and "stock-outs" in the last two years. These supply problems have often resulted from originator companies' efforts to move from strictly commercial marketing and distribution to a more complex system of commercial and differential sales plus donations.

For example, in 2001 Kenyan treatment centres and individual pharmacies experienced shortages of Epivir® (3TC), Stocrin® (EFV), Zerit® (d4t) and Videx® (ddI). This was due both to the unpredictability of the initial ARV demand, and changing the medicines' packaging to comply with differential pricing systems in which less expensive products are sold in distinct packaging.

To ensure a constant supply of drugs to patients, MSF has:

- Maintained buffer stocks at country level.
- Secured a budget for long-term supply of ARVS.
- Secured storage facilities to minimize the possibility of theft or damage.
- Kept careful records of usage and stored supplies.
- Investigated payment terms and requirements when establishing new relationships with suppliers; and included the cost of maintaining adequate buffer stock in budget calculations.

Useful tools for distribution

A public health approach for scaling up ARV treatment: toolkit for programme managers (pre-publication draft, WHO, July 2003).

Managing drug supply, 2nd edition. Management Sciences for Health in collaboration with WHO, 1997.

- Given as much advance warning of needs to manufacturers or distributors as possible to help them assure adequate stocks.

At field level, MSF storage conditions follow good storage practices but the challenge remains at patient level – for example, refrigerating products can be a problem for patients. This needs to be taken into account when developing protocols.

ARV stocks are usually managed separately from other drugs because they require different security standards, specific budgets and special arrangements to avoid shortages. The ARVs currently in the market generally have a short shelf-life (two years). This is why MSF projects place orders for no longer than 6 months. The eventual extension of the shelf-life to three years once stability data become available will facilitate the management of these drugs.

3.4 Rational use

All programmes should work towards rational drug use by building-in tools to ensure appropriate prescription, delivery, adherence and monitoring; however, these factors are beyond the scope of this report and are not discussed here.

4. Country cases

In each country where MSF initiated ARV treatment, potential sources, patent and registration status, prices and distribution options were analysed in depth. The information in the country cases that follow on pages 16 - 43 has been compiled with the help of the MSF teams in those countries, as well as with legal and pharmaceutical experts. The context and international environment change rapidly and access to some information, (e.g. on patents) is limited, so MSF cannot guarantee that the following information is always accurate.

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A group of patients celebrates the 2nd anniversary of MSF's ARV programme in Khayelitsha, South Africa.

4.1 Cambodia

4.1.1 Overview

Cambodia is an LDC with a small market for companies and no central procurement agency for ARVs. Internationally offered prices are often unavailable locally.

Country profile	
Population (millions)[1]	14.1
Level of development: UNDP classification	Medium Human Development Country
UNCTAD classification	Least Developed Country
Number of people living with HIV/AIDS[2]	220,000
National HIV/AIDS prevalence among adults[2]	4%
National drug regulatory authority	Department of Drugs, Food, Medical Material and Cosmetics (under Directorate General of Health)
Authority in charge of patents	Ministry of Commerce/Intellectual Property Division
MSF AIDS programme	
Location	Preah Bat Norodom Sihanouk Hospital
Level of care	National referral hospital
Partners	National health authorities
Initiation of the AIDS programme	1997
Initiation of ART	July 2001
Number of patients on ARVs (April 2003)	660
PMCT	No (referred to another hospital)
ARV protocols selected	
Conformity to national recommendations	No existing recommendations
Regimen used (March 2003)	
- First-line regimen	d4T/3TC/NVP*
- Second-line regimen	ZDV+ddI+LPV/r
ARV procurement	
General situation	Complex supply, with multiple sources of ARVs
Generics purchased	Yes (imported)
MSF price (ppy, March 2003)	
- First-line regimen	US$350
- Second-line regimen	US$1215

1 UN: World Population Prospects: The 2002 Revision. (www.un.org/esa/population/publications/wpp2002)
2 UNAIDS/WHO 2002 Report on the global HIV/AIDS epidemic.
* FDC

4.1.2 Details of procurement

Context

Availability at country level: Both originator and generic pharmaceutical companies have a very limited presence in Cambodia, perhaps due to the population's low income levels. In early 2001 when MSF first started procuring ARVs, only a few drugs from originator companies were available on the private market. Some generic and originator products were available through local distributors, but they only ordered on demand and did not stock these drugs in-country. Long delivery delays were inherent in this system. In May 2003, the National Drug Procurement Centre (CMS) was still not providing ARVs.

Registration: A very limited number of originator or generic ARVs have been registered in Cambodia. For example, of the originator drugs, Roche's Viracept® (NFV) only has a temporary licence,[13] while neither Merck & Co's Stocrin® (EFV) nor Abbott's Kaletra® (LPV/r) are registered yet. Among generics, only Cipla's ZDV was registered in 2001 when MSF began its ARV project.

However, this situation is changing. At the end of 2002, several Cipla and Ranbaxy's WHO pre-qualified ARVs had been temporarily registered. In addition, Thailand's government-led pharmaceutical manufacturer (GPO) has begun the registration process for some of its medicines in Cambodia. During this process, importation authorization is considered on a case-by-case basis.

Patents: Cambodia did not have a patent law until early 2003 so there are no patents on pharmaceuticals in the country. Cambodia is about to join the WTO as an LDC and its new patent law states that patents will not be granted to protect pharmaceutical products until 2016, in accordance with the Doha Declaration on TRIPS and Public Health. This may however have been compromised in accession negotiations with WTO.

Prices at country level: As an LDC, Cambodia should be able to access many originator ARVs at the internationally-offered differential prices. However, in MSF's experience these drugs are often not available in-country at differential prices. For example, in 2002 the local price for Roche's Viracept®, (NFV) was US$4000 ppy, compared to the differential price of US$3172 ppy offered internationally. Similarly, the generic ARVs available in-country through private distributors are much more expensive than those imported directly from manufacturers.

MSF procurement strategy

In February 2001 when Cipla announced that it would sell a first-line ARV treatment for US$350 ppy, MSF decided to look into how to obtain this price in Cambodia.

Since there was no WHO pre-qualification project at the time, MSF conducted its standard review of new products, including a visit to the manufacturer (see page 11).

After validating the drugs for use in MSF programmes, MSF applied for and was granted permission by the Ministry of Health to import and use the drugs. Cambodia was the first country to which MSF imported Cipla ARVs.

MSF routinely asks ARV-producing companies to apply for registration in Cambodia in order to increase access to ARVs at country level. In addition to using generic medicines, MSF imports several drugs from originator companies at differential prices. As with generics, when the medicine is not registered, MSF requests authorization from the national drug authority. This is the case for Stocrin, (EFV) from Merck & Co, Kaletra, (LPV/r) from Abbott and Viread, (TDF) from Gilead.

4.1.3 Comments/analysis

The MSF ARV supply system for Cambodia required considerable resources to set up and it remains extremely complex. Many ARVs are still not registered or locally available. In particular, the drugs that originator firms are offering internationally at differential prices are not available locally *at those prices*. While Cambodia's LDC status makes it eligible for most of the discounts, in practice, taking advantage of them remains logistically difficult. Similarly, the prices of Cipla ARVs are relatively high on the local market, and MSF has had to order directly from Cipla's headquarters to obtain best prices. This lack of local availability of affordable medicines presents a challenge to the scaling-up and sustainability of treatment programmes.

Because of the complexity of procuring ARVs from a fragmented network of producers/suppliers/agents, it would be helpful if a government-led or non-profit central distributor took responsibility for supplying ARVs nationally.

13 Temporary Licence: only the registration dossier has been evaluated, and no analysis has been conducted at the national Laboratory for Drug Quality Control.

Summary of ARV supply in Cambodia in March 2003

Drug Dosage Form	Manufacturer chosen	Supply channel	Comments
ZDV (100 and 300mg tab) ZDV/3TC* (300, 150mg tab) ddI (25, 100, 200mg tab) d4T (30 and 40mg cap) NVP (200mg tab) 3TC (150mg tab) d4T/3TC/NVP* (200+30 or 40+150mg tab) 3TC (50mg/5ml 100 ml Syrup) NVP (50mg/5ml 100 ml Syrup)	Cipla	Imported from Cipla in India	—Of these drugs, only ZDV has been temporarily registered. The other ARVs are imported and used with authorization by the NDRA. —The drugs need to be imported directly from India to get the internationally offered price. The local distributor does not offer prices that are competitive with Cipla in India. —Delivery time (DT): 3 months.
EFV (200 and 600mg cap)	Merck & Co	Imported from the Merck & Co regional branch in Singapore.	—EFV has never been registered in Cambodia. In 2001, Merck & Co shipped the drug from Thailand and asked MSF to obtain an authorization to import. Although Merck & Co had publicized the US$350 price ppy, distribution through Thailand added 20% to that price. It was only after MSF complained about this added charge that Merck & Co sold the product at the publicized differential price. – DT: 4-6 weeks.
NFV (250mg cap)	Roche	Imported from Roche in Switzerland	—Temporarily registered, available locally at the full European price. —In order to get the differential price, the drug had to be imported from Switzerland. At first, MSF experienced some logistical problems due to Roche's request to work through SGS[14] in Cambodia and arrange for a RIA.[15] In principle, pre-shipment inspection is not required for NGOs.[16] After MSF headquarters contacted Roche headquarters, this request was dropped.
LPV/r	Abbott	Imported	—Not yet registered. —MSF applied to AXIOS[17] to get the differential price. —Products come from Indonesia on order. DT: 3 weeks.
TDF	Gilead	Imported	—AXIOS is also the supplier of this drug.
NVP/d4T/3TC (tab) d4T (15 and 20mg caps)	GPO	Imported from Thailand	—Authorization for import and use given by the Cambodian NDRA. —DT: 2 months, production on request.
d4T (syrup) ZDV/3TC* D4T/3TC*	Ranbaxy	Imported from India	—DT: 3 to 4 months (due to new supply channel needing to be put in place).

14 SGS: Société Générale de Surveillance S.A. an organization that controls international shipping
15 RIA: Registered Import Advice
16 In the Cambodian Notice to Importers, Republic of Cambodia, 31 August 2000: donations made by foreign governments or international organizations to foundations, charities and recognized humanitarian organizations are exempt from the pre-shipment Inspection Programme.
17 AXIOS : http://www.axios-group.com or AccesstoHIVCare@axiosint.com.
* FDC

4.2 Cameroon

4.2.1 Overview

A central government-led procurement system, relying on tenders from generic and originator producers, guarantees that ARVs are bought at extremely competitive prices.

Country profile	
Population (million)[1]	16
Level of development: UNDP classification	Medium Human Development Country
Number of people living with HIV/AIDS[2]	920,000
National HIV/AIDS prevalence among adults[2]	11.8 %
National drug regulatory authority	DPM (Direction de la Pharmacie et du Médicament)
Authority in charge of patents	Ministry of Industrial and Commercial Development
MSF AIDS programme	
Location	Yaounde, Military Hospital
Level of care	Referral Hospital
Partners	Institute for Research and Development, Military Hospital
Initiation of the AIDS programme	2000
Initiation of ART	January 2001
Number of patients on ARVs (March 2003)	260
PMCT	No
ARV protocols selected	
Conformity to national recommendations	Yes
Regimen used (March 2003)	
- First-line regimen	- d4T/3TC/NVP*
- Second-line regimen	- ZDV+ddI+NFV
ARV procurement	
General situation	Local purchase through national government procurement centre
Generics purchased	Yes (locally)
MSF price (ppy, March 2003)	
- First-line regimen (d4T/3TC/NVP*)	US$277
- Second-line regimen (ZDV + ddI + NFV)	US$4,763[3]

[1] UN: World Population Prospects: 2002 Revision. (www.un.org/esa/population/publications/wpp2002).
[2] Report on the global HIV/AIDS epidemic. UNAIDS/WHO, 2002.
[3] CENAME tenders are annual, therefore the price of NFV will come down significantly with the next tender.
* FDC

4.2.2 Details of procurement

Context

Availability at country level: Since 2000, the public procurement agency, CENAME,[18] has been handling national ARV procurement. CENAME purchases ARVs through tenders restricted to selected manufacturers. As a result, both branded and generic ARVs have been available in Cameroon since 2001.

Registration: All products purchased by CENAME are approved by the Ministry of Health: they have either been registered or are in the process of being registered.

Patents: Cameroon is a member of OAPI.[19] Before starting an ARV programme in 2000, the MSF team requested and paid for a patent search at the OAPI office in Yaounde to find out which ARVs were protected by patents in the region. Despite long delays, inconsistencies and conflicting information obtained from the OAPI office, patents were found for 3TC, NFV, NVP, ZDV and the ZDV/3TC combinations. Results of the search have been shared with relevant authorities.

OAPI countries also have a common regional patent law, the Bangui Agreement, which was revised in 1999 to comply with the TRIPS Agreement and entered into force in February 2002. Although regulations provided in this agreement appear to be more restrictive than the TRIPS Agreement (such overly restrictive patent rules are sometimes referred to as "TRIPS-plus"), the Director of OAPI declared that interpretation of the new rules allows for some flexibility, and in particular that:

"When a Member State, for purposes of public health, deems that access to medicines should be improved, the competent Minister may, by an administrative decision, designate an administration or an organization to benefit from a non-voluntary licence regime to manufacture, import or sell products protected by patents".[20]

The Ministry of Health authorized CENAME to import generic medicines when available at lower prices than the originator. The importation and use of generic drugs in Cameroon has helped to ensure that needed medicines remain available at affordable prices.

Prices at country level: The Cameroonian government's strategy has evolved. In 2000 all drugs were purchased from originator companies, but since 2001 competitive tenders have included both originator and generic companies. This has led to first-line ARV prices dropping from US$10,000 to US$277 ppy.

MSF procurement strategy

Since ARVs are available at competitive prices in-country, MSF purchases ARVs exclusively from CENAME.

4.2.3 Comments/analysis:

MSF has a collaborative relationship with CENAME, which includes ongoing sharing of information. Problems related to shortages, lack of knowledge about quality or excessive prices have been avoided in Cameroon.

Cameroon has shown clear political will to bring down the prices of ARVs. This has led to developing ARV procurement capacity within the national procurement system, which relies on competitive tenders and quality assessments of producers. Prices paid by CENAME are often amongst the lowest available internationally.

The central procurement system offers a number of other advantages, including the possibility for MSF and other institutions buying ARVs to purchase them at one central point. Time-consuming negotiations with different ARV producers who administer differential pricing schemes are avoided at the local level. In addition, NGOs and other medicine purchasers do not need to get involved in applying for import licences. The government also took the necessary measures to overcome patent barriers, thereby actively implementing the Doha Declaration, which stressed that the TRIPS Agreement "can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all".

18 Centre Nationale d'Approvisionnement en Médicaments et Consommables Médicaux Essentiels
19 OAPI: the 16 members of OAPI in February 2003 were Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Côte d'Ivoire, Gabon, Guinea, Guinea Bissau, Equatorial Guinea, Mali, Mauritania, Niger, Republic of Congo, Senegal, Togo. (www.oapi.wipo.org).
20 http://www.oapi.wipo.net/accordbangui.htm

4.3 Guatemala

4.3.1 Overview

As a Medium Human Development Country, Guatemala has not been eligible for most differential price offers by originator companies. Negotiations with five originator companies in 2003 established some reductions. MSF imports generics from India and also buys from originators.

Country profile	
Population (million)[1]	12.3
Level of development: UNDP classification[2]	Medium Human Development Country
Number of people living with HIV/AIDS[2]	73,000
National HIV/AIDS prevalence among adults	1.4 %
National drug regulatory authority	Departamento regulacion y Control de Productos Farmaceuticos y Similares
Authority in charge of patents	Ministerio de Economia, Registro de la Propiedad Intelectual
MSF AIDS programme	
Location	Guatemala City
Level of care	Roosevelt Referral Hospital, Clinic Yalos (outpatient department)
Partners	Health authorities
Initiation of AIDS programme	1996
Initiation of ART	August 2001 (Hospital); March 2002 (clinic)
Number of patients on ARVs (March 2003)	436
PMCT	No
ARV protocols selected	
Conformity to national recommendations	Yes
Regimen used (March 2003)	
- First-line regimen	- ZDV/3TC* + EFV or ZDV/3TC* + NVP
- Second-line regimen	- d4T + ddI + NFV
ARV procurement	
General situation	Generics imported from India. High-priced originator ARVs purchased locally or regionally. As a Medium Human Development Country, Guatemala does not qualify for most companies' differential pricing schemes (with the exception of Merck and Roche which have publicized reduced prices for Medium Human Development Countries).
Generics purchased	Yes (imported)
MSF price (ppy, March 2003)	
- First-line regimen	- US$867 or US$520 (see protocols above)
- Second-line regimen	- US$1,161

[1] UN: World Population Prospects: The 2002 Revision. (www.un.org/esa/population/publications/wpp2002)
[2] UNAIDS/WHO 2002 Report on the global HIV/AIDS epidemic.
* FDC

4.3.2 Details of procurement

Context

Availability at country level: In 2001, generic ARVs were not available locally, and originator companies did not have local agents, with the exception of Abbott. Merck & Co and Roche have offices in Costa Rica and GSK has a presence in El Salvador. In mid-2003, Ranbaxy's ARVs are expected to be marketed in Guatemala.

Registration: In 2001, few originator and no generic ARVs were registered in Guatemala, but there is no regulation against importing medicines with authorization from the Ministry of Health. By the end of 2002, most originator products still needed to be imported from other countries in the region, although Ranbaxy ARVs had been registered. In addition, in April 2003 the Guatemalan Congress passed a decree that gives originator manufacturers exclusive marketing rights for five years starting from the registration of the product. In practice, this seriously limits access to equivalent generic drugs in the country. MSF has been urging the Congress to repeal the decree.

Patents: Guatemala did not grant patent protection for pharmaceuticals until 2000, so that drugs that came on the market before then cannot be patented. Consequently there is no patent barrier to importing generics (see Registration above for other barriers).

Prices at country level: The Guatemalan government accessed originator price discounts through the Accelerating Access Initiative (AAI) beginning in January 2003. Before that, since Guatemala is classified as a Medium Human Development country, it only benefited from Merck & Co preferential prices as Merck & Co is one of the few companies that consistently offers differential prices to Medium Human Development countries. As a result, prices have often been similar to or higher than those in developed countries. For instance Zerit® (d4T 40 mg) from BMS costs 40% more in Guatemala than in the USA, and Viracept® (NFV) from Roche was more expensive than it is in Switzerland.

Although prices of originator drugs have finally come down after negotiations between Latin American governments and five companies participating in the AAI in early 2003, they are still considerably more expensive than generic equivalents that have been pre-qualified by WHO (e.g. Combivir® 3TC/ZDV) from GSK costs US$0.85/tablet compared to the equivalent fixed-dose produced by Ranbaxy available at US$0.40).

Importing drugs leads to higher prices because there are added fees amounting to 17% of the value (taxes, clearance fees). These fees are also levied on donations. Civil society along with NGOs are advocating for a change of this policy.

MSF procurement strategy

Since there were no patent barriers to importing generic drugs and since they were not available locally, MSF decided to import generics from India. An authorization to do this was obtained from the NDRA, as the generic medicines were not registered.

MSF imported generic ARVs from Cipla at their internationally publicized price for developing countries. Customs costs and taxes had to be added to this base price.

Medicines for which no generics were available, or which had not been validated by either WHO pre-qualification or through MSF's own validation process, were bought from originator companies. Negotiating with both local branches and headquarters of originator and generic companies was time-consuming and often it did not result in affordable prices.

4.3.3 Comments/analysis

Because most ARVs are not patented in Guatemala as the patent law only took effect in 2000, MSF was able to purchase generic drugs by working directly with suppliers. However, national regulations regarding ARV imports led to inflated drug costs (Value Added Tax (VAT) and importation taxes).

Attempting to negotiate prices with originator companies was difficult because most do not have a public policy for Medium Human Development Countries. While most companies have been willing to lower prices for LDCs and sub-Saharan Africa, this has not been the case for other developing countries. In the absence of generic competition, originator companies have usually been unwilling to offer affordable ARV prices in Central America. Intense negotiations between BMS and MSF for reduced prices of Videx® (ddI) and Zerit® (d4T) in Guatemala failed completely. However, recently, subsequent to the start of generic competition in the region and negotiations including the government and both originator and generic companies, originator companies are finally reducing their prices.

Ranbaxy, one of the generic producers whose ARVs have been pre-qualified by WHO, has recently registered ARVs locally. Buyers can now access lower-priced generics without incurring the logistical complications and taxes caused by importing.

Summary of ARV supply in Guatemala in March 2003

Drug Dosage Form	Manufacturer chosen	Supply channel	Comments
ZDV/3TC* tab 3TC 150 mg tab d4T 30 and 40 mg tab ddI 100 and 200 mg tab NVP 200 mg tab	Cipla	Import	Order from India Prices are the ones offered internationally by Cipla, but full cost includes transport, insurance and customs charges + taxes (12% Value Added Tax (VAT).
EFV 200 mg cap IDV 400	Merck & Co	Import	Costa Rica: Distribution costs + customs fees + taxes add 25 % to internationally offered CIF (Cost Insurance Freight) prices.
NFV 250 mg caps	Roche	Import	Costa Rica: until February 2003, no differential price was available in Guatemala, but 20% rebate in kind was offered off the European price + 2% in reduction for immediate payment. A 5 % customs fee is charged by the government. This brings the cost of a pill to US$1.28 (yearly ppy of US$4672).
LPV/r r 100 mg	Abbot	Local purchase	Guatemala: until February 2003, no internationally offered price for Medium Human Development Countries. After negotiation, 20% rebate in kind + 3% reduction for immediate payment. Taxes and customs fees have to be added.

* FDC

4.4 Honduras

4.4.1 Overview

Initially MSF imported generics to Honduras, but once these became available through local distributors it switched to local purchase.

Country profile	
Population (million)[1]	6.9
Level of development: UNDP classification	Medium Human Development Country
Number of people living with HIV/AIDS[2]	63,000
National HIV/AIDS prevalence among adults	1.9 %
National drug regulatory authority	Departamento de Farmacia, Secretaria de Salud
Authority in charge of patents	Secretaria de Industria, Comercio y Turismo, Direccion General de la Propiedad Intelectual
MSF AIDS programme	
Location	Tela
Level of care	MSF HIV Clinic
Partners	Ministry of Health
Initiation of the AIDS programme	2001
Initiation of ART	July 2002
Number of patients on ARVs (March 2003)	65
PMCT	No
ARV protocols selected	
Conformity to national recommendations	Yes
Regimen used	
- First-line regimen	- d4T / 3TC / NVP*
- Second-line regimen	- ZDV + ddI + NFV; d4T + ddI + NFV
ARV procurement	
General situation	Local purchase of Cipla ARVs + regional purchase of originator ARVs
Generics purchased	Yes
MSF price (ppy, March 2003)	
- First-line regimen	US$288
- Second-line regimen	US$3796 for NFV only

[1] UN: World Population Prospects: The 2002 Revision. (www.un.org/esa/population/publications/wpp2002).
[2] Report on the global HIV/AIDS epidemic. UNAIDS/WHO, 2002.
* FDC.

4.4.2 Details of procurement

Context

Availability at country level: Originator companies do not have agents in Honduras, but do have a presence in the region (Merck & Co and Roche in Costa Rica and Abbott in Guatemala). This means that all originator drugs must be imported. Cipla and Ranbaxy have agents in the country.

Registration: It is not easy to obtain information about the registration status of drugs in Honduras. Sometimes MSF received conflicting information from the regulatory authority and in most cases was forced to rely on information provided by the companies themselves.

When MSF started its ARV project in 2001, few ARVs were registered. MSF was authorized to import non-registered products. By March 2003, most of Cipla's ARVs had been registered and Ranbaxy had filed for registration for its products. Registration for Merck & Co's Stocrin® 600 mg (EFV) is pending.

Patents: MSF requested a patent search at the Honduran patent office with the help of a local lawyer. The results of the search were inconclusive: it was found that only the ZDV/3TC combination, better known by its brand name Combivir®, was protected by a Honduran patent. However, a closer look at the country's 1999 intellectual property law revealed that such a combination should not have been granted a patent, because it is not considered to be an invention (as specified in Article 5 of the law). MSF decided to import the generic ZDV/3TC combination despite the GSK patent, which can be regarded as invalid.

Prices at country level: As regards originator products, the situation in Honduras is the same as in all Medium Human Development Countries (see Guatemala page 21). Generics are competitively priced and available through private distributors.

MSF procurement strategy

Cipla ARVs were first imported from India in 2002, with an import authorization from the Ministry of Health. Once generics were registered, MSF bought them through local distributors demanding and receiving internationally publicized prices. Originator ARVs are purchased from distributors in Costa Rica and Guatemala.

4.4.3 Comments/analysis

MSF's demand for ARVs stimulated generic producers to initiate local sales activity for ARVs in Honduras: Cipla has established a local sales office and Ranbaxy is doing so. MSF advocated for local company presence because direct purchase from the companies' headquarters was slow and complex. In 2003 MSF is buying d4T/3TC/NVP* at US$288 ppy - slightly less than the US$304 internationally publicized price.

Most originator companies do not have a differential pricing policy for middle-income countries and have no distributors in Honduras. Although they led to price reductions, negotiations held between governments of Central American countries and five pharmaceutical companies (BMS, Merck & Co, GSK, Roche, BI) in January 2003 did not result in the price levels available from generic producers. Historically in Central America it has not been originator companies that have facilitated access to ARVs at affordable prices, but rather the generic companies.

Honduras has been granted financing from the Global Fund for HIV/AIDS, TB and Malaria. If the Global Fund procurement policy is followed, the government will be obliged to buy from the least expensive quality producer. There are no intellectual property barriers that prevent Honduras from doing so.

Summary of ARV supply in Honduras in March 2003

Drug Dosage Form	Manufacturer chosen	Supply channel	Comments
ZDV 100mg tab ZDV/3TC tab ddI 25 mg tab ddI 100 mg tab D4T 30 mg cap NVP 200 mg tab 3TC 150 mg tab NVP+d4T 30 + 3TC tab NVP + d4T 40 + 3TC tab ZDV 50mg/5ml 100 ml syrup 3TC 50mg/ml 100ml Syrup NVP 50mg/ml, 100 ml syrup	Cipla	Local purchase	It took about 4 months to receive the first shipment from India. Now drugs are purchased through a local distributor with a month's delay. MSF actively lobbied for the creation of a local supply system to avoid having to purchase directly from India.
EFV 200 mg cap IDV 400 mg caps	Merck & Co	Import	Merck & Co has a differential price policy for Middle-Income Countries and Honduras benefits from it. MSF imports the drug from a distributor based in Costa Rica.
NFV 250 mg cap	Roche		Distributor is based in Costa Rica. Since Roche administers its differential pricing system from it headquarters, orders have to be made directly to Switzerland.

4.5 Kenya

4.5.1 Overview

The national procurement centre does not supply ARVs but a local non-profit supplier and MSF are importing generic drugs from India. Some originator drugs are purchased at differential prices through local distributors.

Country profile	
Population (million)[1]	31.9
Level of development: UNDP classification	Medium Human Development Country
Number of people living with HIV/AIDS[2]	2,200,000
National HIV/AIDS prevalence among adults	13.9 %
National drug regulatory authority	Pharmacy and Poison Board
Authority in charge of patents	KIPI (Kenyan Industrial Property Institute) Ministry of Trade and Industry
MSF AIDS programme	
Location	Homa Bay Hospital
Level of care	District Hospital
Partners	National Health Authorities
Initiation of the AIDS programme	1996
Initiation of ART	November 2001
Number of patients on ARVs (March 2003)	270
PMCT	No (UNICEF is operating MTCT programmes)
ARV drugs selected	
Conformity to national recommendations	Yes
Regimen used (March 2003)	
- First-line regimen	- d4T/3TC/NVP*
- Second-line regimen	- ZDV+ddI+NFV
ARV procurement	
General situation	Use of multi-source ARVs, with import of generic drugs and local purchase of originator ARVs at companies' representatives
Generics purchased	Yes
MSF price (ppy, March 2003)	
- First-line regimen	US$292
- Second-line regimen	US$1,594

[1] UN: World Population Prospects: The 2002 Revision. (www.un.org/esa/population/publications/wpp2002).
[2] Report on the global HIV/AIDS epidemic. UNAIDS/WHO 2002.
* FDC.

4.5.2 Details of procurement

Context

Availability at country level: In 2001, despite the presence of local generic manufacturers and importers, only originator ARVs were available in the country.

Despite the presence of BMS, Merck & Co, BI, GSK and Roche, as the demand for ARVs increased, doctors and patients were plagued by periodic shortages. For example, in 2001, treatment centres experienced shortages of Epivir® (3TC), Stocrin® (EFV), Zerit® (d4T) and Videx® (ddI).

In May 2003, the National Procurement Centre was still not supplying or distributing ARVs. However, a well-established non-profit organization, Mission for Essential Drugs and Supplies (MEDS), has become a major distributor and supplier of both originator and generic ARVs, and provides an integrated procurement and distribution service for the mission sector in Kenya. MEDS has also been supplying public sector facilities and NGOs.

Registration: By 2000, all originator ARVs were registered in Kenya. At this time generic manufacturers (Indian) were reluctant to apply for registration because they feared they might be infringing patents. Generic importers and producers have not been confident that the government would support widespread use of their products.

As of March 2003, although generic drugs were reaching some patients through special arrangements for the non-profit sector, the products have still not been registered.

Registration dossiers for many generic ARVs have been filed but approvals are still pending at the Pharmacy and Poisons Board.

Patents: Most ARVs are under patent in Kenya and this has severely limited access to less expensive sources of medicines in the country.

Drugs under patent in Kenya

GSK :	ZDV	until 2006
	3TC	until 2010
	ZDV/3TC*	until 2017
BI :	NVP	until 2010
Roche[21] :	NFV	until 2014

In May 2002, the new Kenyan Industrial Property Act 2001 came into force. It made the rules for importing generics more flexible in certain circumstances. (See: "Drug patents under the spotlight: sharing practical knowledge about pharmaceutical patents". MSF, 2003).

Prices at country level: With the exception of Roche, originator companies dramatically reduced their prices in Kenya in 2001. However, their programmes had limited impact because of the lack of a national AIDS programme, and despite these reductions prices remained nearly three times higher than in countries using generic suppliers.

The situation began to change in July 2002, when MSF and MEDS decided to begin using generic drugs from Indian suppliers and the ppy price of the first-line drug dropped from US$825 to US$300 in one go. However, in May 2003, these less expensive medicines were still only available in a limited number of treatment centres primarily supplied by MEDS or MSF.

MSF procurement strategy

MSF has been working on ARV procurement in collaboration with the Kenya Coalition For Access to Essential Medicines,[22] since 2000. Because of the lack of government focus on this issue, progress has been painstakingly slow. In 2001, MSF had no access to generic sources of ARVs and was still buying these drugs exclusively from originator companies at differential prices.

A breakthrough came with the entry into force of the IP Act in May 2002, which allows the importation of products that have been "legitimately" put on the market. Having requested an authorization from the Ministry of Health to import the ARVs needed, MSF gave the first order to Cipla in July 2002, and soon after Ranbaxy's drugs were also ordered for use in MSF programmes. But as of June 2003 each generic order still required a special import authorization since these drugs are still not registered. Generic supplies have been supplemented by originator drugs when these were either less expensive or the sole source of a particular drug.

4.5.3 Comments/analysis

In Kenya, MSF has been able to bring down the cost of treatment in its own projects because of access to generic ARVs. Subsequently, some other non-profit medical providers and medicine suppliers have gained access to the same sources. The per patient costs that MSF and other non-profit orgnizations have been paying has been continuously dropping due to the availability of generic medicines and the differential pricing from originator companies.

21 On their website, Roche announces that "Roche will not act against infringement of patents Roche holds on HIV/AIDS drugs in sub-Saharan Africa and UN defined Least Developed Countries, nor will Roche file patents on new or investigational HIV/AIDS medications in these countries."

22 The Kenya Coalition for Access to Essential Medicines; Members are local community-based and national NGOs, international NGOs, healthcare providers, journalists, lawyers and other individuals.

* FDC

The fact that some drugs are currently imported directly from India and are not available through local distributors is an ongoing administrative and logistical burden. Anyone importing medicines is obliged to continuously apply for authorizations. Although using unregistered generics has had a dramatic impact on the price of ARV therapy in Kenya, it is an ad-hoc approach and difficult to sustain in the long-term. Until the government registers generics most individuals and organizations in Kenya will continue to pay a premium over the prices paid in many African countries.

Summary of ARV supply in Kenya in March 2003

Drug Dosage Form	Manufacturer chosen	Supply channel	Comments
ZDV/3TC* 300/150 mg tab ZDV 300 mg tab NVP 200 mg tab d4T 30, 40 mg caps IDV 400 mg d4T/3TC/NVP* 30 and 40 tab d4T/3TC* 30 and 40 caps 3TC 150 mg tab	Ranbaxy	Import from India	Some of the prices obtained locally are even lower than the ones offered at international level. MSF requests an NDRA authorization to import and use medicines that are not registered. One-to-two months of delivery delay. Prices can be negotiated when ordering a drug, depending on the quantity.
3TC,ZDV,NVP syrup ZDV 100 mg tab	Cipla	Local purchase	Even if the drugs are not registered, it is possible to purchase small quantities of Cipla ARVs locally, but the prices are higher than if imported from India.
EFV 200,50,600 mg caps	Merck & Co	Local purchase	Although the price offered internationally is supposed to be CIF, the product costs 15 % more locally due to distributor's costs.
ddI 25, 100, 200 mg tab d4T 15, 20 tab + suspension	BMS	Local purchase	Same as for Merck & Co (see above) since it is the same distributor: the local price is 15% more than the one announced internationally. Available upon request. Delivery delay for the first order: between 8 to 12 weeks.
NFV 250 mg caps	Roche	Local purchase	Kenya has benefited from the last price reduction for NFV, but 25% for transport and distribution costs are added.

* FDC

4.6 Malawi

4.6.1 Overview

This is an LDC with multiple sources of ARVs and generic competition, which has led to low prices. There is strong political will to expand access to ARVs.

Country profile	
Population (million)[1]	12.1
Level of development: UNDP classification	Low Human Developed Country
UNCTAD classification	Least Developed Country
Number of people living with HIV/AIDS[2]	800,000
National HIV/AIDS prevalence among adults	15.9 %
National drug regulatory authority	Pharmacy, Medicines and Poisons Board
Authority in charge of patents	Ministry of Justice Department of the Registrar General
MSF AIDS programme	
Location	Chiradzulu Hospital
Level of care	District Hospital
Partners	Ministry of Health
Initiation of the AIDS programme	1997
Initiation of ART	August 2001
Number of patients on ARVs (April 2003)	607
PMCT	Yes
ARV drugs selected	
Conformity to national recommendations	Yes
Regimen used	
- First-line regimen	- d4T / 3TC / NVP*
- Second-line regimen	- ZDV + ddI + NFV
ARV procurement	
General situation	Local purchase through private distributors representing generic and originator companies
Generics purchased	Yes (locally)
MSF price (ppy, March 2003)	
- First-line regimen	US$288
- Second-line regimen	US$1875

[1] UN: World Population Prospects: The 2002 Revision. (www.un.org/esa/population/publications/wpp2002).
[2] Report on the global HIV/AIDS epidemic. UNAIDS/WHO 2002.
* FDC.

4.6.2 Details of procurement

Context

Availability at country level: When the MSF team started purchasing ARVs in May 2001, the government was already importing some generic products from Cipla (ZDV/3TC*), and a local distributor was also selling several generic products. The only originator products available on the local market at this time were ZDV and ZDV/3TC*, both from GSK.

In March 2003, all needed ARVs were available in Malawi through local distributors except for Merck's EFV 600 mg capsules and Roche's NFV powder. Generic producers Ranbaxy and Cipla both have an active presence and their products are registered and available. Since patient numbers are growing steadily in Malawi, MSF conducts competitive bids to ensure the lowest possible prices.

Registration: By May 2001, ZDV, 3TC, ZDV/3TC* from Cipla were already registered by the Medicines and Poisons Board. Cipla had also applied for registration of d4T, ddI and NVP. AZT and 3TC from GSK and NVP from BI were registered.

Patents: Malawi has had a patent law for years and is a member of ARIPO[23], which grants patents in accordance with the national patent law of each member. Little or no patent information is available locally because of the limited capacity of the Malawian patent office. However, as an LDC, Malawi is not obliged to enforce patents on pharmaceuticals until 2016, as stated in paragraph 7 of the WTO Doha Declaration on TRIPS and Public Health.

Prices at country level: Cipla's local distributor offered Cipla ARVs at nearly the same price as the ones offered internationally to MSF, other NGOs and governments. Theoretically, all originator products should be available at the lowest publicized differential price since Malawi is both an LDC and is in sub-Saharan Africa. (See Annex III for sample prices.)

MSF procurement strategy

When the MSF programme began in Malawi, given the scant information available on patents and the local availability of Cipla ARVs, MSF decided to purchase the drugs locally. MSF chose a solution that would be sustainable from both a financial and logistical standpoint. Before procurement began, an MSF pharmacist visited the country to assess the potential local distributors of generic and branded products. Based on this assessment, manufacturers of unregistered products were asked by MSF to file registration dossiers. While waiting for products to become available in-country, purchases were made from originator companies in Europe. By November 2001, MSF had managed to obtain all needed ARVs through local distributors.

4.6.3 Comments/analysis

MSF's procurement strategy in Malawi relies on dynamic private sector distributors and is reproducible for other local organizations and the government. The fact that the government has registered generic products facilitates a coherent system that does not rely on special authorizations. These government actions seem to be motivated by an overall political objective of scaling up ARV treatment. Intense competition from multiple generic companies has, in most cases, reduced prices to the lowest levels available internationally.

As Malawi is both a sub-Saharan country and an LDC, in theory all the originator ARVs should be available at the best preferential prices. In fact prices fluctuate considerably because drugs are sold from South Africa. This means that prices are influenced both by fluctuations of the South African *rand* and the Malawian *kwacha,* and additional fees are often added for shipping and distributor margins. Lack of a central purchasing authority or agent means that buyers are forced to constantly negotiate with multiple sellers and their agents.

23 ARIPO: the African Regional Industrial Property Organization.
* FDC

Summary of ARV supply in Malawi in March 2003

Drug Dosage Form	Manufacturer chosen	Supply channel	Comments
ZDV 100, 300 mg tab ZDV/3TC* tab ddI 25, 100 mg tab ddI 100 mg tab d4T 30, 40 mg cap NVP 200 mg tab 3TC 150 mg tab NVP/d4T/ 3TC * tab ZDV, 3TC, NVP 50mg/5ml 100 ml syrup	Cipla	Local purchase	Delivery delay up to 3 months. At the end of 2002, Cipla HQ gave authorization to their distributor to keep a local stock. But in exchange for this service, MSF was requested to supply an annual order plan. The local Cipla distributor did not automatically charge internationally publicized prices but negotiation with Cipla headquarters was needed.
d4T 30/3TC 150 mg tab d4T40/3TC150 mg tab	Ranbaxy		MSF began purchasing Ranbaxy ARVs when they were registered and available locally (in 2003).
d4T 20 mg cap	BMS		
EFV 200 mg cap EFV 600 mg cap	Merck & Co		MSF identified a local distributor for Merck & Co products but this agent does not offer EFV at the internationally offered price. Between Nov 2001 and January 2003, the price of EFV 200 mg increased 36 % in Malawi. DT is one month from placing an order. Not available
NFV 250 mg cap NFV powder for suspension	Roche		Despite the announcement that Roche was offering NFV powder at a dramatically reduced price for LDCs, MSF was never able to access this product in Malawi. The price of Viracept® capsules periodically increased and between June 2001 and January 2003, the increase was 23%. As of March 2003, the MSF team was still trying to get NFV capsules at the newly announced differential price.

* FDC

4.7 Mozambique

4.7.1 Overview

The country has no central ARV drug procurement to date but both generic and originator drugs are available through a variety of local distributors. Price negotiations are done on a case-by-case basis.

Country profile	
Population (million)[1]	18.8 million
Level of development: UNDP classification	Low Human Development country
UNCTAD classification	Least Developed Country
Number of people living with HIV/AIDS[2]	1.7 million
National HIV/AIDS prevalence among adults	14.6%
National drug regulatory authority	Conselho de Medicamento (COMED)
Authority in charge of patents	Ministry of Industry, Commerce and Tourism, National Directorate of Industry, Industrial Property Department
MSF AIDS programme	
Location	Cidade de Maputo, Cidade de Tete, Distrito de Angonia and Cidade de Lichinga
Level of care	District or provincial hospital: Tete, Angonia & Lichinga, Health Centre: Tete, Lichinga & Maputo
Partners	Ministry of Health
Initiation of the AIDS programme	October 2001
Initiation of ART	December 2002
Number of patients on ARVs (March 2003)	85
PMCT	Yes
ARV drugs selected	
Conformity to national recommendations	Yes
Regimen used (from the beginning)	
- First-line regimen	d4T/3TC/NVP* (or EFV)
- Second-line regimen	ZDV, ddI, NFV
ARV procurement	
General situation	Local purchase through private distributors for both originator and generic products
Generics purchased	Yes, locally
MSF price (ppy, March 2003)	
- First-line regimen	US$463
- Second-line regimen	Not yet purchased

[1] UN: World Population Prospects: The 2002 Revision. (www.un.org/esa/population/publications/wpp2002).
[2] Report on the global HIV/AIDS epidemic. UNAIDS/WHO 2002.
* FDC.

4.7.2 Details of procurement

Context

Availability at country level: Mozambique has so far been perceived by drug manufacturers as a small market and therefore most companies do not have direct representation in the country. GSK is the only originator company that is present.

Both originator and generic companies tend to sell their products through private importers/distributors who are often supplied from South Africa. In addition to originator companies' ARVs, Ranbaxy and Cipla products are readily available.

Registration: Mozambique does not yet have a registration system but there are controls on the importation of medicines and in principle, only drugs included in the National Formulary can be imported. However, special permission for the use of unauthorized drugs can normally be obtained through the Ministry of Health.[24]

Patents: Mozambique enacted its first Intellectual Property Code in 1999 and joined ARIPO in 2000. That is why no ARVs are patented in the country. In any case, patents should not constitute a problem since Mozambique is an LDC and therefore doesn't need to enforce pharmaceutical protection until 2016 according to the WTO Doha Declaration (paragraph 7).

Prices: ARV drug pricing is regulated by government control on price mark-ups. For example, drug importers are allowed to add a maximum 10% margin on imported drugs and retailers are allowed to add up to 15% to their purchase price. In practice, implementation of the system is inconsistent and private pharmacies sometimes sell ARVs at inflated prices.

MSF procurement strategy

When the programme began MSF sourced many drugs from abroad, as few ARVs were available locally and they were being sold at premium prices. When local distributors began selling ARVs, MSF procurement switched to local purchases. In some cases, local distribution only began when MSF suggested local distributors to companies, e.g. MSF facilitated contacts for Roche and Merck & Co.

The case of Merck & Co's 600 mg formulation of EFV is illustrative. Although the company had made an international announcement about a differential price and widespread availability of this product in developing countries, when the MSF team attempted to order the product in Mozambique, they were told that it was not available. It was only after discussions with Merck & Co headquarters and its South African office that the company found a way to deliver the drug to Mozambique from Europe. In June 2003, the team was also attempting to gain access to Roche's NFV at the newly communicated differential price but at the time of writing had had no response from their local agent.

4.7.3 Comments/analysis

In the absence of a central purchasing agency, MSF has relied on local distributors who represent originator and generic producers. By informing distributors of the international price offers MSF was often able to get prices that were close to these international offers. Some originator products have been the exception, for example, MSF paid 35% more than Merck & Co's publicized price for EFV 200 mg.

The fact that the Mozambique government has been quick to give authorizations for the import of generics has fostered competition between manufacturers, and brought prices down.

With the assistance of both the Bill Clinton Foundation and the Global Fund, the Mozambique government is embarking on ambitious plans to increase access to treatment. The immediate plan is to have 8,000 people on treatment by the end of 2003. This will be done partly by strengthening CMAM, the centralized national drug procurement centre, so that it can handle the nationwide supply of ARVs.

24 Article 22 of the Medicine Act 4/98: "When, against clinical justification, they are considered as being indispensable for the treatment or diagnosis of certain pathologies" or "exclusively aimed at clinical research and tests".

Summary of ARV supply in Mozambique in October 2002

Drug Dosage Form	Manufacturer chosen	Supply channel	Comments
3TC/d4T/NVP (150+40+200) tab d4T 40 and 30 mg caps 3TC 150 mg tab ZDV/3TC (300+150) tab	Cipla	Local purchase through Cipla private distributor	Direct import from India, no stock available in-country. Prices are similar to internationally publicized prices DT = 4-6 weeks
3TC+d4T+NVP (150+30+200) tab NVP 200 mg	Ranbaxy	Local purchase through state-owned distributor	DT = 4-10 weeks Prices are similar to internationally publicized prices
EFV 200 mg cap EFV 600 mg cap	Merck & Co	In 2002: Import from private South African pharmacy In 2003: Local purchase through private distributor	MSF has been paying US$675 ppy instead of the internationally publicized price of US$500 for the 200 mg formulation. EFV 600 mg has not yet been registered as of May 2003.
NFV 250 mg caps	Roche	Plan to purchase through local distributor	Quotation is pending.

4.8 South Africa

4.8.1 Overview

MSF imports generic drugs from Brazil to South Africa and can now treat five people for the price of one, but these less expensive versions of the drugs are not widely available because most are still not registered.

Country profile	
Population (million)[1]	45.0
Level of development (UNDP classification)	Medium Human Development Country
Number of people living with HIV/AIDS[2]	4,200,000
National HIV/AIDS prevalence among pregnant women	24.5 %
National drug regulatory authority	Medicine Control Council (MCC)
Patent office	Department of Trade and Industry, Companies and Intellectual Property Registration Office (CIPRO)
MSF AIDS programme	
Location	Khayelitsha township (Cape Town)
Level of care	MSF HIV clinics
Partners	Provincial Administration of the Western Cape
Initiation of AIDS programme	1999
Initiation of ART	May 2001
Number of patients on ARVs (June 2003)	540
PMCT	Yes
ARV protocols selected	
Conformity to national recommendations	No public sector national guideline
Regimen used (from the beginning)	
- First-line regimen	- ZDV/3TC*+EFV or NVP
- Second-line regimen	- ddI+d4T+LPV/r
ARV procurement	
General situation	No generics available on the market. MSF imports generics with a special authorization and locally purchases originator ARVs at differential prices.
Generics purchased	Yes (imported)
MSF price (ppy, March 2003)	
- First-line regimen	US$400 with NVP or US$1,000 with EFV
- Second-line regimen	US$1203

1 UN: World Population Prospects: The 2002 Revision. (www.un.org/esa/population/publications/wpp2002).
2 Report on the global HIV/AIDS epidemic. UNAIDS/WHO 2002.
* FDC.

4.8.2 Details of procurement

Context

Availability at country level: As of March 2003, generic ARVs are still not available commercially in South Africa and originator ARVs are only available in the private sector. This means that generics are only available to a small number of projects (see below under MSF procurement strategy).

In theory, because of voluntary licences that have been granted by GSK and BI to a local manufacturer (Aspen Pharmacare), generic versions of ZDV, 3TC and NVP should become available soon. However, this only applies to the public sector.

Registration: Most originator ARVs are registered, as are a handful of generics (3TC 150 mg from Cipla, ZDV 100 mg from Apotex and Garec). The regulatory authority, the South African Medicines Control Council (MCC), has set a target of registering between 7 to 10 generic ARVs by mid-2003. It is possible to import unregistered generics by requesting special importation and use authorization from the MCC (section 21 of the Medicines Act). There is also concern that the terms and conditions of the voluntary licences granted to Aspen Pharmacare may prevent the company from offering their ARVs at internationally competitive prices.

Patents: Originator companies have patents in South Africa for all ARVs except zalcitabine (Hivid®, a drug which is not recommended in WHO treatment guidelines) and saquinavir (Invirase®), two Roche drugs.

Daily price per patient (USD)		
ZDV/3TC*+ NVP	Private sector (originator ARVS in a pharmacy)	Imported generics by MSF
January 2002	5.50	1.55
January 2003	4.40	1.08

Prices at country level: Patents and the lack of registered generics have seriously handicapped access to low-cost ARV drugs. In the absence of generic competition, differentially priced originator products are the only ones available to patients outside pilot programmes such as MSF's.

In March 2003, the lowest annual cost for a triple therapy regime purchased in South Africa was US$400 ppy (ZDV/3TC*+NVP) for the NGO and public sectors. The same treatment costs US$2007 ppy in the private sector.

MSF procurement strategy

Initially MSF was procuring ARVs from a private pharmacy at full price while exploring less expensive alternatives. The project is attempting to demonstrate the feasibility of more widespread treatment in South Africa, and drug affordability has been a key objective. For this reason MSF obtained permission from the MCC to use less expensive but as yet unregistered generic ARVs.

In January 2002 MSF managed to establish a collaborative agreement in which the Brazilian state manufacturer, FarManguinhos, supplies ARVs to MSF in Khayelitsha. Since the introduction of generic sources in the MSF programme, the price of first-line treatment (ZDV/3TC + NVP) ppy has been reduced from US$2000 to US$400. Using the same provision of the Medicines Act, MSF is currently importing several generic ARV products. Originator products are now used only when generic alternatives cannot be sourced.

4.8.3 Comments/analysis

Although MSF has found a means of accessing affordable ARVs in South Africa, the section 21 provision is a complex administrative procedure. South Africa has recently announced that it will develop a comprehensive plan to treat people living with HIV/AIDS ensuring that they can access ARVs to extend their lives. The authorization for use and distribution of generic versions of these drugs must come from the national government.

* FDC

4.9 Thailand

4.9.1 Overview

Thailand has a significant domestic market and local production of generics. The government shows there is political will and a strong activist movement that helped challenge a drug patent.

Country profile	
Population (million)[1]	62.8
Country development (UNDP classification)	Medium Human Development Country
Number of people living with HIV/AIDS[2]	755 000
National HIV/AIDS prevalence among adults[2]	2.15
National drug regulatory authority	Food and Drugs Administration, Ministry of Public Health
Authority in charge of patents	Department of Intellectual Property, Ministry of Commerce
MSF AIDS programme	
Location	Surin Provincial Hospital, Phrachomklao Provincial Hospital, Petchburi Ban Laem District Hospital, Petchburi Bang Kruai, District Hospital, Nonthaburi Guccinarai District Hospital, Kalasin
Level of care	Provincial and District Hospital, home-based care
Partners	Ministry of Public Health, Surin Provincial Hospital, HPO, TNCA (Network of local NGOs), TNP+ (Network of people living with HIV/AIDS)
Initiation of AIDS programme	1995
Initiation of ART	2000 (home-based care), 2001 (hospital)
Number of patients on ARVs (June 2003)	615
PMCT	Yes
ARV protocols selected	
Conformity to national recommendations	Yes
Regimen used	
- First-line regimen	- d4T/3TC/NVP*
- Second-line regimen	- ZDV + ddI+ SQV/r
ARV procurement	
General situation	Local production of generic ARVs
Generics purchased	Yes (locally)
MSF price (ppy, March 2003)	
- First-line regimen	US$352
- Second-line regimen	US$3500

1 UN: World Population Prospects: The 2002 Revision. (www.un.org/esa/population/publications/wpp2002).
2 Report on the global HIV/AIDS epidemic. UNAIDS/WHO 2002.
* FDC

4.9.2 Details of procurement

Context

Availability at country level: Thailand is the first South-East Asian country to have documented the extent of the HIV/AIDS epidemic and to have developed a national AIDS policy. The procurement of AIDS medicines is in line with Thailand's national pharmaceutical policy, which favours domestic production by forbidding the import of medicines that are already available locally.

Thailand has been able to mobilize its generic capacity in both the public and private sectors. The Governmental Pharmaceutical Organization[25] (GPO) started to produce generic ZDV in 1995 and now produces seven ARVs, including some FDCs. GPO plans to start production of generic versions of NFV, ABC, r, IDV and SQV hard-gel by the end of 2003.

In addition to covering domestic needs, GPO has started to apply for registration of their products in neighbouring countries, such as Cambodia, and has offered technology transfer to a few African countries. Originator ARVs are available in Thailand but companies do not maintain permanent stocks in the country.

Registration: GPO products and all originator ARVs are registered in Thailand. Some Indian companies have applied for registration for certain products but none have been granted marketing authorization.

Patents: Patent protection for pharmaceuticals has only been possible since 1992, meaning that drugs that were marketed before this date cannot be under patent. Thailand is not listed in any of the international patent databases and patent information is thus only available through the Thai patent office. Thai patents have been found for the improved oral formulation of ddI,[26] EFV and LPV/r. In addition, several patent applications are currently under examination, notably for IDV, the syrup formulation of NVP and the ZDV/3TC combination.

To avoid patent infringement, GPO has developed alternative drug formulations, such as the oral powder form of ddI.

Prices at country level: As a Medium Human Development country, Thailand is only eligible for Merck & Co's and Roche's preferential pricing schemes. In 2000, the average ppy treatment cost was US$4,620, and in 2001, it fell to US$1,300, a 72% drop. At the end of 2002, the least expensive triple therapy was an FDC (d4T/3TC/NVP) produced by GPO at a price of US$350 ppy.

MSF procurement strategy

Since drug imports are restricted to pharmaceutical entities in Thailand, MSF purchases all ARVs either from manufacturers or distributors in the country. The primary source of ARVs is GPO. Products not available through GPO are purchased from originator company agents.

MSF has also been involved in offering technical support to a network of buyers' clubs. To increase access to more affordable drugs, TNP+ (a network of people living with HIV/AIDS) manages buyers' clubs where members unable to afford the prices charged by hospitals can buy ARVs at the lowest possible prices. In March 2003, approximately 600 people were purchasing ARVs through this network.

4.9.3 Comments/analysis

The availability and affordability of ARVs in Thailand has been constantly improving as a result of local production. This system has benefited from the strong political support of the Thai government.

However, GPO has been blocked from producing some drugs by patents. For example, it was forced to produce a less convenient powder form of ddI because of a patent on the tablet formulation. This patent has recently been invalidated by a Thai court, however BMS is appealing the decision.

It is extremely difficult to obtain lower prices for drugs that are either under patent in Thailand or not produced by GPO. The use of compulsory licensing provisions in the Thai intellectual property law will be key to maintaining competition in the future. Merck & Co is the only originator company with a clear policy that is being put into practice. Abbott's drugs are needed in MSF projects but no discount is available in Thailand. After MSF publicly criticized Roche for its inconsistent pricing policy for NFV, the company finally announced a Lower-Middle Income Country price in March 2003. This drug is not yet available in Thailand as Roche demands that purchases are made directly with their Swiss headquarters. This makes the lower price inaccessible in reality, as Thai law restrict imports of medicines.

Thailand will soon be receiving Global Fund money earmarked for scaling up ARV treatment in the public sector. Local production is likely to play a pivotal role in supplying this new national programme, as was the case in Brazil.

25 GPO, The Governmental Pharmaceutical Organization, was founded 35 years ago and it manufactures 300 different pharmaceuticals for the Government's own needs.
26 This patent was challenged by AIDS activists and NGOs who won their case against the patent holder Bristol-Myers Squibb in 2002, when the Thai Central Intellectual Property and International Trade Court found that the amendment the company had made to the original patent, and which the Thai patent authority had approved, was unlawful.

Summary of ARV supply in Thailand in June 2003

Drug Dosage Form	Manufacturer chosen	Supply channel	Comments
ABC 300 mg ABC 20mg/ml (240ml)	GSK		
ZDV 100 and 300 mg tab ZDV/3TC tab ddI 25, 50 , 100, 150, 200 mg tab d4T 15, 20, 30, 40 mg caps NVP 200 mg tab, NVP 240 ml syrup 3TC 150 mg tab NVP +D4T + 3TC 200 + 30 + 150 tab NVP +D4T + 3TC 200 + 40 + 150 tab ZDV 50mg/5ml 100 ml syrup 3TC 50mg/5ml 100 ml syrup	GPO		GPO has been producing a powder form of ddI because the tablet form was under patent. However, as a result of a recent court decision which invalidated the BMS patent, GPO should now be able to produce ddI tablets. BMS is appealing this decision.
EFV 50 and 200 mg cap IDV 400 mg caps	Merck & Co		Merck & Co products are supplied through a distributor in Thailand at differential prices offered by Merck worldwide. (Thailand is classified as a Medium Human Development Country with adult prevalence of 1% or greater), the following charges are added to this base price: 5 % handling fee (to cover importation fees, customs clearance and local freight costs), and a 7 % value added tax.
NFV 250 mg tabs	Roche		In April 2003, NFV from Roche was still sold at US$4,170 ppy, although theoretically Thailand could benefit from the price offer (US$2,967 ppy) if bought in Switzerland.
LPV/r r 100 mg caps r 80 mg/ml, 90 ml SQV 200 mg soft gel	Abbott		As a Medium Human Development Country, Thailand is not eligible for a preferential price for Abbott drugs. The price of LPV/r in April 2003 was US$5102 ppy while it is US$500 ppy for LDCs and African countries.

4.10 Ukraine

4.10.1 Overview

Ukraine is a Medium Human Development Country with one of the highest first-line treatment prices presented in this report. When MSF started ARV procurement, the country was considered a small market, and it was not benefiting from company offers. Local distributors do not stock products, which can cause shortages.

Country profile	
Population (million)[1]	48.5
Country development (UNDP classification)	Medium Human Development Country
Number of people living with HIV/AIDS[2]	240,000
National HIV/AIDS prevalence among adults	0.9 %
National drug regulatory authority	State Committee on Pharmaceutical and Medical Products Safety and Quality Control
Authority in charge of patents	Ukrainian Industrial Property Institute (Ukrpatent), State Department of Intellectual Property (SDIP) Ministry of Education and Science
MSF AIDS programme	
Location	Odessa, Mikolayev, Simferopol
Level of care	Regional Hospital, Maternities
Partners	Ministry of Health
Initiation of the AIDS programme	1999
Initiation of ART	June 2000 (PMCT), April 2002 (ART)
Number of patients on ARVs (March 2003)	18 children (from 617 mother and child pairs)
PMCT	Yes
ARV protocols selected	
Conformity to national recommendations	Yes
Regimen used (June 2002)	
- First-line regimen	- AZT/3TC*+NVP (or NFV for NVP exposed children)
- Second-line regimen	- ddI+D4T+LPV/r
ARV procurement	
General situation	Recent importation of generics, and local purchase of originator ARVs at minimum discounts
Generics purchased	Yes (imported)
MSF price (ppy, March 2003)	
- First-line regimen	US$500
- Second-line regimen	Not yet purchased

1 UN: World Population Prospects: The 2002 Revision. (www.un.org/esa/population/publications/wpp2002).
2 Report on the global HIV/AIDS epidemic. UNAIDS/WHO 2002.
* FDC

4.10.2 Details of procurement

Context

Availability at country level: Until recently, the only ARVs available in Ukraine were originator products supplied by local private distributors. But because of the low volumes of ARVs sold, these medicines are usually not stocked locally. In order to avoid supply shortages, MSF has sometimes had to contact originator companies directly.

For prevention of mother to child transmission (PMTCT), NVP has been supplied through a BI donation programme, which began in 2001. No generic formulations were available at the time. This programme was plagued by shortages of the syrup formulation for two reasons. First, the company suspended commercial importation before donation supplies were available. Second, although BI provided the drug in the requested quantities in absolute terms, because only large (240 ml) bottles were provided, some clinics had more than they needed and others had none. This problem was resolved when BI started supplying 20 ml bottles.

Registration: Most originator ARVs are registered, but there are some exceptions, such as AZT oral solution from GSK and some doses of d4T and ddI from BMS. The first generic ARVs were registered in May 2003.

Patents: After intensive research by MSF at the Ukrainian patent office, it seems that the following ARVs are under patent in Ukraine: abacavir (GSK), efavirenz and indinavir (Merck & Co), the crystalline form of lamivudine (GSK) and nevirapine. Ukraine does not have to comply with the TRIPS Agreement as it is not a member of the WTO. But it is an observer and thus are in the process of becoming compliant with the WTO rules.

Prices at country level: In 2001, the average cost of a yearly first-line treatment was US$8,500 ppy, which is close to the price in Western European countries. Ukraine is a Medium Human Development Country, for which only Merck and Roche have set levels of differential prices. Therefore negotiations were necessary, and have led to a ppy price of US$1,700. After the introduction of generics, the prices available to MSF plunged to US$500.

Despite the lack of patent barriers, the Ukrainian government chose to negotiate exclusively with originator companies. As a result, the government is paying three times more than necessary for the existing first-line therapy.

MSF procurement strategy

Considering the large price difference between originator and generic products, MSF has been advocating for the introduction of imported generics and seeking permission to import. However, despite long-standing support from the Ministry of Health, MSF was denied import permission until generics had been registered in May 2003.

MSF is currently in the process of importing generic drugs directly from India, which has helped reduce prices further.

Originator ARVs are purchased locally in most cases except when the price charged locally is higher than in Western Europe. In the latter case MSF headquarters makes the purchase. An example of this was Roche's Viracept® which was priced at US$520 per pack in Ukraine and less than half that in The Netherlands.

4.10.3 Comments/analysis

Since a number of ARVs are not under patent in Ukraine, there is no legal barrier to importing generic versions of these drugs. Registering additional generics has brought down prices further, but to dramatically improve availability, local distributors will need to stock generic and originator products.

Summary of ARV supply in Ukraine in March 2003

Drug Dosage Form	Manufacturer chosen	Supply channel	Comments
d4T 40mg caps IDV 100mg caps	Ranbaxy	Import	Most Cipla and Ranbaxy products were registered in Ukraine in May 2003. All generic products were imported until June 2003.
ZDV 100, 300 mg tab ddI 200mg ZDV+3TC NVP 200mg	Cipla	Import	
NFV syrup NFV 250 mg caps	Roche	Import	In 2002 as the price of NFV was twice the price of NFV in Europe, MSF imported.
EFV 200 mg cap EFV 600 mg cap	Merck & Co	Local purchase Not available	Medicines are ordered at Merck & Co's local agent which imports the drugs on order from their regional office (in Russia).

5. Main findings and recommendations

The following section draws together the common themes and findings from the 10 country cases. No ideal ARV procurement model was identified but analysis of the cases illustrated which factors had the most significant impact on availability and affordability of ARVs.

Government HIV/AIDS strategy:
The most critical factor affecting ARV procurement is a clear government commitment and policy to include treatment in a national HIV/AIDS strategy and securing the funding for this. Next come the registration status of medicines; the patent situation and the government's approach to overcoming patent barriers; accessibility to best prices by ensuring competition including originator and generic companies; and setting up an effective mix of public/private and NGO procurement and service delivery systems that best serve treatment programmes nationwide.

Political will:
Whether it led to the decision to produce locally (Thailand) or to a system whereby imported drugs are made available at competitive prices (Cameroon and Malawi), national political will was a critical factor in ensuring the availability and affordability of quality selected drugs. MSF's procurement experience was profoundly influenced by governments' policies, whether written or implied. In some countries (Kenya and South Africa), the lack of political will led MSF to identify and apply "exceptional" strategies. Such strategies need case-by-case government approval, and therefore have only demonstrative potential but do not significantly improve access across-the-board to patients in need.

Drug registration:
Having a limited number of registered generics and originator products created a serious barrier to ARV affordability and availability. Government policy regarding registration and other factors, such as the size of the market or a country's wealth, played critical roles in which drugs were registered.

Manufacturers are not always keen to register their products in Low- and Middle-Income countries where the market remains small; for instance, in Cambodia and Mozambique few originator drugs are registered. This is true even in countries included in international offers. Therefore price offers remain "virtual" unless temporary authorization for import and use can be attained.

Governments were often ready to give MSF special authorization when drugs were not registered, which has helped to foster competition between producers.

Patents:
In most of the 10 countries MSF had difficulty finding reliable information on the patent status of particular drugs, although some patents existed. MSF spent considerable time and resources hiring lawyers in various countries to analyse the national patent system and to ascertain the patent status of needed ARVs.

But it is clear that some countries are using the maximum flexibility allowed under TRIPS and strengthened in the Doha Declaration by ensuring accessibility of generic ARVs when patents were granted. Also, whether there was a government policy or not, MSF and its suppliers have had no legal problems (have never been sued or received legal threats) when using generic drugs.

Generic competition:
The most significant factor in lowering prices was the introduction of generic sources in a country. Prices for first-line therapy in the 10 countries ranged from US$277 ppy in Cameroon to US$867 in Guatemala.

Generally prices are significantly lower for generics than then they are for even differentially priced originator products. South Africa provides a good example. The differential price offered by originator companies for ZDV/3TC* and NVP in May 2003 was US$767 ppy, while MSF was paying US$400 for generic drugs from Brazil.

In some LDCs or sub-Saharan countries generic prices have dropped to less than US$300 ppy. But countries that are not LDCs or not in sub-Saharan Africa are only getting significantly reduced prices when they have access to generics. Country cases show that generic producers are willing to charge their lowest prices in some mid-level countries, for example, Honduras, where the first-line treatment costs US$288 ppy.

However, generic companies did not always make their internationally publicized prices available at country level. This was the case in Cambodia for most Cipla drugs, which forced the MSF team to import the drugs from the manufacturer.

ARVs are still unaffordable for people living in developing countries. Large scale-up will depend on further price reductions. MSF estimates that with a combination of large production volumes and generic competition,

* FDC

a price of US$50-100 ppy for triple therapy is achievable.

Differential prices:
In general, MSF found that it took extraordinary measures to get the published differential prices at country level. The drugs were often unregistered, unavailable or available from local agents that were adding surcharges. But with a lot of persistence, many of these problems were resolved for LDCs and sub-Saharan African countries. It should be noted that a number of originator companies are offering some of the best prices available internationally in LDCs and sub-Saharan Africa, as some BMS and Merck & Co products show.

MSF's experiences in Guatemala, Honduras, Thailand and Ukraine show that in UNDP-classified Medium Human Development Countries not in sub-Saharan Africa, differential prices are not usually available. Merck & Co's products are the exception as the company has publicized differential prices for Medium Human Development countries. Roche now has a policy of differential prices for World Bank-classified Lower-Middle Income Countries, but only accepts orders in Basle, Switzerland, and charges transport, insurance and freight costs to the customer (up to 20% surcharge).

Procurement system:
Procurement systems are partly driven by a country's political will to tackle the HIV/AIDS epidemic. From MSF's perspective, the most effective and easiest procurement systems are:

1) a strong public procurement agency: For instance, the Cameroon government takes full responsibility for authorizing the use of drugs of assured quality, purchasing through competitive bidding (tenders) and managing stock to avoid supply interruption.

2) private sector distributors: Another more complicated but equally effective system is purchase through dynamic private sector distributors. Malawi's first-line ARV combination price is one of the lowest in the world (US$288/ppy) because of local distributors' ability to act as agents of originator and generic manufacturers. This spares MSF or other buyers the administrative burden of importing, which is handled by the distributor. The low prices have partly been achieved by demanding that local distributors charge prices that have been publicized by the manufacturers. When surcharges were added, MSF complained to the manufacturer as well as the local distributor.

3) direct from manufacturers: In some cases, because ARVs were unavailable or were over-priced, MSF imported needed ARVs directly from manufacturers (Cambodia and Guatemala). This is the most difficult means of procurement, as the full burden of registration (provisional) and importation falls on the organization. Also this supply line is more vulnerable because of long-delivery times and the lack of a local buffer stock.

local manufacturers: Like Brazil, Thailand is an example of a country that produces ARVs locally. Local production has led to affordable, straightforward procurement of some drugs but for those that need to be imported, difficult price negotiations have been necessary.

In some countries, such as Kenya and Ukraine, MSF used a dual approach, buying from both private sector distributors and importing directly from manufacturers. This approach imposes a heavy administrative burden but does bring down medicine prices. (Note: importation is only just beginning in Ukraine).

Recommendations for ministries of health/ national AIDS programmes/policy-makers:
In countries where national HIV/AIDS guidelines are not yet developed, ARVs should be added to a country's EML and should include specific formulations, such as double and triple FDCs and paediatric formulations. WHO treatment guidelines are good references. When drugs are in the national EML, it simplifies procurers' work in purchasing ARVs.

National governments should consider fast-track registration of originator and generic ARVS, especially when drug/suppliers have been pre-qualified by WHO.

Governments should lower or abolish taxes, duties and wholesaler and dispenser mark-ups on ARVs, to ensure that the prices obtained through competition or differential pricing mechanisms are not being increased prohibitively.

Governments should work more effectively with national and regional patent offices to increase information on the patent status of ARVs.

LDCs should take advantage of the fact that under the terms of the Doha Declaration they do not need to grant or enforce patents on pharmaceuticals until 2016.

Subject to certain safeguards and limitations, governments can exercise their right to issue compulsory licences on patents on public

health grounds. This provision is made under the WTO TRIPS Agreement.

Recommendations for ARV procurers:
The procurement agent should endeavour to make the best clinical choice of ARVs of assured quality at the lowest available price.

The lesson learned on registration is that buyers should advocate full registration rather than rely on special authorizations wherever possible. Pressure may have to be applied on both manufacturers or their representatives and NDRAs to achieve this.

Procurers need not assume that patents are barriers if generic products are available in-country. In actual practice it may be possible to purchase generic versions of drugs which are theoretically patented.

If publicized originator or generic prices are unavailable from local or regional subsidiaries or agents, it is advisable to contact the company headquarters, which will often provide information about prices and conditions. Procurers should insist that the company's global offers are respected by local agents.

To access the best possible prices and avoid shortages, it is important to plan drug requirements as far in advance as possible. Suppliers should also receive this information in advance, even if actual orders are placed at a later date, as quantities can always be adjusted if necessary.

If the government procurement agency in the country does not supply ARVs, it might be possible to get local importers or agents to stock them locally, rather than being forced to buy ARVs direct from each supplier. Manufacturers sometimes ask local buyers to recommend agents to represent their products if they do not yet have distributors.

When national procurement agencies are supplying ARVs, customers can demand that they use generic competition rather than negotiation. Customers can help by supplying these agencies with information on sources and prices.

The Global Fund will cover medicines approved by local regulatory authorities even if they are not yet pre-qualified by WHO and therefore countries need not limit their use of generics to pre-qualified drugs. Currently the Global Fund's intention is to continue this policy until the end of 2004[27].

Recommendations for manufacturers:
As part of the global commitment to scaling up access to treatment, manufacturers should support the development of FDCs, paediatric formulations and user-friendly, affordable diagnostics that will enable simplification of treatment.

Manufacturers should participate in the development of differential pricing and join WHO's pre-qualification project through expressions of interest.

Recommendations for UN and other international agencies:
A differential pricing system for new drugs that are not available in generic forms should be explored internationally. This is particularly important for "mid-level" countries that are still often faced with prices that put needed drugs out of reach. International agencies should also support regional ARV procurement initiatives.

Since national procurement agencies can work effectively, the international community should support countries' efforts to expand national procurement agencies' capacity to procure, distribute and manage stocks of ARVs.

On behalf of countries, international procurement agencies (UN and non-profit) should consider stocking a full range of generic and originator ARVs, in countries that cannot build procurement capacity easily. Pooled procurement would also increase volumes, and so decrease prices.

Recommendations for NGOs:
NGOs should work together to avoid duplication of effort and maximize their contribution to global scaling up of ARV treatment. Collaboration with governments is particularly important when encountering problems.

27 http://www.globalfundatm.org/publicdoc/Third%20Board%20Meeting.pdf

6. Annexes

Annex I: Index of useful tools, references and sources of information

- Pilot Procurement, Quality and Sourcing Project: Access to HIV/AIDS drugs and diagnostics of acceptable quality, 6th edition. WHO, 2003.
http://www.who.int/medicines/organization/qsm/activities/pilotproc/suppliers.doc

A project initiated by WHO in 2002 and developed in collaboration with other United Nations Organizations (UNAIDS, UNICEF, UNFPA). Drugs on the list are commonly referred to as "pre-qualified". An international reference for regulatory authorities and procurement agencies. The project was recently expanded to include TB and malaria drugs in addition to ARVs.

- Sources and prices of selected medicines and diagnostics for people living with HIV/AIDS
A joint UNICEF, UNAIDS, WHO and MSF project, June 2003 (also available in French and Spanish).
http://www.accessmed-msf.org

Joint UNICEF-UNAIDS-WHO-MSF database on possible sources of HIV/AIDS-related medicines. The quality of the sources is only evaluated on the basis of manufacturer's file assessment. The information in this database needs to be confirmed by a proper quality assessment.

- Untangling the web of price reductions: a pricing guide for the purchase of ARVs for developing countries, 4th edition. MSF, 2003 (also available in French and Spanish).
http://www.accessmed-msf.org

Guide to navigating the complex world of preferential ARV prices: data compiled by MSF and checked by the companies involved. Includes prices offered by originator companies and by some generic companies in low- and middle–income countries. Aimed at potential buyers, including government, non-profit procurement agencies, health facilities and NGOs.

- WHO model formulary, WHO 2002.

Intended to improve patient safety and limit superfluous medical spending, the formulary is the first ever publication to give comprehensive information on all 325 medicines contained in the WHO Model List of Essential Drugs. Presents information on the recommended use, dosage, adverse effects, contraindications and warnings of these medicines.
http://www.who.int/medicines/organization/par/who_model_formulary.pdf

- Simplified HIV drug dosing table for children. MSF document available upon request at msfbthai@ksc.th.com

- Drug patents under the spotlight: sharing practical knowledge about pharmaceutical patents. MSF, 2003.
http://www.accessmed-msf.org

- Patent situation of HIV/AIDS related drugs in 80 countries. WHO/UNAIDS, 2000
http://who.int/medicines/library/par/hivrelateddocs/patentshivdrugs.pdf

- Globalization and access to drugs, perspectives on the WTO/TRIPS Agreement revised. Health Economics and Drugs, EDM Series N° 7, WHO, 1999.
http://who.int/medicines/library/dap/who-dap-98-9-rev/who-dap-98-9-rev.j

■ Scaling up antiretroviral therapy in resource-limited settings, guidelines for a public health approach. WHO, 2002.
http://www.who.int/hiv/topics/arv/ISBN9241545674.pdf

■ Managing drug supply, 2nd edition. Management Services for Health in collaboration with WHO, 1997.

■ Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents, by the Panel on Clinical Practices for the Treatment of HIV, 2002.
http://www.aidsinfo.nih.gov.

■ Operational principles for good pharmaceutical procurement (Interagency document). WHO, Geneva, 1999. WHO/EDM/PAR/99.5.
http://www.who.int/medicines/library/par/who-edm-par-99-5/who-edm-par-99-5.htm

■ Hivatis guidelines:
http://www.aidsinfo.nih.gov/guidelines/pediatric/pediatric.pdf
http://www.aidsinfo.nih.gov/guidelines/perinatal/Perinatal.pdf

Annex II: List of abbreviations

(For a full glossary of terms, see www.accessmed-msf.org)

AAI	Accelerating Access Initiative
AIDS	Acquired immune deficiency syndrome
ARIPO	African Regional Industrial Property Organization
ART	Antiretroviral therapy
ARV	Antiretroviral
BI	Boehringer Ingelheim
BMS	Bristol-Myers Squibb
CIF	Cost, insurance, freight
DT	Delivery time
EML	Essential medicines list
FDC	Fixed-dose combination
GMP	Good manufacturing practices
GSK	GlaxoSmithKline
HIV	Human immunonodeficiency virus
ICH	International Conference for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
LDC	Least developed country
Merck & Co	Merck, Sharp & Dohme
MSF	Médecins Sans Frontières
NDRA	National drug regulatory authority
OAPI	African Organization of Intellectual Property (L'Organisation Africaine de la Propriété Intellectuelle)
NGO	Non-governmental organization
PLWHA	People living with HIV/AIDS
PMTCT	Prevention of mother-to-child-transmission
Ppy	per patient per year
RIA	Registered import advice
TB	Tuberculocis
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNCTAD	United Nations Conference on Trade and Development
UNDP	United Nations Development Programme
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
VAT	Value added tax
WHO	World Health Organization
WIPO	World Intellectual Property Rights Organization
WTO	World Trade Organization
3TC	lamivudine (Epivir®); nucleoside analogue reverse transcriptase inhibitor
ABC	abacavir (Ziagen®); nucleoside analogue reverse transcriptase inhibitor
d4T	stavudine (Zerit®); nucleoside analogue reverse transcriptase inhibitor
ddI	didanosine (Videx®): nucleoside analogue reverse transcriptase inhibitor
(AZT or) ZDV	zidovudine (Retrovir®): nucleoside analogue reverse transcriptase inhibitor
NVP	nevirapine (Viramune®): non-nucleoside analogue reverse transcriptase inhibitor
EFV	efiravenz (Stocrin®): non-nucleoside analogue reverse transcriptase inhibitor
NFV	nelfinavir (Viracept®): protease inhibitor
LPV/r	lopinavir/ritonavir (Kaletra®): protease inhibitor
TDF	tenofovir (Viread®): nucleotide reverse transriptase inhibitor
IDV	indinavir (Crixivan®): protease inhibitor
r	ritonavir (Norvir®): low dose ritonavir used as a booster; protease inhibitor
SQV	saquinavir (Invirase®): protease inhibitor
ddC	zalcitabine (Hivid®): nucleotide reverse transriptase inhibitor

Annex III: Prices of selected ARVs in some MSF projects

Prices of selected ARVs used within the MSF project in Malawi, March 2003

Drug	Dosage Form	Source	Price per pack (US$)	Price per unit US$
ZDV	100 mg tab	Cipla	8/60's	0.133
ZDV	300 mg tab		12/60's	0.2
ZDV/3TC*	tab		20/60's	0.33
ddI	25 mg tab		5.5/60's	0.09
ddI	100 mg tab		15.5/60's	0.26
d4T	30 mg caps		3.25/60's	0.05
d4T	40 mg caps		3.25/60's	0.05
NVP	200 mg tab		11/60's	0.18
3TC	150 mg tab		8.5/60's	0.14
NVP/d4T30/3TC*	tab		23.5/60's	0.39
NVP/d4T40/3TC*	tab		23.5/60's	0.39
ZDV	50mg/5ml,100 ml		1.55/bottle	1.55
NVP	50mg/ml, 100ml		2.45/bottle	2.45
NVP	50mg/ml, 25 ml		0.65/bottle	0.65
3TC	10mg/ml 100ml		2/bottle	2
EFV	200 mg caps	Merck & Co	38/60's	0.63
EFV	600 mg caps		38/60's	0.63
NFV	250 mg caps	Roche	100 /270's	0.37
NFV	50mg/g, susp		30 / bottle	30
d4T40/3TC*	tab	Ranbaxy	12.7 /60's	0.21
d4T30/3TC*	tab		14.1/60's	0.235

Sample prices paid by MSF for Cipla products in Malawi. Purchases were made through a local distributor.

Drug dosage	Source	Unit price publicized by Cipla headquarters (in dollars)	Wholesaler price per unit (in US$) in Malawi				
			June 01	Sep 01	Dec 01	Dec 02	March 03**
ZDV/3TC* tab	Cipla	0.40 (ex-works in India: transport and insurance to be added)	0.76	0.67	0.55	0.41	0.33
NVP 200 mg tab	Not available	0.46 (May 2001) 0.285 (Apr 02)	Registered 0.52	0.33	0.29	0.183	

** after competition with Ranbaxy products
* FDC

Drug prices in Mozambique, October 2002

ARV		Price per box (for one month)	
		Ranbaxy	Cipla
3TC+d4T+NVP (150+40+200),	*60 tab*	US$32.95	US$32.00
3TC+d4T+NVP (150+30+200),	*60 tab*	US$26.92	US$32.00
d4T 40mg,	*60 caps*	US$6.52	US$4.90
d4T 30mg,	*60 caps*	US$4.99	US$4.30
3TC 150mg,	*60 tab*	US$14.70	US$11.30
NVP 200mg,	*60 tab*	US$18.30	US$18.30
ZDV+3TC (300mg + 150mg),	*60 tab*	US$41.50	US$26.50

EFV 200 mg (Stocrin®) from Roche: not available in Mozambique.

Drug quotations in Mozambique (first round and not yet finalized) in May 2003

ARV		Price per box (for one month)	
		Ranbaxy	Cipla
3TC+d4T+NVP (150+40+200)	*60 tab*	N/A	US$28.50
3TC+d4T+NVP (150+30+200)	*60 tab*	US$31.29	US$28.10
3TC+d4T(150+40)	*60 tab*	US$18.52	US$16.90
3TC+d4T(150+30)	*60 tab*	US$18.70	US$17.70
d4T 40mg	*60 caps*	N/A	US$6.89
d4T 30mg	*60 caps*	US$4.99	US$6.99
3TC 150mg	*60 tab*	US$14.96	US$12.90
NVP 200mg	*60 tab*	US$18.25	US$18.90
ZDV+3TC (300mg + 150mg)	*60 tab*	US$42.21	US$26.10
ddI 25 mg	*60 tabs*	N/A	US$6.95
ddI 50 mg	*60 tabs*	N/A	US$9.95
ddI 100 mg	*60 tabs*	N/A	US$14.00
ddI 2000 mg	*60 tabs*	N/A	US$24.90
ZDV 300 mg	*60 tabs*	US$28.56	US$23.90

EFV (Stocrin®) 200 mg from Roche: 56.26 USD/box of 90 capsules;
EFV (Stocrin®) 600 mg: N/A (not yet registered);
NFV 250 mg (Merck & Co): Price still under request;
NFV 250 mg (CIPLA): 59.50 USD/box of 100 pills.

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