UNITAID

Increasing access to quality medicines and diagnostics for HIV/AIDS, TB and Malaria

The HIV Medicines Patent Pool Initiative

Briefing for Delegates to the 62nd WHA, Geneva, 20 May 2009

Ellen 't Hoen
Senior Adviser Intellectual Property and Patent Pool
UNITAID, 20 Avenue Appia, 1211 Geneva 27, Switzerland
thoene@who.int
UNITAID's Mission

Is to contribute to scale up access to treatment for HIV/AIDS, malaria and tuberculosis for the people in developing countries by leveraging price reductions of quality drugs and diagnostics, which currently are unaffordable for most developing countries, and to accelerate the pace at which they are made available.

To fulfill its mission, UNITAID will use sustainable, predictable and additional funding to help generate a steady demand for drugs and diagnostics, thereby significantly impacting market dynamics to reduce prices and increase availability and supply. UNITAID will base its price reduction strategy on market competition.

Where intellectual property barriers hamper competition and price reductions, it will support the use by countries of compulsory licensing or other flexibilities under the framework of the Doha declaration on the Trade-Related Aspects on Intellectual Property Rights (TRIPS) Agreement and Public Health, when applicable.

Any other innovative solution that may overcome limitations to market diversification in developing countries will also be pursued.

Source: www.unitaid.eu
• CIPIH 2006 recommendation "Patent pools of upstream technologies may be useful in some circumstances to promote innovation relevant to developing countries. WHO and WIPO should consider playing a bigger role in promoting such arrangements, particularly to address diseases that disproportionately affect developing countries."

• 2006 MSF and KEI proposed to UNITAID to set up a medicines patent pool.

• May 2008 WHO Global Strategy and Plan of Action Public Health, Innovation and Intellectual Property recognised the role of patent pools to increase access to medicines.

• July 2008 UNITAID EB decided in principle to establish a voluntary medicines patent pool and work is on its way to develop a full implementation plan.
• A Patent Pool is a portfolio of assets consisting of the entire set of patents and other relevant IP held by various actors (companies, universities, government institutions) related to a particular technology that are made available on a non-exclusive basis to third parties, (e.g. generic manufacturers) against the payment of royalties.
• 2007- 2008, 92% of patients on antiretroviral use generic drugs in low and middle income countries.. (Source: WHO Global Price Reporting Mechanism).

• Vast majority uses d4T/3TC/NVP fixed dose combination

• Until 2005 India ’s excluded pharmaceutical products from patenting (1970 Patents Act)
Effect of Generic Competition

New ARVs More Costly

Source: http://www.msfaccess.org
"The battle to start providing antiretroviral therapy in the developing world has been won. The battle to provide the best care we can is just beginning."

Rationing Antiretroviral Therapy in Africa – treating too few, Too Late. Ford, Mills, Calmy, N Eng J Med 360;18, April 30 2009

http://content.nejm.org/cgi/reprint/360/18/1808.pdf
Patent Pool Process

- The 'standard': Missing Essential ARVs
  - In collaboration with WHO HIV and Essential Medicines Department
- Identify the relevant patents
- Call for patents
- Start of negotiations with patent owners
- Establishment of the licensing agency (The 'Pool')
- Day to day operation of the Pool
• In collaboration with the WHO HIV department and the WHO Essential Medicines and Pharmaceutical Policies department, a list of priority products was developed and submitted for discussion at the 17th WHO Expert Committee on Essential Medicines on 23 - 27 March 2009.

• The Expert Committee:
  – welcomed the patent pool proposal as an example of a new initiatives to develop desirable new products
  – identified the need for the development of fixed dose combination products for HIV especially where they improve efficacy and adherence;
  – acknowledged the need for paediatric dosage forms;
  – identified the need for additional classes of medicines for HIV and acknowledges research in developing new drugs in existing classes of medicines as well as in new classes;
  – noted that to date a wide selection of fixed dose combination products was not available needed in developing the list of essential medicines;
  – Acknowledged the lists of 'missing priority ARVs' proposed and annexed them to the report.
  – Noted the potential value of applying the patent pool approach to other major public health problems

A Successful Pool will:

• Accelerate the availability of generic versions of new ARVs
• Enable the development of FDCs of which the patents are held by different entities
• Enable the development of adapted formulations for children
• May provide a model for the future…
Is the Patent Pool Feasible?

• Part of the WHO Global Strategy
• UNITAID commitment
• Companies’ initial responses positive
• NGO Support
• Political momentum and growing support
• **Increase Access to Affordable Drugs:** Barack Obama and Joe Biden believe that people in developing countries living with HIV/AIDS should have access to safe, affordable generic drugs to treat HIV/AIDS. They will break the stranglehold that a few big drug and insurance companies have on these life-saving drugs. They support the rights of sovereign nations to access quality-assured, low-cost generic medication to meet their pressing public health needs under the WTO’s Declaration on Trade Related Aspects of Intellectual Property Rights (TRIPS). Barack Obama and Joe Biden also support the adoption of humanitarian licensing policies that ensure medications developed with U.S. taxpayer dollars are available off-patent in developing countries.
UNITAID Patent Pool Summary Statement

Gregg Alton, Gilead Sciences, Inc.

The UNITAID patent pool proposal is an important initiative, and Gilead Sciences is committed to participating in the discussions about how this kind of innovative approach will move forward. We believe if structured appropriately, UNITAID’s patent pool can play a critical role in expanding access to antiretroviral treatment for patients around the world by encouraging the development of new fixed-dose combinations and pediatric formulations, lowering prices, while respecting intellectual property.

Gilead sees many similarities between UNITAID’s proposal and our company’s licensing agreements with Indian generic manufacturers, given the shared belief that these approaches promote innovation and offer a mechanism for increased access at lowered cost. Two manufacturers, Matrix and Aurobindo, are already having an impact by lowering the price of tenofovir disoproxil fumarate by 50 percent below Gilead’s current access price, developing fixed-dose combinations and providing more than 200,000 patients with high-quality, low-cost treatment. Today, together with the generics, over 500,000 patients are receiving Viread representing approximately 13 percent of those accessing treatment in low- and lower middle-income countries.

As the patent pool proposal takes shape, important opportunities exist for relevant stakeholders to help define the pool’s scope, structure and associated terms. Key questions that remain to be addressed include: What entity will actually administer the pool? What would be the pool’s governance structure? How would critical regulatory, medical information and other processes be supported? The answers to these questions will provide concrete details that will allow involved stakeholders to evaluate the core elements of the proposal.

With these questions in mind, we believe the following are important to consider as the patent pool takes shape:

* Flexibility in the pool, above all else, will be critical
* Structure should allow for creativity in building unique partnerships to create new development and delivery pathways
* Adjustment and re-evaluation will be vital as the patent pool develops
* Basic factors driving drug development today – cost, risk and reward among them – should be taken into account to ensure broad participation in the patent pool
* Development of processes to help manage the intellectual property aspects of this model should be clearly defined
Gilead looks forward to continuing to work with UNITAID and other partners in meeting the urgent need for expanded HIV treatment access, and we welcome the opportunity for future discussions about patent pools and other access-related topics.
An estimated 33 million people worldwide are living with HIV, of which at least 95 percent live in the developing world. Although more than four million people in developing countries are now receiving antiretroviral medicines, this figure represents only about 45 percent of total need. While collaborative efforts around the globe have helped create better therapies for patients, increased access to these critical medicines remains a significant global health challenge. Gilead Sciences is a research-based biopharmaceutical company that works to expand treatment options and improve the care of people with life-threatening diseases such as HIV/AIDS.

As the market leader in the development of therapeutics for the treatment of HIV, it is our responsibility to help ensure that our innovative medicines are available and accessible to all who can benefit from them. This requires developing new approaches to accelerate treatment access. In 2003, we established the Gilead Access Program to ensure sustainable access for patients suffering from HIV in developing countries around the world.

We offer substantial price reductions through our Access Program in some 130 countries, representing two-thirds of the countries in the world, and the regions hardest hit by the HIV/AIDS epidemic.

**Tiered Pricing**

Gilead has developed a tiered pricing system for our HIV medicines, Viread® (tenofovir disoproxil fumarate) and Truvada® (emtricitabine and tenofovir disoproxil fumarate), through which pricing discounts are given in low- and lower middle-income pricing tiers based on a country’s ability to pay. The main criteria used in determining the tier in which a specific country falls are economic status (using gross national income per capita) and HIV prevalence. With these tiers as guidelines, we work independently and in collaboration with partners to establish fair pricing.

**Industry Partnerships**

Gilead has established partnerships with 13 Indian companies, providing a full technology transfer to enable them to produce and distribute quality, low-cost generic versions of Gilead’s HIV medications in 95 developing countries. These companies have extensive expertise in achieving efficiencies in manufacturing and distributing HIV medicines in the developing world. Our partners have the freedom to establish pricing for their products, while Gilead receives a 5 percent royalty on sales. Several partners have already received tentative U.S. Food and Drug Administration approval through the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR) program for generic Viread, generic
Truvada and other tenofovir-based fixed-dose combinations, thereby significantly increasing patient access to high-quality, low-cost HIV treatment.

We believe these partnerships are a model for innovative collaboration between the research-based industry and generic manufacturers and have the potential to lower costs by ensuring competitive pricing. Our other industry collaborations include local manufacturing and distribution by South Africa’s Aspen Pharmacare of Gilead’s branded HIV medications and generic versions of them; our partnership with Merck & Co., Inc. for the distribution of Atripla® (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) in developing countries; and our manufacturing collaboration in The Bahamas with PharmaChem Technologies and the Grand Bahama Port Authority. These efforts showcase how companies can work together to increase access to HIV medicines.

**Distribution Network**

Gilead has established a network of distribution partners to accelerate the regulatory process in the developing world by leveraging their knowledge of local systems, to manage outreach and on-the-ground logistics and to ensure secure distribution of Gilead’s HIV drugs. Gilead provides comprehensive training for our distribution partners on the treatment and access challenges specific to their region. This training effectively helps to ensure that our distribution partners gain a solid understanding of Gilead’s products and how they may be marketed most effectively in order to provide clinical and community-based education, address medical information requests and establish pharmacovigilance systems in the manner most appropriate for the territories where they operate.

**Comprehensive Approach**

Additionally, Gilead works to advance global anti-HIV efforts by supporting clinical research and health and education programs around the world, particularly in resource-limited settings. We provide our HIV medications at no cost for use in clinical studies that evaluate HIV treatment strategies tailored for the developing world. Our partnerships with healthcare organizations, patient advocacy groups and public health institutions help to raise awareness and increase diagnosis and treatment of HIV/AIDS.

**For More Information**

To learn more about Gilead Sciences and our efforts to increase HIV drug access in the developing world, please visit our Web site, www.gilead.com, or call International Access Operations at +1-650-522-5101.
Partnerships are a critical element of increasing access, and Gilead has implemented several collaborative initiatives to help improve care and treatment for those individuals living with HIV/AIDS in the developing world.

**Manufacturing**

In 2005, Gilead established a facility in The Bahamas to manufacture tenofovir DF, the active drug substance in Viread, for resource-limited countries through a cooperative effort with PharmaChem Technologies and the Grand Bahama Port Authority. That same year, Gilead entered into a non-exclusive partnership with South Africa-based Aspen Pharmacare, under which Aspen manufactures finished product for low pricing tier countries and distributes Gilead therapies throughout Africa. In late 2007, Aspen was extended the option to manufacture and distribute generic versions of Gilead's products in Africa, while Gilead receives a 5 percent royalty on sales. Aspen is also sourcing active pharmaceutical ingredient (API) from our Indian Generic partners.

**Generics**

Gilead has also entered into non-exclusive license agreements with 13 generic manufacturers in India - Alkem Laboratories Ltd., Aptuit Laurus Private Ltd., Aurobindo Pharma Ltd., Cadila Healthcare Ltd., Emcure Pharmaceuticals Ltd., FDC Ltd., Hetero Drugs Ltd., Matrix Laboratories Ltd., Medchem International, Ranbaxy Laboratories, SeQuent Scientific Ltd., Shasun Chemicals & Drugs Ltd. and Strides Arcolab Ltd. Under these license agreements, our partners will produce active pharmaceutical ingredient and tablets and distribute high-quality generic versions of Gilead's HIV medications in 95 resource-limited settings.

View list of countries

These agreements have been established based on these companies' expertise in achieving efficiencies in manufacturing, breaking down in-country barriers, navigating healthcare systems and distributing HIV products in countries most affected by the HIV/AIDS epidemic. These arrangements include a full technology transfer to enable faster ramp-up of production of high-quality product, and allow for the manufacture of commercial quantities of both active pharmaceutical ingredient (API) and finished product. The generic companies are free to establish pricing for their products and Gilead receives a 5 percent royalty on sales of finished product. Gilead expects that multiple manufacturers will ensure competitive pricing, thus helping to achieve broader access for patients with HIV/AIDS. Several partners have already received tentative U.S. Food and Drug Administration approval through the U.S. President's Plan for AIDS Relief (PEPFAR) program for generic Viread and Truvada, thus significantly increasing patient access to high-quality, low-cost HIV treatment.

**Distribution**

Gilead has established a network of distributors to assist with forecasting, registration, importation and distribution of our products. Our distribution partners are chosen based on their ability to accelerate the regulatory process by leveraging their knowledge of local systems, to manage outreach and on-the-ground logistics, and to provide medical education and to secure distribution of Gilead's HIV drugs where and when they are needed most.

We provide comprehensive, regional-specific training for our distribution partners. This training helps to effectively ensure safe use of Gilead's products by helping our distributors gain a solid understanding of our products in order to provide clinical and community-based education, address medical information requests and set up standard reporting systems within their respective regions.

Gilead and our distribution partners share a common commitment to provide sustainable access for patients suffering from HIV, and have worked with us to keep distribution costs low.
A summary of the presentation made by Greg Perry, Director General of the European Generic Medicines Association.

“The patent pool concept is one of the most innovative ideas that have been presented as a means of dealing with lack of R&D and access for certain key medicines. It is clear that where normal market mechanisms do not work, for example in areas where the diseases is most prevalent in developing countries, new mechanisms need to be found.

The patent pool proposal by UNITAID for the moment only covers HIV combination products and pediatric formulations but this is in a sense a pilot project. If it can work here, not only will it deal with one of the most important humanitarian needs of our time but will also be the foundation stone for future projects in other disease areas.

For the pool to work it clearly needs the support of both patent holders and governments. In a sense there are two types of patent pool.

The first envisages cooperation between various patent holders and others in the R&D development chain which helps to reduce costs, pool resources, maximizes innovation resources and share ideas. This is a model we see in other industries such as mobile telephones where knowledge sharing is frequent and the rate of innovation change is high. This may become a model for future developments in the pharmaceutical sector as many companies seek new business models for pharmaceutical development. It may be a key model for neglected diseases.

A second type of pool is where the patent holders place their rights into a public pool and where the knowledge is accessible to any other companies (on payment of a royalty) including those with no patents or contributions to the pool itself. These partners would be able use the invention to manufacture, and possibly develop the products further, to ensure wider access and create new forms of incremental innovation.

Both models can have an important role for improving innovation and increasing access for medicines for developing countries. The two models can work in conjunction. However, it is this second form of patent pool that I see provides major opportunities for increasing access to medicines by increasing the number of suppliers of certain medicines. It is also in the second model where generic manufacturers could have a role. Where the “invention” is already developed and gone through clinical trials, generic manufacturers, which in many regions have highly advanced manufacturing plants, could be partners to the pool in obtaining licenses for the manufacturing of the medicinal products. Moreover certain generic companies, which have experience in developing products, a history of incremental innovations and advanced clinical experience, might also be pool partners for research and development - as well as the manufacturing- of certain new formulations such as pediatrics, fixed dosed combinations and other product developments.

However, to encourage generic companies certain needs would have to be met. This would include access to registration through the WHO pre-qualification procedure or recognition of authorizations granted by advanced regulatory agencies such as exist in the EU (i.e. the 27 Member States agencies and the EMEA) the USA and Japan. There would also have to be some guarantee of market conditions such as price and market stability. In case of research and development costs, access to funding could also be important.

In conclusion the patent pool proposal should be actively supported but must be built on a spirit of partnership between patent holders, generic and originator manufacturers, governments and international agencies.”
Technology Transfer for Global Access: Guiding Principles

Emory University is committed to “working collaboratively for positive transformation in the world through courageous leadership in teaching, research, scholarship, health care, and social action.”1 As a leading research institution, Emory will endeavor to fulfill this commitment by helping make Emory-developed innovations accessible to people in the developing world whose lives depend on their use. This work is part of a broader effort to address the challenges of global health through a multi-disciplinary approach, from the development of knowledge and technologies to the delivery of treatment and care. Toward this goal, the Office of Technology Transfer will adopt the following guiding principles into its licensing program:

1. **Emory reaffirms its commitment to seek out global licensing partners for new and neglected technologies that may be of significant interest to the developing world.**

   Emory has a history of licensing technology to corporate partners that develop drugs and vaccines to address diseases affecting the developing world. Emory reaffirms its commitment to these efforts by seeking out industry partners and creating new companies that work to increase access in the developing world to therapies developed by Emory scientists.

   We recognize that some corporate partners may not immediately recognize the value in global access strategies, and we are committed to being vigorous advocates for licensing technology in ways that promote global access.

2. **Emory will engage in open and honest discussions with its industry partners to develop creative and effective licensing strategies that promote global access.**

   As market conditions evolve, licensing with global access clauses will, we believe, become less threatening to licensees. Governmental and philanthropic resource availability, socially conscious investors and activists, threats of compulsory licensing, and improved technology to prevent re-importation are just a few of the developments that are changing the once-settled assumption that the promotion of global access is not a rational financial strategy.

   As a result, we believe that Emory has more common ground with industry partners than previously recognized with respect to global access licensing. Through open discussion and creative thinking, Emory and its licensing partners can develop licensing terms with which both parties are comfortable in order to promote global access.

---

1 Emory University Strategic Vision Statement
3. Emory supports making new products available in the developing world and therefore will negotiate with licensing partners in a manner that encourages them to make those products available to people who need but cannot afford them.

Emory values the importance of access as well as the value of financial return. Recognizing that aspirational statements are not sufficient, Emory is committed to seeking incentives for actual results—including, e.g., shared reduction in financial return on sales in the developing world.

4. Emory will continue to follow effective global access principles when licensing Emory inventions.

We understand that the dynamic nature of licensing and the rapidly increasing attention to global access would render any list of socially responsible licensing strategies incomplete. While we will continue to think creatively about the issue, some of the potential strategies include:

(a) Structuring royalty payments to reward companies that succeed in making new products available at an affordable cost to the developing world.
(b) Structuring diligence obligations that facilitate widespread availability of new products.
(c) Encouraging licensees to sublicense to manufacturers in developing countries.
(d) Incorporating intellectual property terms that allow or encourage licensees to forego patent protection in developing countries when doing so will promote global access.
(e) Partnering with government entities and not-for-profit organizations who share in the vision of making technologies more available and accessible in the developing world.
Annex 1

Cost Benefit Analysis for UNITAID Patent Pool

20 June 2008

Introduction

The feasibility and sustainability of treatment for HIV/AIDS in developing countries will depend upon the ability of donors and developing country governments to obtain an inexpensive supply of new medicines, including those that are adapted or designed to address the health needs of people living in developing countries. The following analysis examines the costs and benefits of a UNITAID Patent Pool focusing the open licensing of inventions used for the treatment of HIV/AIDS. Specifically, the analysis compares the estimated $1.5 million annual cost of operating such a pool to the benefits as measured by expected lower prices for second line and second generation AIDS drugs. These lower prices are expected to flow from a greater degree of generic competition, as a consequence of enhanced global norms in favor of open licensing, and by measures that make the open licensing of inventions easier, less costly and more compelling for patent owners.

As noted in the report, there are limits to this analysis. Most importantly, the UNITAID Patent Pool is designed and expected to improve the management of patent portfolios so that the competitive sector can develop better manufacturing processes, new fixed dose combinations (FDCs) or other improvements in delivery methods, such as simplified dosing, heat stabilization of products, oral delivery of injectable treatments, and the development of appropriate formulations such as triple FDCs, FDCs for Preventing Mother-to-Child Transmission (PMTCT) of HIV, and pediatric formulations. These important benefits are noted but not quantified in this analysis.

First and Second Treatments for AIDS

In HIV/AIDS treatment a “first line” regime is the initial treatment regime given to a patient. While the first line regime would ideally be chosen strictly upon medical criteria, in practice, particularly in developing countries, it may also be based on the price. A “second line” regime is used when a patient fails on their first line regime, commonly due to the development of resistance. This requires the patient to change all three drugs in their first line regime. Patients who experience intolerable side effects may need to change one of the ARVs in their first line regime; this is called a first line alternative regime.

---

2 This report was initially prepared by James Love of Knowledge Ecology International (KEI) and finalized with contributions from several others including David Serafino and Michelle Childs of KEI, Ellen ‘t Hoen, Karen Day, Selina Lo and Laurent Gadot of MSF, Professor Brook Baker of Northeastern University School of Law and Frederic Martel, Kathleen Strong and Paulo Meireles of UNITAID. The views presented here are those of the author and do not necessarily reflect those of the members of the UNITAID Patent Pool Expert Group, the World Trade Organization, the World Intellectual Property Organization, the World Health Organization, UNITAID or DFID.
The terms “first generation” and “second generation” are normally used to describe older and newer treatments. Second generation products tend to have better (or different) medical properties including, lower toxicity, different delivery mechanisms (simpler dosing regimes, heat stabilization, etc.) or some other characteristics that make them attractive to patients and medical professionals alike.

In the United States, the most popular first line regime today includes a second generation ARV incorporated in a FDC. This particular FDC consists of TDF+FTC+EFV, and is a once-a-day treatment. Gilead reports that this combination is used by approximately 30 percent of U.S. patients receiving antiretroviral treatment (ART). In the developing world, the most commonly used first line regime is a combination of first generation ARVs, d4T+3TC+NVP, which is available as an FDC, but is one pill to be taken twice a day.

People who receive ART often have compelling medical reasons to switch to a different drug combination. Resistance to ARVs is a natural process that develops as a consequence of long term treatment. “In one of MSF’s long-standing HIV/AIDS projects, in Khayelitsha, South Africa, one in five patients needs to be switched to second line therapy after five years of treatment because they have developed resistance to their initial treatment. Indeed, in wealthy countries, many people living with AIDS have changed their treatment lines four, five or even six times. With two million people on ARVs across the developing world, the need for access to newer ARV options is growing rapidly.”

Unfortunately, the prices for the second generation ARV medicines are far higher than the prices for the first generation ARVs now being used in developing countries. In many cases, the prices are an order of magnitude (or more) higher. These higher prices threaten the sustainability of AIDS treatment in developing countries.

**Demand for Second Line AIDS Drugs**

At present, approximately 3 million persons living in developing countries are receiving treatment for AIDS, a number that is expected to increase with expanded donor investments in treatment and improved treatment infrastructure.

According to the WHO, where data are available, 94 percent of existing patients who have access to treatment are reported to be receiving first line treatments, and six percent are receiving second line treatments. There are considerable differences between regions. For example, within Latin America and Western and Central Europe, 26 to 27 percent of the population reporting is on second line regimes. In South & Southeast Asia, only 4 percent of the reporting population is on second line regimes. In sub-Saharan Africa, only 1 percent is on second line treatments.

---

3 On June 13, 2008, Gilead said that 150,000 of approximately 500,000 persons on ART were using Atripla.
4 “Tenofovir (TDF) is now included as a preferred first-line NRTI, because of its efficacy, ease of use and safety profile. This is a change from the 2003 guidelines, which recommended reserving the use of TDF as part of second-line regimens.” Antiretroviral therapy for HIV infection in adults and adolescents, 2006 Revision, WHO.
Table 1: Use of First and Second Line AIDS Drugs

<table>
<thead>
<tr>
<th>UNAIDS Region</th>
<th>First Line</th>
<th>Second Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caribbean</td>
<td>89%</td>
<td>11%</td>
</tr>
<tr>
<td>East Asia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern Europe &amp; Central Asia</td>
<td>92%</td>
<td>8%</td>
</tr>
<tr>
<td>Latin America</td>
<td>74%</td>
<td>26%</td>
</tr>
<tr>
<td>Middle East &amp; North Africa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oceania</td>
<td>99%</td>
<td>1%</td>
</tr>
<tr>
<td>South &amp; South East Asia</td>
<td>96%</td>
<td>4%</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>99%</td>
<td>1%</td>
</tr>
<tr>
<td>Western and Central Europe</td>
<td>73%</td>
<td>27%</td>
</tr>
</tbody>
</table>

Source: WHO 2008 (Towards Universal Access Report)

Estimates about the future demand for second line treatments (often based on second generation medicines) are based upon incomplete data, particularly concerning the degree of compliance for those now receiving drugs. A high rate of adherence to treatment, such as the rates reported by some MSF-run programs, is not necessarily typical for the average patients receiving ART. Patients who have lower rates of compliance will develop drug resistance earlier, and become candidates for new (and often more expensive) drug regimes.

The Clinton Foundation recently estimated that, annually, at least 2 percent of patients in Africa and Asia and 4 percent of patients living in Latin America should be migrated from first line treatment to second line treatment for medical reasons.

**Increased Prices for Second Generation Drugs**

As noted above, in developing countries the most widely used first line treatment is based on first generation ARVs: the d4T+3TC+NVP (30mg, 150mg, 200mg) Highly Active Antiretroviral Therapy (HAART) regime. This consists of one pill with a combined 380 milligrams of active pharmaceutical ingredients (APIs), given twice a day, or 0.2774 kg of API per patient per year (PPY). This regime is now available for less than $100 per year from some generic suppliers.

Second generation products are more expensive, for several reasons.

1. All other combinations now available require larger amounts of APIs. For example, a second generation/first line treatment of TDF+FTC+EFV (300mg, 200mg, 600mg) involves 0.4015 kg per year of APIs. The second line protease inhibitor regime consisting of AZT+3TC+LPV/r (600mg, 300mg, 800mg/200mg) is 0.6935 kg of APIs per year.

2. The term “second generation” is typically given to AIDS drugs invented after Brazil changed its patent law in 1996. Prior to the creation of the Global Fund, Brazil was “making
the market” for generic ARVs, but only for the products invented before the 1996 change in the Brazil patent law.

3. As the developing country with the oldest AIDS treatment program, Brazil is the largest purchaser of second generation AIDS drugs, mostly from brand name suppliers. Brazil issued its first compulsory license on an AIDS drug, efavirenz, which is used in both first and second line treatment, in 2007. Prices in the global market for APIs are much higher for products only purchased from the patent owner in Brazil.

4. Universal access to knowledge of manufacturing processes does not exist for new products, leading to fewer competitors entering the market unless they have developed their own expertise.

5. With fewer people using second generation generic products, the economies of scale are not as good as for the widely used, older products such as d4T+3TC+NVP.

The following table shows global prices for pharmaceutical APIs for eleven ARVs.

### Impact of Brazil Purchases of Generic APIs

Until the Global Fund and PEPFAR were created, the government of Brazil was the only significant purchaser of generic AIDS medicines. While many of the final products were formulated and manufactured domestically, Brazil also purchased APIs from generic manufacturers in India and China. The Brazil purchases of generic APIs had an enormous impact on the global prices for APIs. For example, the global prices of generic APIs for 3TC fell from more than $20 thousand per kilo in 1996, to less than $300 per kilo in 2004. These global price decreases not only benefited Brazil, but also created the possibility of low-cost ARV production for Africa and other countries.

When Brazil introduced patent protection for pharmaceutical products in 1996, it stopped buying generic APIs for the newer ARVs invented after 1996. This had the practical effect of creating a dual market for ARV APIs. API prices for products invented before the patent law change were much cheaper than products invented after the patent law change. The table below illustrates the difference in global API prices. Using data collected by the WHO in 2004 from ARV API suppliers, the table compares the global prices for APIs for eleven ARVs, based upon the patent status of the products in Brazil.

For the six products that were off-patent in Brazil, the average (low/high) price was $382/$582 per kilo for the raw APIs. For the five patented products only purchased from brand name suppliers, the average global API prices were $1,540/$2,760.
Table 2: Difference in Raw Global API prices (2004) and Patent Status in Brazil

<table>
<thead>
<tr>
<th>Drug API</th>
<th>Low Price $ per kilo</th>
<th>High Price $ per kilo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purchased as Generics in Brazil</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Didanosine (ddI)</td>
<td>450</td>
<td>850</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>295</td>
<td>480</td>
</tr>
<tr>
<td>Stavudine (d4T)</td>
<td>580</td>
<td>775</td>
</tr>
<tr>
<td>Zidovudine (AZT)</td>
<td>360</td>
<td>510</td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td>320</td>
<td>475</td>
</tr>
<tr>
<td>Indinavir (IDV)</td>
<td>285</td>
<td>400</td>
</tr>
<tr>
<td><strong>Average:</strong></td>
<td><strong>382</strong></td>
<td><strong>582</strong></td>
</tr>
<tr>
<td><strong>Purchased from Brand Name Manufacturers in Brazil</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efavirenz (EFV)</td>
<td>1,200</td>
<td>1,600</td>
</tr>
<tr>
<td>Abacavir (ABC)</td>
<td>1,500</td>
<td>3,500</td>
</tr>
<tr>
<td>Lopinavir (LPV);</td>
<td>2,900</td>
<td>4,000</td>
</tr>
<tr>
<td>Nelfinavir (NFV)</td>
<td>900</td>
<td>1,400</td>
</tr>
<tr>
<td>Saquinavir (SQV)</td>
<td>1,200</td>
<td>3,300</td>
</tr>
<tr>
<td><strong>Average:</strong></td>
<td><strong>1,540</strong></td>
<td><strong>2,760</strong></td>
</tr>
</tbody>
</table>

Source: Source and Prices of Active Pharmaceutical Ingredients, WHO/HIV/AMDS.

As noted, this is an important illustration of the relationship between purchases of generic products in middle-income countries and the prices of drugs in low-income countries, and it should inform the decision of UNITAID in considering geographic coverage of the patent pool. The larger the global market for APIs, the more the investment, entry and competition by generic suppliers.

Global Prices for First and Second Generation AIDS Drugs (2007)

The difference in prices for first and second generation AIDS drugs is illustrated below. Using data from the 2007 MSF survey of AIDS drug prices, prices are presented in terms of U.S. dollars per formulated and delivered kilo of active pharmaceutical ingredient (API). Included in the table are eight products, including two fixed dose combinations that are widely used first generation drugs, and eight products, including three FDCs, which are important second generation drugs. (As discussed above, the components of all of the first generation products were developed before the 1996 changes in the Brazil patent law, and have long been sold as generics in Brazil and in some other middle-income countries.)

The first line FDC product d4T+3TC+NVP, which is the most widely used treatment in the developing world, is also highlighted as an important benchmark.
Table 3: Prices per Formulated API for First and Second Generation AIDS Drugs

<table>
<thead>
<tr>
<th>Product</th>
<th>Category</th>
<th>Unit Price</th>
<th>Unit Price</th>
<th>Number of</th>
<th>Price Per</th>
<th>Price per</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Brand</td>
<td>Lowest</td>
<td>Suppliers</td>
<td>Kilo Brand</td>
<td>Kilo Lowest</td>
</tr>
<tr>
<td><strong>First Generation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AZT</td>
<td>All Cats</td>
<td>0.290</td>
<td>0.142</td>
<td>6</td>
<td>$967</td>
<td>$473</td>
</tr>
<tr>
<td>3TC</td>
<td>All Cats</td>
<td>0.095</td>
<td>0.059</td>
<td>7</td>
<td>$633</td>
<td>$393</td>
</tr>
<tr>
<td>AZT+3TC</td>
<td>All Cats</td>
<td>0.325</td>
<td>0.183</td>
<td>7</td>
<td>$722</td>
<td>$407</td>
</tr>
<tr>
<td>ddI</td>
<td>Cat 1</td>
<td>0.789</td>
<td>0.363</td>
<td>4</td>
<td>$1,973</td>
<td>$908</td>
</tr>
<tr>
<td>d4T+3TC+NVP</td>
<td>Cat 1</td>
<td>0.470</td>
<td>0.159</td>
<td>6</td>
<td>$1,205</td>
<td>$356</td>
</tr>
<tr>
<td>IDV</td>
<td>Cat 1</td>
<td>0.274</td>
<td>0.220</td>
<td>4</td>
<td>$685</td>
<td>$550</td>
</tr>
<tr>
<td>ddI</td>
<td>Cat 2</td>
<td>0.846</td>
<td>0.363</td>
<td>4</td>
<td>$2,115</td>
<td>$908</td>
</tr>
<tr>
<td>d4T+3TC+NVP</td>
<td>Cat 2</td>
<td>0.784</td>
<td>0.139</td>
<td>6</td>
<td>$2,010</td>
<td>$356</td>
</tr>
<tr>
<td>IDV</td>
<td>Cat 2</td>
<td>0.470</td>
<td>0.220</td>
<td>4</td>
<td>$1,175</td>
<td>$550</td>
</tr>
<tr>
<td>d4T</td>
<td>Cat 2</td>
<td>0.089</td>
<td>0.033</td>
<td>7</td>
<td>$2,225</td>
<td>$825</td>
</tr>
<tr>
<td>NVP</td>
<td>Cat 2</td>
<td>0.600</td>
<td>0.066</td>
<td>8</td>
<td>$3,000</td>
<td>$330</td>
</tr>
<tr>
<td><strong>Unweighted average:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>$1,195</strong></td>
<td><strong>$530</strong></td>
</tr>
<tr>
<td><strong>Second Generation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF+FTC</td>
<td>All Cats</td>
<td>0.875</td>
<td>0.750</td>
<td>2</td>
<td>$1,750</td>
<td>$1,500</td>
</tr>
<tr>
<td>AZT+3TC+ABC</td>
<td>All Cats</td>
<td>1.167</td>
<td>0.750</td>
<td>5</td>
<td>$1,556</td>
<td>$1,000</td>
</tr>
<tr>
<td>ATV</td>
<td>Cat 1</td>
<td>0.484</td>
<td>0.484</td>
<td>1</td>
<td>$3,227</td>
<td>$3,227</td>
</tr>
<tr>
<td>SQV</td>
<td>Cat 1</td>
<td>0.288</td>
<td>0.270</td>
<td>3</td>
<td>$1,440</td>
<td>$1,350</td>
</tr>
<tr>
<td>LPV/r</td>
<td>Cat 1</td>
<td>0.228</td>
<td>0.228</td>
<td>3</td>
<td>$1,373</td>
<td>$1,373</td>
</tr>
<tr>
<td>NFV</td>
<td>Cat 1</td>
<td>0.293</td>
<td>0.277</td>
<td>4</td>
<td>$1,465</td>
<td>$1,385</td>
</tr>
<tr>
<td>TDF</td>
<td>Cat 1</td>
<td>0.567</td>
<td>0.534</td>
<td>4</td>
<td>$1,890</td>
<td>$1,780</td>
</tr>
<tr>
<td>EFV</td>
<td>Cat 1</td>
<td>0.650</td>
<td>0.506</td>
<td>7</td>
<td>$1,083</td>
<td>$843</td>
</tr>
<tr>
<td><strong>Unweighted average:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>$1,723</strong></td>
<td><strong>$1,557</strong></td>
</tr>
<tr>
<td>ATV</td>
<td>Cat 2</td>
<td>0.582</td>
<td>0.582</td>
<td>1</td>
<td>$3,880</td>
<td>$3,880</td>
</tr>
<tr>
<td>TDF+FTC+EFV</td>
<td>Cat 2</td>
<td>2.830</td>
<td>1.333</td>
<td>2</td>
<td>$2,573</td>
<td>$2,121</td>
</tr>
<tr>
<td>SQV</td>
<td>Cat 2</td>
<td>0.603</td>
<td>0.270</td>
<td>3</td>
<td>$3,015</td>
<td>$1,350</td>
</tr>
<tr>
<td>LPV/r</td>
<td>Cat 2</td>
<td>0.457</td>
<td>0.457</td>
<td>3</td>
<td>$2,753</td>
<td>$2,753</td>
</tr>
<tr>
<td>NFV</td>
<td>Cat 2</td>
<td>0.603</td>
<td>0.277</td>
<td>4</td>
<td>$3,015</td>
<td>$1,385</td>
</tr>
<tr>
<td>TDF</td>
<td>Cat 2</td>
<td>0.567</td>
<td>0.546</td>
<td>4</td>
<td>$1,890</td>
<td>$1,820</td>
</tr>
<tr>
<td>EFV</td>
<td>Cat 2</td>
<td>1.800</td>
<td>0.506</td>
<td>7</td>
<td>$3,000</td>
<td>$843</td>
</tr>
<tr>
<td><strong>Unweighted average:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>$2,875</strong></td>
<td><strong>$1,892</strong></td>
</tr>
</tbody>
</table>

Consistent with the theory that economies of scale, manufacturing know-how and competition are important, the lowest prices per kilo of API are available for the most widely used first generation/first line products. The highest prices are for second generation products that are sold by brand name companies under tiered pricing agreements in middle-income countries.

**Patents**

In the past seven years, there has been a significant increase in the number of patents on pharmaceutical inventions and other relevant fields of technology. WIPO reports the following trends in Patent Cooperation Treaty (PCT) patent filings, as measured by the number of inventions claimed.

| Table 4: PCT Applications Published by Field of Technology |
|-------------------------------|------|------|------|------|------|------|------|------|
| Macromolecular Chemistry, Polymers | 3690 | 4152 | 4252 | 4367 | 4365 | 4881 | 5908 | 5989 | 62% |
| Macromolecular Macromolecular Chemistry, Polymers | 3640 | 4223 | 4545 | 5242 | 5705 | 6226 | 6515 | 6168 | 59% |
| Pharmaceuticals & Cosmetics | 7384 | 9561 | 9653 | 9979 | 9488 | 11252 | 13925 | 14096 | 91% |
| Biotechnology | 6795 | 9282 | 8996 | 8605 | 7663 | 7504 | 7422 | 7308 | 8% |
| Chemical Engineering | 3851 | 4455 | 4767 | 5367 | 4907 | 4950 | 5685 | 5899 | 53% |

Source: WIPO Statistics Database.

We have less information regarding the granting of patents in developing countries, but some data suggest that patent filings will be more extensive in developing countries than in the past. First, the WTO TRIPS Agreement came into force on January 1, 1995, and the ten-year transition period for non-LDCs expired in January 2005. Despite the fact that LDCs are not obligated by the WTO to issue or enforce patents on pharmaceutical products until 2015, and LDCs are excluded from the US 301 List, only 3 LDCs in Africa have reportedly exploited this flexibility in their national laws. The creation and strengthening of regional patent offices in Africa, combined with the creation of new, donor-funded markets for medicines in low-income countries may have also contributed to an increase in patent registrations in low-income countries. For example, Gilead sells two important AIDS drugs: TDF and FTC. TDF was brought to market in 2001, before the creation of the Global Fund, and is only patented in 2 of 99 low-income countries. FTC was brought to market in 2003, after the creation of the Global Fund, and patents were reportedly filed in 45 countries of the 99 countries, including 38 countries in Africa.

**Patents that Are Funded or Owned by Non-Profit Institutions**

AIDS, Tuberculosis and Malaria are areas of global concern, and there is considerable public sector and philanthropic donor investment in innovation to treat these diseases. Patents that are a consequence of government or philanthropic support, or which are owned by non-profit institutions, including government or private sector research institutions and universities, would
be among those solicited for the licensing to the pool. In some cases, researchers and donors, including but not limited to governments, may have certain rights in inventions.

For example, among the AIDS drugs that are subject to various public interest clauses in the United States under the U.S. Bayh-Dole Act are patents on d4T, ddC, ddI, ritonavir, lopinavir, FTC, T-20 and abacavir.⁷

**Relationship between the Patent Pool and Other Measures to Promote Competition and Effective Procurement**

The proposed UNITAID Patent Pool would be one of several efforts to promote competition and efficient procurement. Brazil, Thailand and many other countries have achieved considerable cost savings through price negotiations that are strengthened by the possibility of issuing compulsory licenses. Several countries have directly used TRIPS flexibilities to limit patent coverage, issue compulsory licenses, or authorize parallel trade in medicines. The Clinton Foundation HIV/AIDS Initiative, with the support of UNITAID, has played a very important role in improving procurement practices, including virtual pooling and joint price negotiations. All of these efforts are very important and effective. The UNITAID patent pool would complement each of these efforts. The existence of the patent pool would likely influence competition and prices, even when the patent owners were not directly licensing patents to the pool, because the enhanced global norms for open competition would raise expectations that products would be priced closer to manufacturing costs. When patents are licensed to the pool, efforts like pooled procurement or price negotiations should be more effective than they would be in the absence of transparent open licenses for generic products. The challenge for this cost-benefit analysis is to assign a value to the patent pool in terms of increased competition, lower prices, and benefits in terms of innovation.

**Costs of the Pool**

As estimated and proposed by the UNITAID Secretariat, the initial start-up costs of the pool should total $1.5 million per year for three years, or $4.5 million. The $1.5 million budget is anticipated to be sufficient to pay for the hiring of at least two senior and two support staff and pay for office expenses, travel for the board, staff and advisory boards, as well as insurance, accounting, legal, consulting, and public relations services.

**Benefits of the Patent Pool**

---

⁷ For example, under 18 USCS 202(c)(4), a U.S. Federal agency that funds research “shall have a nonexclusive, nontransferrable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any subject invention throughout the world: Provided, That the funding agreement may provide for such additional rights, including the right to assign or have assigned foreign patent rights in the subject invention, as are determined by the agency as necessary for meeting the obligations of the United States under any treaty, international agreement, arrangement of cooperation, memorandum of understanding, or similar arrangement, including military agreement relating to weapons development and production.”
For patent owners, a patent pool with widely accepted standardized licenses and good relationships with users of patents (generic suppliers), regulators, governments and donors can offer a cost-effective and rapid method of implementing open licensing of inventions that appropriately addresses such issues as the quality of licensed products, royalty rates and collection methods, and the management of intellectual property rights for improvements on licensed inventions, consistent with transparency and the rule of law.

For drug developers, access to the portfolio of patents in the pool can make it easier to develop new fixed dose combinations for other improvements in delivery methods, such as simplified dosing, heat stabilization of products, oral delivery of T-20, etc.

For patients, the patent pool can contribute to more competition and better products, particularly in the development of appropriate formulations such as triple FDCs, FDCs for Preventing Mother-to-Child Transmission (PMTCT), and pediatric formulations, as well as better prices and assurances regarding the quality of products. It will also help to ensure early entry of improved treatments into the market in developing countries.

For donors, the patent pool provides a mechanism to enhance the transparency of the patent landscape, enhance and expand the role of open licensing of inventions, and to increase competition, innovation, and to lower prices for products.

Brook Baker, of Health GAP and Northeastern University, estimates that open licensing of AIDS drugs through the patent pool could lower the prices of second line treatments by 50 percent (below originator prices) in low-income countries and by 70 percent in middle-income countries. (See attachment)

In sub-Saharan Africa alone, the WHO estimates that each year 2 percent of the more than 2 million patients receiving treatment will need to shift to second line treatments. Holding this rate steady, the number of patients requiring second line treatments will increase by more than 200,000 within five years.

**Benefits and Contributions of the Patent Pool to Open Licensing**

Originator prices and licensing strategies for second generation products are heterogeneous, and difficult to predict. Rather than present a single prediction, one can consider a range of possible scenarios, each based on a different set of assumptions regarding demand for second line/second generation products, originator prices and the estimated savings from open competition.

Each scenario presents the possible savings achieved by a patent pool in terms of a percentage. This percentage can be said to represent both the share of the products subject to open competition, as well as the impact of the pool in promoting competition by introducing open licensing norms in countries where patents exist.
In the most optimistic cases, the patent pool would be widely supported by donor and recipient
governments, civil society, socially responsible investors and opinion leaders, and it would be
decisive in making open licensing the norm for second line/second generation markets in low-
and middle-income countries. In less optimistic cases, the patent pool would be less effective in
promoting open licensing, particularly for middle-income countries. These calculations are not
ideal and lack, for example, feedback between the role of open competition in middle income
countries and the price savings in low-income countries. They do illustrate, however, the
possible benefits of measures to strengthen competition, demonstrate the importance of such
interventions, and justify the relatively modest funding requirements of a patent pool.

Several scenarios are presented below. Low-income countries are designated as Category 1, and
middle-income countries are designated as Category 2.
## Scenarios

### Scenario 1

<table>
<thead>
<tr>
<th>Assumptions:</th>
<th>Cat. 1</th>
<th>Cat. 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients requiring second generation/second line treatments</td>
<td>200,000</td>
<td>40,000</td>
</tr>
<tr>
<td>Innovator Price</td>
<td>750</td>
<td>3,000</td>
</tr>
<tr>
<td>Generic Savings</td>
<td>30%</td>
<td>70%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Savings Given Impact Factor</th>
<th>10%</th>
<th>25%</th>
<th>50%</th>
<th>75%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat. 1</td>
<td>4,500,000</td>
<td>11,250,000</td>
<td>22,500,000</td>
<td>33,750,000</td>
<td>45,000,000</td>
</tr>
<tr>
<td>Cat. 2</td>
<td>8,400,000</td>
<td>21,000,000</td>
<td>42,000,000</td>
<td>63,000,000</td>
<td>84,000,000</td>
</tr>
</tbody>
</table>

### Scenario 2

<table>
<thead>
<tr>
<th>Assumptions:</th>
<th>Cat. 1</th>
<th>Cat. 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients requiring second generation/second line treatments</td>
<td>300,000</td>
<td>60,000</td>
</tr>
<tr>
<td>Innovator Price</td>
<td>750</td>
<td>3,000</td>
</tr>
<tr>
<td>Generic Savings</td>
<td>50%</td>
<td>70%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Savings Given Impact Factor</th>
<th>10%</th>
<th>25%</th>
<th>50%</th>
<th>75%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat. 1</td>
<td>11,250,000</td>
<td>28,125,000</td>
<td>56,250,000</td>
<td>84,375,000</td>
<td>112,500,000</td>
</tr>
<tr>
<td>Cat. 2</td>
<td>12,600,000</td>
<td>31,500,000</td>
<td>63,000,000</td>
<td>94,500,000</td>
<td>126,000,000</td>
</tr>
</tbody>
</table>

### Scenario 3

<table>
<thead>
<tr>
<th>Assumptions:</th>
<th>Cat. 1</th>
<th>Cat. 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients requiring second generation/second line treatments</td>
<td>500,000</td>
<td>100,000</td>
</tr>
<tr>
<td>Innovator Price</td>
<td>750</td>
<td>3,000</td>
</tr>
<tr>
<td>Generic Savings</td>
<td>50%</td>
<td>87.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Savings Given Impact Factor</th>
<th>10%</th>
<th>25%</th>
<th>50%</th>
<th>75%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat. 1</td>
<td>18,750,000</td>
<td>46,875,000</td>
<td>93,750,000</td>
<td>140,625,000</td>
<td>187,500,000</td>
</tr>
<tr>
<td>Cat. 2</td>
<td>26,250,000</td>
<td>65,625,000</td>
<td>131,250,000</td>
<td>196,875,000</td>
<td>262,500,000</td>
</tr>
</tbody>
</table>
Break-Even Analysis

<table>
<thead>
<tr>
<th>Undiscounted savings:</th>
<th>Scenario 1</th>
<th>Scenario 2</th>
<th>Scenario 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat 1</td>
<td>45,000,000</td>
<td>112,500,000</td>
<td>187,500,000</td>
</tr>
<tr>
<td>Cat 1 + Cat 2</td>
<td>129,000,000</td>
<td>238,500,000</td>
<td>450,000,000</td>
</tr>
</tbody>
</table>

The break even “impact” probability @ $1.5 million annual budget for patent pool

<table>
<thead>
<tr>
<th></th>
<th>Scene 1</th>
<th>Scene 2</th>
<th>Scene 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat 1</td>
<td>3.33%</td>
<td>1.33%</td>
<td>.80%</td>
</tr>
<tr>
<td>Cat 1 + Cat 2</td>
<td>1.16%</td>
<td>0.63%</td>
<td>.3%</td>
</tr>
</tbody>
</table>

Concluding Summary and Comment

This analysis has looked at the costs and expected benefits of the proposed UNITAID patent pool. The costs of the pool are assumed at $1.5 million per year.

The quantified benefits of the pool include expected lower prices for second generation/second line products, as a consequence of a higher level of generic competition.

The most important assumptions that drive the results in this analysis are:

1. The expected originator prices and the savings from generic competition, and
2. The expected number of patients requiring access second generation/second line products.

Of these two assumptions, the most conservative assumption is in the number of patients that will require access to second generation/second line productions. Of the approximately two million patients today receiving treatment in sub-Saharan Africa, only an estimated one percent is reportedly receiving WHO defined second line treatments. This is far below the numbers of patients who receive second line treatments in Europe, the United States or Latin America.

Scenario 1 predicts only 200,000 patients in all low-income countries requiring treatment with second generation/second line products. Scenario 3, in theory the most aggressive, only assumes 500,000 patients requiring such treatments. Based purely on the rate of use of both second generation and second line treatments in the Europe and the United States, even the Scenarios 3 figures may be low for the Category 1 low-income countries.

The same can be said of the assumptions regarding patients in the Category 2 countries. The WHO data suggests 92 thousand persons in Latin America alone are already receiving second line treatments, a figure that is only slightly lower than the 100,000 patients used in Scenario 3, which is the most optimistic in terms of estimated benefits. The relatively low numbers used in the scenarios above for both Category 1 and Category 2 are designed to reflect expected additional demand for second generation and second line products. However, clearly the benefits of open generic competition will flow also to the patients already using second line/second
generation products, so the estimated benefits are systematically underestimated for Categories 1 and 2, and particularly for Category 2.

The assumptions regarding originator prices are based upon recent prices by originators, before facing serious competition from generic manufacturers. The estimated savings from competition are based upon data from the MSF surveys of ARV drug prices, recent data from Thailand and Brazil following the introduction of generic competition for second line/generation products, and estimates by several drug pricing experts.

The assumptions regarding originator prices, generic savings and demand for second line/generation products are used to calculate the raw, undiscounted benefits of open licensing. In the first three tables, these benefits are then considered at 10, 25, 50, 75 or 100 percent, to reflect the expected savings under different assumptions regarding the impact of the pool on outcomes.

A patent pool will be only one factor among several in determining outcomes. In the absence of such a pool, generic suppliers, treatment activists, procurement managers, and developing country governments have managed to implement generic competition to some extent for many important products. The “impact” of the pool is an assumption regarding the degree to which open competition is expanded by the existence and activities of a UNITAID patent pool. A 10, 25 or 50 percent impact factor would give the pool the relevant share of credit for expected savings from competition in the area of new products. By showing a range of possible impact factors, readers can consider several possible values.

In the table labeled “Break-Even Analysis,” there is a calculation of the impact factor that would just break even with the estimated $1.5 million annual budget of the patent pool. This includes two rows of figures, one for Category 1-only savings, and the other for the combined value of Category 1 and Category 2 savings.

The most conservative approach is to consider only the expected the impact of the pool for Scenario 1/Category 1. Here, savings are only considered for low-income countries, in the most conservative assumptions regarding demand. For this combination, the pool would be justified if it has a combined impact of 3.3 percent on expected competition for second generation/second line products. Looking only at Category 1 savings, the break-even impact would be 1.33 or .8 percent for Scenarios 2 and 3.

When one takes into account both Category 1 and Category 2 savings, the break-even impact figures are 1.16, .63 and .33 percent, respectively, for Scenarios 1, 2 and 3. In other words, if the pool only has a 1 percent impact on generic competition, it will pay for itself.

As noted in the introduction, the quantitative analysis presented above does not capture other possible benefits to be derived from the pool. There is no quantification of the benefits of increased competition and better management of patent portfolios in the development of better manufacturing processes, new fixed dose combinations (FDCs) or other improvements in delivery methods, such as simplified dosing, heat stabilization of products, oral delivery of

---

8 If this analysis was done in 2000, the originator prices would have been far higher -- $10,000 for the most common first line regime used today, for example.
injectable treatments, and the development of appropriate formulations such as triple FDCs, FDCs for Preventing Mother-to-Child Transmission (PMTCT), and pediatric formulations. These yet-to-be-quantified benefits are likely to be very large, and almost any success in this area would easily justify the entire start-up cost of the patent pool. (The expected quantified benefits for innovation could be addressed in a subsequent analysis.)

In terms of considering the proposal to establish the UNITAID patent policy, policy makers may find it useful to consider the 10 and 25 percent impact calculations from Scenario 2. These seem to require only modest expectations of the impact of a UNITAID patent pool on competition for second line/second generation products.

### Low End of Scenario 2 Benefits

<table>
<thead>
<tr>
<th>Savings Given Impact Factor</th>
<th>10%</th>
<th>25%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat. 1</td>
<td>11,250,000</td>
<td>28,125,000</td>
</tr>
<tr>
<td>Cat. 1 plus Cat. 2</td>
<td>33,850,000</td>
<td>59,625,000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Benefit-Cost Ratio</th>
<th>10%</th>
<th>25%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat. 1</td>
<td>7.5</td>
<td>18.8</td>
</tr>
<tr>
<td>Cat. 1 plus Cat. 2</td>
<td>22.6</td>
<td>39.5</td>
</tr>
</tbody>
</table>
Drug firms 'must pool patents'

Drug firms must allow the generic production of their HIV medication if the deaths of millions of people are to be avoided, British MPs warn.

The All Party Parliamentary Group on Aids wants to see a patent pool in which firms would give up their rights in exchange for a royalty fee.

They describe a "treatment timebomb" in which the number of people with HIV will increase fivefold by 2030.

Growing resistance to basic drugs means millions need more expensive ones.

"We are sitting on a treatment timebomb," said David Borrow, chair of the group of MPs who wrote the report.

"We must reduce the price of second-line medicines and less toxic first-line medicines before millions need them. We cannot sleepwalk into a situation where we can only afford to treat a tiny proportion of those infected."

Governments around the world, including the UK, have signed up to the goal of 'Universal Access to HIV treatment, prevention, care and support' by 2010.

But the report warns that the world is not on track to meet this target, noting that only a third of the 9m people who need it have access to HIV treatment.

Good will

The majority of people who are being treated in the developing world are treated with a combination of cheaper drugs which can have serious side effects. Because of this they are barely used in the West.

"The pharmaceutical industry has an opportunity to act now to help prevent future human catastrophe"

Mike Foster International Development Minister

Three years ago, the World Health Organisation recommended a shift away from these medications to less toxic ones based on either Zidovudine or Tenofovir.

But these remain significantly pricier than the older ones: currently the Tenofovir-based combination is more than twice as expensive as the traditional combination.

This is despite the fact, the report notes, that a voluntary license scheme for this drug has allowed eleven different generic manufacturers - all in India - to produce it.

A much broader form of licensing is being proposed by Unitaid, the UN body on drugs for killer diseases.

This would involve drug firms voluntarily putting their patents into a single pool in return for a royalty. Manufacturers or researchers who wish to use the relevant patents are then able to do so for a fee.

International Development Minister, Mike Foster, said: "The simple fact is that the HIV epidemic continues to outstrip our best efforts. Five people are infected with HIV every minute and for every two people put on treatment, there are 5 people newly infected with HIV.

"The pharmaceutical industry has an opportunity to act now to help prevent future human catastrophe. It is time for them to state their clear commitment to make new HIV medicines affordable to those who need them most, by working with Unitaid to develop a patent pool."

GlaxoSmithKline (GSK) is cited by the report as saying it did not at present see the point of putting its HIV patents in a pool.

"For HIV, we believe that extensive research is already underway, and thus it is not a neglected disease. Millions of dollars are ploughed into research into HIV every year by the pharmaceutical industry.

"To improve access, we already have an extensive voluntary licensing programme for HIV across Sub Saharan Africa, involving eight licensees. These licensees are free to develop FDCs [Fixed-Dose Combination retrovirals] and paediatric versions and we believe this is a much simpler approach than the creation of a patent pool."

Gilead, which makes Tenofovir, has said it is interested in the idea.

"We believe if structured appropriately, Unitaid’s patent pool can play a critical role in expanding access to antiretroviral treatment for patients around the world by encouraging the development of new fixed-dose combinations and pediatric formulations, lowering prices, while respecting intellectual property," said the company’s senior vice president Gregg Alton.
International development minister urges firms to pool HIV patents

- 50 million will need new drugs by 2030, MPs warn
- Resistance growing to basic combinations

Sarah Boseley, health editor
guardian.co.uk, Sunday 12 July 2009 20.34 BST

Drug companies should give up their patent rights to HIV medicines to help prevent the deaths of millions of people in poor countries, a British government minister will say this week.

The international development minister, Mike Foster, will call on pharmaceutical companies to put lives before profits, as the all-party parliamentary group on Aids publishes a report this week detailing the scale of the "treatment timebomb". By 2030, they estimate, 50 million people will need new drugs, which are currently prohibitively expensive, to keep them alive.

Three million people are on cheap, basic HIV drug combinations, but they are only a third of those in need and resistance is growing to these drugs both in the developing world and in the west.

New and improved drugs are urgently required, but they are expensive, and cheap generic copies of the newest drugs can no longer easily be made and sold because of tightened intellectual property rules in India and China.

The UK generally has a very close relationship with the drug companies, which regard patents as the means of recouping the substantial costs of researching and developing new drugs.

But Foster says they must change their stance on HIV. He wants companies to contribute to a "patent pool", which the international drug-purchasing facility, Unitaid – set up by a number of donor countries, including the UK – is trying to establish.

"While it is absolutely vital that we work to reduce the human cost of HIV by focusing our efforts on preventing new infections, we must also face up to the stark reality of the treatment challenge we face. The pharmaceutical industry has an opportunity to act now to help prevent future human catastrophe. It is time for them to state their clear commitment to make new HIV medicines affordable to those who need them most."

According to the all-party report, if HIV patents are put in a pool, generics companies – which make the cheap combinations now used in Africa – will be permitted to make low-cost copies of newer drugs and devise new combinations in a single pill, which is important for people living in poverty.

The report lays out in stark terms the coming crisis. "It took political activism almost a decade ago to make life-saving drugs available to the poor in developing countries," it says. "Only a third of those who need it are on treatment and this treatment will not work for them forever. Political activism is needed once more to ensure that the next generation of drugs is available to the world's poorest in future."

MP David Barrow, who chairs the group, said: "We are sitting on a treatment timebomb. We must reduce the price of second-line medicines and less toxic first-line medicines before millions need them. We cannot sleepwalk into a situation where we can only afford to treat a tiny proportion of those infected."

The only way to end the HIV/AIDS epidemic is to prevent infection, the report says, but because the drugs suppress the virus, those receiving treatment are much less likely to pass it on.
Contrary to the impression given in your report (GlaxoSmithKline urged to pool its patents on HIV drugs, 7 September), GSK has been in discussions with Unitaid to better understand their objectives regarding an HIV patent pool. In fact, Unitaid's own progress report references two meetings with GSK in May and July of this year, and we are open to further meetings. We have not ruled out the possibility of participating in the pool, but have yet to see any real proposal that provides benefits beyond GSK's existing approach.

In our view the notion of a patent pool is to stimulate research, which is why GSK was the first company to create a patent pool focused on 16 neglected tropical diseases where there is a severe lack of research. This patent pool demonstrates our flexible approach to intellectual property rights.

We are in no way complacent about HIV. For the last 20 years GSK has made concerted efforts to help tackle the epidemic. We have offered all our Aids medicines to the world's poorest countries at not-for-profit prices since 2001, and have granted eight voluntary licences to African generic companies to enable them to make versions of our Aids medicines. In the last two months alone, we announced a series of targeted commitments around HIV in children, including creation of a new fund to help prevent mother-to-baby transmission of HIV and seed funding for public-private partnerships to research Aids medicines for children. Fighting this disease requires a multilateral approach and we are fully committed to playing our part.

Chris Strutt

Senior vice-president, GlaxoSmithKline, government affairs, public policy and patient advocacy
Unitaid welcomes GlaxoSmithKline’s renewed interest in the Unitaid patent pool initiative for HIV/Aids medicines and its openness to taking a flexible approach to managing intellectual property (Letters, 10 September); and GlaxoSmithKline urged to pool its patents on HIV drugs, 7 September). Wherever multiple patents owned by different companies are required to make a product, patent pools may offer a useful solution. Pills that combine three medicines into one tablet to treat HIV/Aids are a good example of such products.

The World Health Organisation recommends the use of such pills because they make it easier for patients to take their treatment and reduces the risk that viral resistance will render the drugs useless. However, patents from two to three different companies are usually required, meaning that single-company initiatives will not do the trick. The Unitaid pool will facilitate the development of combination pills and children's formulations of HIV/Aids medicines for use in developing countries, based on voluntary patent contributions from pharmaceutical companies. Those companies will receive royalty payments for doing so. The pool will also enable robust competition among drug producers to ensure that international resources to fight Aids, currently under severe strain, are spent as efficiently as possible.

The situation is urgent. An estimated 6 million people needing access to Aids treatment, including hundreds of thousands of children, still do not receive it. This number will only grow in the years to come. We ask GSK and other Aids drug patent-owners to work with us to make this initiative a success.

Ellen 't Hoen

Senior adviser IP & medicines patent pool, Unitaid