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## *Estimating Resource Requirements for AIDS Treatment*

### **Case study: Estimating resource requirements for AIDS treatment in Burkina Faso**

A recent World Bank supervision mission to Burkina Faso provided technical support to government counterparts in launching an ART project. The mission was expected to review and agree on a set of priority interventions to be funded during 2002, taking into account activities of other key development partners; review implementation and institutional arrangements; and initiate work on the ART to respond to the government's request for International Development Association assistance in this area.<sup>1</sup>

In 2003 Burkina Faso's HIV prevalence rate was 4 percent.<sup>2</sup> The key decision facing the government was whether, in what form, how, and when to embark on ART for people affected with HIV/AIDS.

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<sup>1</sup> This case write-up is based on the mission report. But some data and results have been adjusted or further elaborated in order to better fit the purposes of this Guide.

<sup>2</sup> "Prevalence" measures the percentage of the population in question estimated to be affected. Schneidman, Miriam. 2002. *The Health System and the Poor: Draft Report on Burkina Faso*. World Bank, Washington, D.C.

### ***Relevant data and information***

To make an acceptably accurate assessment of an ART program in Burkina Faso, at least the following information should be available. Otherwise, the best available estimates must be used:

- GDP of the country
- Amount of government spending on health care
- Budget shares for government spending in all sectors, including health
- Prevalence of HIV
- Current acquisition price of ARVs
- Potentially available best prices of ARVs in the world market
- Amount of donor funds available to the country to implement ART
- Current allocation of funds within HIV/AIDS issues, especially on prevention
- Currently prevailing health and development challenges facing the country
- Documented experiences of ART in Burkina Faso, if any.

#### **Key statistics within Burkina Faso in 2003 were:**

- Average household spending for health: \$8 (rural \$4, urban \$21)
- Share of total household health spending going to medicines: 83 percent (rural 89 percent, urban 78 percent)
- Public health spending as a share of GDP, 2001: 2.1 percent
- Public health spending as a share of government spending, 2003: 9.8 percent
- Total expenditure on health, 2003: 4 percent of GDP

### ***Analysis***

Projections of the evolution of the HIV/AIDS epidemic (based on the most recent available data) under alternative assumptions resulted in different future scenarios.<sup>3</sup> Assuming a 4 percent HIV prevalence in 2005, the consultant calculated the most conservative of these scenarios.

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<sup>3</sup>Neither the information nor the time available for the study allowed for considering the long-term consequences, or for directly assessing existing health capacity to treat HIV/AIDS.

To account for the impact of a hypothetical ARV program on the survival of people living with AIDS, the consultant assumed that the number of people with AIDS under the 4 percent scenario would increase in 2005 from 33,245 (report estimation) to 35,723 and in 2010 from 40,000 to 54,646 (table A.1).

### **Cost of ARVs**

The average price negotiated by the Purchasing Agency of Generic Essential Medicines and Medical Supplies (CAMEG) of an ARV combination available to Burkina Faso was \$1,000 (per person per year). In a proposal to the Global Fund to Fight AIDS, Tuberculosis and Malaria, it was estimated that ARVs would cost \$1,410. At the same time, ARVs were available from Cipla (a low-cost generic manufacturer) for about \$333 per person per year and from the Clinton Foundation's initiative on HIV/AIDS at a further discounted price of \$140 per person per year<sup>4</sup> (table A.2).

Under the more optimistic assumptions, the projected cost of ART for all people with AIDS in Burkina Faso would be 0.14% of GDP and

**Table A.1 People living with HIV/AIDS in Burkina Faso, 2003–10**

<b>Group</b>	<b>2003</b>	<b>2005<sup>a</sup></b>	<b>2010</b>
Population with HIV/AIDS	270,000	305,0000	365,000
Population with AIDS	29,500	33,245	40,000
Population with AIDS (receiving ART)	29,500	35,723	54,646

a. Estimated assuming an 4% baseline prevalence of HIV in 2005.

Source: Estimates from World Bank mission report.

<sup>4</sup>Quoted in, among other sources, "Clinton Program Would Help Poor Nations Get AIDS Drugs"—*Wall Street Journal*—October 23, 2003.

**Table A.2 Projected cost of ART (drugs only) for all people with AIDS under high cost (\$1000), low cost (\$333), and lowest cost (\$140) price scenarios, 2003–10**  
(millions of U.S. dollars unless otherwise specified)

Price scenario	2003	2005	2010
<b>At the CAMEG negotiated price (\$1,000)</b>	<b>29.5</b>	<b>35.7</b>	<b>54.6</b>
–As share of GDP	0.98	1.07	1.26
–As share of health budget	42.9	46.7	54.9
<b>At Cipla’s price offer to Médecins Sans Frontières (\$333)</b>	<b>9.8</b>	<b>11.9</b>	<b>18.2</b>
–As share of GDP	0.33	0.36	0.42
–As share of health budget	14.3	15.6	18.3
<b>At Clinton Foundation price (\$140)</b>	<b>4.1</b>	<b>5.0</b>	<b>7.7</b>
–As share of GDP	0.14	0.15	0.18
–As share of health budget	6.0	6.5	7.7
<b>GDP projections<sup>a</sup></b>	<b>2,847</b>	<b>3,334</b>	<b>4,336</b>
Health budget projections	65.3	76.5	99.5

a. Projections assume an annual real growth of 5.4% in 2003 and thereafter.

Sources: World Bank mission report, Budget Projections: IDA Program Document for a PPRS Credit to Burkina Faso, April 15, 2002, p.8, table 1; Sources and prices of selected medicines and diagnostics for people living with HIV/AIDS, A joint UNICEF—UNAIDS—WHO—MSF Project, June 2003 and Clinton Program Would Help Poor Nations Get AIDS Drugs, *Wall Street Journal*, October 23, 2003

6.0 percent of the health budget in 2003. The pessimistic case projects 0.98 percent of GDP and 42.9 percent of the health budget. These percentages would likely increase in the medium-term because ART increases survival and, hence, the prevalence of AIDS.

### *Other costs*

The main health care costs in ART, other than the cost of ARVs themselves, are associated with: non-ARVs, diagnostic tests, personnel, and equipment (table A.3).

**Table A.3 Projected total cost of ART, per person per year, 2003 (U.S. dollars)**

Cost category	Lowest-cost scenario	High-cost scenario
ARV drugs	140	1,000
Other drugs	80	80
Biological monitoring	150	400
Personnel	200	200
Equipment	50	50
Total cost	620	1,730

In 1999 Burkina Faso's health budget was \$57.2 million, with 40 per cent funded from external sources. Providing treatment to all people with AIDS would imply a significant increase in budget for 2005 (table A.4).

### *Implications of the cost scenarios*

The price of ARV drugs is a major variable in the total cost of an ARV program. Depending on the country, other associated costs (such as

**Table A.4 Projected total cost of ART for all people with AIDS in Burkina Faso, under high cost (\$1,730), and lowest cost (\$620) price scenarios, 2003–10 (millions of U.S. dollars)**

	2003	2005	2010
High-cost scenario	51.0	61.8	94.5
Lowest-cost scenario	18.3	22.1	33.9

Source: Estimates from World Bank mission report.

personnel) also contribute significantly to total cost. Up to 2,000 patients might be cared for within the existing infrastructure in Burkina Faso. Significantly increasing that figure would probably require important investments in physical capacity and human resources. It is essential that the country procurement agency—the CAMEG—is able to take advantage of market conditions.

With an annual budget of \$2 million it would be possible to provide ARVs for 2,000 to 14,285 patients, depending on the unit cost of the treatment obtained. If the full cost of treatment were covered, the number of patients treated would range between 1,156 and 3,225 in high and low cost scenarios.

Given the government's financial constraints, one possibility is introducing user fees (that is, having patients pay for all or part of their treatment). But this may radically affect the selection of patients, broadening the health divide and highlighting privileges and class differences among people living with HIV/AIDS.

Likely problems from small ART programs include:

- *Pressure to be selected.* Poorer people likely to be discriminated against.
- *Significant stress on health staff* from having to apply eligibility criteria.
- *Potential sharing of medication* among family members if not all those with the disease are selected for treatment.
- *A black market.* Even in the optimistic case that 14,285 patients (48 percent of people living with AIDS) are treated, a strong unsatisfied need, fueled by the likely political publicity of the program, could increase demand from relatively affluent people. People with low incomes might have an incentive to divert part of the \$1,000 worth of medication to the market, especially if there are adverse effects in the course of treatment. Noncompliance, the loss of effectiveness, and the appearance of resistance could also result.

## Complicating the resource estimation model and applying it to other contexts

Program implementation requires investments in physical and human capital that cannot be estimated simply by multiplying patients treated and average cost. For large increases in the number of patients treated, it

is essential to assess the used and unused health system capacity and the additional investments in physical and human capital required for attaining specific coverage targets.

Introducing ART implies possible changes in the lifelong profile of treatment costs, an additional complication. The likely short-term effect of introducing or scaling up ART is an immediate increase in the health expenditures of the HIV/AIDS program. In the long term, the ART may reduce the rate of opportunistic infections and their associated costs, especially hospitalization. But improving ART allows people with HIV to live longer. So the life cycle costs for a single patient and the total spending on AIDS treatment are likely to grow if individual patterns and costs of care are maintained for an initial cohort of patients. The net impact on the costs of an individual's treatment, or on the total expenditure of an HIV/AIDS program, is thus uncertain and difficult to assess.

The parameters that define the epidemic and the required costs of treatment are likely to change. Simple statistical extrapolation of past data might be highly misleading, especially if the model aims at a distant time horizon. In any case, estimated numbers of people living with HIV/AIDS provided by statistical or epidemiological methods usually represent the maximum number of people to be treated, because only a proportion of the estimated number of people living with HIV/AIDS are likely to seek and obtain care. That proportion can also be extrapolated from past data, but it may change with ART programs. Experience from other countries where such change has already occurred might prove useful in assessing the likely effects.

Estimating the future evolution of an epidemic—and its associated costs—is highly speculative, due to the lack of information and the inherent uncertainty of the cost and effectiveness of available and future treatments. Transparency in the analytical procedures and assumptions for making projections will allow these projections to be easily adjusted as the parameters of the epidemic change, new treatments are introduced, or new evidence becomes available.

A simple model of financial resource estimation for an ART program would take at least the following factors into account:

- HIV prevalence rate and projections for the near future.
- GDP per capita and economic outlook for the country.

- Cost of ARVs (at current and best world prices, if different).
- International and national aid funding available for an ART program.

In addition to the factors detailed in the simple model, a complex model of resource estimation would take into consideration at least (and not conclusively) the following:

- Health infrastructure capacity (physical and human).
- Cost assumptions for scaling-up capacity to meet increased need.
- Different predictive assumptions of the impact of behavioral change.
- Different scenarios of new HIV incidence.
- An estimate of financial outflows and inflows (hospital care, productivity).
- Changes in household economic situations and the ability to pay for treatment.

Applying a simple model of resource requirements estimation to Kenya and South Africa, estimates of government spending and health sector budget outlays required for treating HIV/AIDS with ARVs, under different cost assumptions (tables A.5–A.8), are as follows:<sup>5</sup>

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<sup>5</sup> This illustration for Kenya and South Africa estimates the growth in the HIV/AIDS epidemic and the growth rate in the number of people with clinical AIDS along the same assumptions as those used for Burkina Faso. In reality, it is likely that the rate of growth of HIV incidence differs across countries, due to a host of complex socioeconomic and political factors.

**Table A.5 Projected number of people living with HIV/AIDS in Kenya and South Africa, 2002–10**

	2002	2005	2010
<b>Kenya</b>			
Population with HIV/AIDS <sup>a</sup>	2,500,000	2,825,000	3,390,000
Population treated with ARVs (10%)	250,000	282,500	339,000
<b>South Africa</b>			
Population with HIV/AIDS <sup>b</sup>	5,000,000	5,650,000	6,780,000
Population treated with ARVs (10%)	500,000	565,000	678,000

a. Data assume HIV/AIDS prevalence rate of ~8 percent, adult prevalence of ~15 percent.

b. Data assume HIV/AIDS prevalence rate of ~12 percent, adult prevalence of ~20 percent.

Source: www.unaids.org.

**Table A.6 Projected cost of ART (drugs only) for all people with AIDS in Kenya, under high cost (\$1,000), low cost (\$333), and lowest cost (\$140) price scenarios, 2002–10 (millions of U.S. dollars unless otherwise specified)**

Price scenario	2002	2005	2010
GDP projections <sup>a</sup>	11,296	11,860	12,453
Health budget projections <sup>b</sup>	271.1	284.6	298.9
ARV cost of \$1,000 per person per year	250	282.5	339
–As share of GDP	2.2	2.4	2.7
–As share of health budget	92.2	99.3	113.4
ARV cost of \$333 per person per year	83.3	94.2	113
–As share of GDP	0.7	0.8	0.9
–As share of health budget	30.7	33.1	37.8
ARV cost of \$140 per person per year	35.0	39.6	47.5
–As share of GDP	0.3	0.3	0.4
–As share of health budget	12.9	13.9	15.9

a. GDP projections are taken at 5 percent a year (consistent with Burkina Faso assumptions).

b. Health budget projections are held constant at 2002 (percentage of total GDP) terms. Source: GDP projections from World Bank country GINA data, [www.worldbank.org](http://www.worldbank.org). Health budget data from UNDP *Human Development Report 2003*, [www.undp.org/hdr2003/indicator/cty\\_f\\_KEN.html](http://www.undp.org/hdr2003/indicator/cty_f_KEN.html).

**Table A.7 Projected cost of ART (drugs only) for all people with AIDS in South Africa, under high cost (\$1,000), low cost (\$333), and lowest cost (\$140) price scenarios, 2002–10 (millions of U.S. dollars unless otherwise specified)**

Price scenario	2002	2005	2010
GDP projections <sup>a</sup>	113,492	119,167	125,125
Health budget projections <sup>b</sup>	4,199	4,409	4,630
ARV cost of \$1,000 per person per year	500	565	678
–As share of GDP	0.44	0.47	0.54
–As share of health budget	12	12.8	14.6
ARV cost of \$333 per person per year	166.6	188.3	225.8
–As share of GDP	0.15	0.16	0.18
–As share of health budget	4.0	4.3	4.9
ARV cost of \$140 per person per year	70.0	79.0	94.9
–As share of GDP	0.06	0.07	0.08
–As share of health budget	1.7	1.8	2.1

a. GDP projections are taken at 5 percent a year (consistent with Burkina Faso assumptions).

b. Health budget projections are held constant at 2002 (percentage of total GDP) terms.

Source: GDP projections from World Bank country GINA data, [www.worldbank.org](http://www.worldbank.org). Health budget data from UNDP Human Development Report 2003, [www.undp.org/hdr2003/indicator/cty\\_f\\_ZAF.html](http://www.undp.org/hdr2003/indicator/cty_f_ZAF.html).

**Table A.8 Projected total costs of ART, per person per year, in Kenya and South Africa (U.S. dollars)**

Cost category	Lowest-cost scenario		High-cost scenario	
	Kenya	South Africa	Kenya	South Africa
ARVs	140	140	1,000	1,000
Other drugs	80	80	80	80
Biological monitoring	150	150	400	400
Personnel <sup>a</sup>	200	1,020	200	1,020
Equipment	50	50	50	50
Total	620	1,440	1,730	2,550

a. For illustrative purposes, we assume similar wage structures in Kenya and Burkina Faso. Wage structures in South Africa were estimated using figures reported in UNDP's *Human Development Report 2003*. The average GDP per capita for the poorest 80 percent of South Africans is compared with the average GDP per capita for all of Kenya to find an illustrative wage multiplier (the figure used here is 5.1).

Source: Author calculations based on UNDP *Human Development Report 2003*.

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## *Intellectual Property Rights: How They Affect Procurement and What Steps Can Be Taken*

Intellectual property rights affect all kinds of commodities, but they are especially important for HIV/AIDS medicines and related goods. Intellectual property rights influence:

- The availability of goods in a country.
- The opportunities for importing goods from another country.
- The competition between equivalent goods from different producers, specifically between products of originator (or innovator) companies and those of generic producers.
- Price competition and getting value-for-money in public health.

Many HIV/AIDS medicines and laboratory products are relatively new, still protected by patents granted to the originators, usually within countries where the originator has, or expects to have, a significant market. But the patent situation varies widely across countries, affected by such international agreements as the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). That makes it important for staff responsible for project implementation to assimilate the information in this chapter. Early clarification of the intellectual property rights situation (and of registration requirements and import reg-

ulations) will prevent frustration, wasted time and money, and possible litigation. The chapter covers:

- Intellectual property rights—what are they?
- The TRIPS Agreement—the international regulatory situation of intellectual property rights.
- National regulatory situations and TRIPS-compliant flexibilities for least developed and developing WTO member countries.
- Determining the patent status of HIV/AIDS medicines in a particular country.
- The chapter ends with a brief consideration of the relevance of trademarks and copyrights.

## Intellectual property rights—what are they?

Intellectual property rights include patents, trademarks, copyrights, and rights in data assembled for regulatory purposes (rights in data are not strictly “intellectual property”). HIV/AIDS medicines may be subject to claims based on any of these rights, which may affect medicine procurement in different ways.

A *patent* is granted to the inventor of a product or process and gives the inventor the right to exclude others from making, using, selling, offering for sale, and importing a product covered by a “product” patent,<sup>1</sup> and from using a process covered by a “process” patent.<sup>2</sup> Patents 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. Because of cost and other factors (including differences in national legislative arrangements) associated with patenting, it is common for a particular medicine to be patented in some countries and not in others. This is the case for many HIV/AIDS medicines, including ARVs and medicines used to treat opportunistic infections, cancer, and other AIDS-related conditions. There are limitations on and exceptions to patent protection that benefit public procurement authorities.

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<sup>1</sup> The right to prevent importation does not prevent “parallel importation” of a patented medicine when a rule of international exhaustion of patent rights is followed. This is discussed later.

<sup>2</sup> As well as to exclude others from using, selling, offering for sale, and importing a product produced by a patented process.

A *trademark* is a sign used to distinguish the products of one enterprise from those of other enterprises. A trademark gives its holder the right to prevent others from using it in commerce in a manner likely to confuse consumers. Most medicines are known by the trademark(s) of one or more producers (the exclusive commercial name), as well as by a scientific or generic name (such as the international nonproprietary name that can be used by anyone).<sup>3</sup> Like patents, trademarks are granted on a country-to-country (and regional) basis. The registered trademark applicable to the same medicine may differ from country to country.<sup>4</sup> Trademark protection is limited by important “fair use” rights that permit common references to trademarked medicines.

A *copyright* is granted to the author of an expressive work (such as a book or design) and gives its holder the right to exclude others from reproducing or distributing the copyrighted work. Copyright protection does not extend to information (such as historical data and records) or to ideas (such as scientific content).<sup>5</sup> Although copyright is not commonly associated with medicines, it is sometimes claimed (and sometimes misused) by producers to preclude the duplication or distribution of the packaging or information materials accompanying a medicine (such as doctor and patient leaflets).

*Rights in data* may be asserted on the basis of national (or regional) legislation covering information submitted to drug regulatory authorities, such as the authority that approves the safety, efficacy, quality, or bioequivalence of a medicine in the registration process. Rights in data

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<sup>3</sup> A list of international nonproprietary names for pharmaceutical substances (such as amoxicillin, ampicillin, nandrolone, temazepam, phenobarbital, amphetamine, ibuprofen, chloroquine, and retinol) is maintained by the WHO. WHO members are expected to refrain from granting trademark status to international nonproprietary names.

<sup>4</sup> Medicines are sometimes referred to as “branded” or “brand name” medicines. Sometimes that means the same thing as “trademarked” medicine. At other times, “branded” or “brand name” is used to refer in a more general way to the company that makes the medicine, for example, a “Glaxo”-brand or “Pfizer”-brand product. A major producer might market the same medicine under a number of different trademarks (or specific names), but all those medicines would be “branded” medicines of the company that produces them. From a legal standpoint, the concept of “branded” or “brand name” in the sense of the company (or “trade name”) is not usually the basis for a formal legal action. Such actions, rather, are brought on the basis of the specific “trademark” for the medicine that is registered within a particular country.

<sup>5</sup> Copyright law distinguishes between expression and information (such as historical data or scientific content). Some countries have adopted unique “database” protection laws to address what they consider a gap in protection. Other countries have rejected this approach.

protect against the “unfair commercial use” of certain information contained in regulatory submissions. Rights in data are limited by public interest considerations. Public noncommercial use of data generally does not interfere with such rights.

## **The TRIPS Agreement—the international regulatory situation of intellectual property rights**

On January 1, 1995, the WTO was established as successor to the General Agreement on Tariffs and Trade (GATT). The WTO includes agreements regulating trade in goods and services. The most important from the standpoint of medicines procurement is the TRIPS Agreement, which obligates the nearly 150 members of the WTO to effect certain rules on the protection of intellectual property rights.

To take account of the different economic and social circumstances of WTO members, the TRIPS Agreement includes various “transitional” arrangements that directly affect patents on medicines and other intellectual property rights. In addition—as a consequence of the WTO Ministerial Declaration on the TRIPS Agreement and Public Health, adopted in Doha on November 14, 2001—transitional arrangements in favor of “least developed” WTO members were extended in important ways.

TRIPS Agreement rules affecting medicines, including those for treatment of HIV/AIDS, have been the subject of substantial and sometimes heated controversy between WTO members. To a large extent, this has reflected a difference between developed and developing members in their perceptions of the costs and benefits of protecting patents in medicines.

The idea behind granting patents is that by providing a potential financial reward to the inventor of a new product, such as a medicine, innovation and investment are encouraged to the benefit of the public. A new medicine may be costly (and risky) to develop, but easy to reverse-engineer and copy. Patents provide a means to allow innovators to recover their investments and to make profits that could be used to further develop new medicines.

The TRIPS Agreement takes into account the potential social cost of medicines patents in a variety of ways, acknowledging and allowing certain flexibilities. Despite the inclusion of these flexibilities in the TRIPS

Agreement, developing country WTO members were concerned with pressures being exerted on them to rigidly apply a fixed set of patent rules. They demanded that WTO Ministers expressly acknowledge and affirm their right to flexibly implement TRIPS obligations.

In the Doha Declaration on the TRIPS Agreement and Public Health,<sup>6</sup> WTO Ministers:

- Agreed that the TRIPS Agreement “does not and should not prevent Members from taking measures to protect public health” and “that the 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.”<sup>7</sup>
- Recognized that each WTO member is permitted to adopt its own regime for the “exhaustion of intellectual property rights without challenge.”<sup>8</sup> This means that members are free to permit “parallel importation” of medicines.
- Recognized that “Each Member has the right to grant compulsory licenses and the freedom to determine the grounds upon which such licenses are granted.”<sup>9</sup>
- In connection with a rule that permits the granting of compulsory licenses without prior negotiations with the patent holder when there is a national emergency, other circumstances of extreme urgency or for public noncommercial use, recognized that “Each Member has the right to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency.”<sup>10</sup>

The Doha Declaration, in its paragraph 6, made provision for further negotiations on the effective use of compulsory licensing by members with insufficient or no manufacturing capacity. The results of these negotiations will be discussed later.

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<sup>6-10</sup> WTO Ministerial Conference, Declaration on the TRIPS Agreement and Public Health, adopted November 14, 2001, Fourth Session, Doha, WT/MIN(01)/DEC/2 (November 20, 2001).

WTO Ministers agreed in paragraph 7 of the Doha Declaration that least developed members should not be obligated to implement or apply TRIPS provisions for pharmaceutical product patents or data protection until January 1, 2016. Just as important, they agreed that least developed members already allowing for such protection did not need to “enforce” such rules until that later date.<sup>11</sup> The TRIPS Council adopted a decision confirming this flexibility.<sup>12</sup> And the WTO General Council added a waiver of least developed members’ obligations regarding so-called exclusive marketing rights that might otherwise have been used as a substitute for patent protection to block production, import, and sale of medicines.

To sum up this far:

- The WTO TRIPS Agreement establishes minimum standards of intellectual property rights protection. It also incorporates basic “flexibilities” that can be used to overcome intellectual property rights-related barriers to acquiring low-cost medicines.
- The Doha Declaration on the TRIPS Agreement and Public Health strongly affirmed the right of governments to promote and protect public health by taking advantage of the flexibilities in the TRIPS Agreement to provide access to medicines “for all.” Special new rules were adopted in favor of least developed countries.
- “Least developed” countries are specially favored under new TRIPS Agreement rules. They have maximum flexibility to disregard patents and data protection rules until at least 2016.

## National regulatory situations and TRIPS-compliant flexibilities for different countries

Every nation has an inherent right to protect the health of its people. Intellectual property rules cannot take away this fundamental right.

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<sup>11</sup> Providing in relevant part: “We also agree that the least-developed country Members will not be obliged, with respect to pharmaceutical products, to implement or apply Sections 5 and 7 of Part II of the TRIPS Agreement or to enforce rights provided for under these Sections until 1 January 2016, without prejudice to the right of least-developed country Members to seek other extensions of the transition periods as provided for in Article 66.1 of the TRIPS Agreement. We instruct the Council for TRIPS to take the necessary action to give effect to this pursuant to Article 66.1 of the TRIPS Agreement.” (Declaration on the TRIPS Agreement and Public Health, para. 7).

<sup>12</sup> Decision of the Council for TRIPS of June 27, 2002 ([www.wto.org/english/tratop\\_e/trips\\_e/public\\_health\\_e.htm](http://www.wto.org/english/tratop_e/trips_e/public_health_e.htm))

To facilitate the low-cost acquisition of HIV/AIDS-related medicines and supplies, national laws and regulations generally should provide for the flexibilities permitted by the TRIPS Agreement. But even without pre-existing national legislation, the government always retains the power to act to protect the public interest. The TRIPS Agreement does not require that all necessary measures a government may take shall have been the subject of pre-existing legislation.

It is important in the formulation of national legislation and regulations that the various departments with responsibilities for importing and distributing medicines cooperate and coordinate their activities. It is all too common that the departments responsible for public health, trade, and intellectual property rights regulation do not communicate with each other in the development of their regulatory authority. As a result they may end up working with inconsistent rules.

The term “generic” is used in different ways for medicines.<sup>13</sup> Here it refers to originally patented medicines that are later produced off patent. If a generic medicine is lawfully available in an exporting country, a procurement authority in an importing country is concerned only with the patent situation in its own market.

Some HIV/AIDS-related medicines are not under patent in potential exporting countries. Why? Because patent protection for pharmaceutical products was made available only recently in those countries—or has not yet come into force. In some cases, the patent on a medicine will already have expired. In others, the medicine may be produced and marketed by a licensee under a government authorization that does not require the patent holder’s consent.<sup>14</sup> Such generic (or off patent) medicines can be obtained in the exporting country without difficulty in the

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<sup>13</sup> The term “generic” is also used more generally to refer to multisource products normally available from a wide range of manufacturers. Many drugstore retail chains, for example, sell their own generic brand of aspirin.

<sup>14</sup> Article 31(f) of the TRIPS Agreement provides that the predominant part of production under compulsory license shall be for supply of the domestic market of the country issuing the license. Medicine that would be available for export without additional measures would be the nonpredominant part of such production under compulsory license. On August 30, 2003, a new legal mechanism was adopted at the WTO that allows for the issuance of compulsory licenses for export at the request of eligible importing countries. This legal mechanism is discussed in note 27. Under this mechanism, additional measures are required in the exporting country.

sense that patents should not constitute an obstacle. Similarly, the producer of a generic medicine in an exporting country will typically use an identifier that either is an international nonproprietary name or that differs from the originator's brand name to avoid potential trademark infringement in its local market.

For medicines that are generic in the country of export, the potential intellectual property rights obstacles to procurement of HIV/AIDS-related medicines generally arise in the importing country, not the exporting country. (This assumes that there are generic medicines for purchase in an exporting country, and that is a question discussed later.)

If a medicine or supply is not protected by intellectual property rights (such as a patent) in the country of importation, intellectual property rights will not constitute an obstacle for the procurement authority.

The acquisition of HIV/AIDS-related medicines or supplies is complicated by the fact that intellectual property rights are generally granted for a particular country (or region). The presence or absence of a patent in one country does not ensure the presence or absence of a patent in another country. Even though a medicine, such as an ARV, may be off patent in India, it may not be in South Africa. Because of this, a patent holder in an importing country may object to the import of a medicine that has been lawfully produced and sold (is generic) in an exporting country, based on a patent in the importing country.

Whether the patent holder in the importing country will be able to block importation and distribution depends on various factors, including the legislation of the importing country, steps the government has taken or may take under that legislation, and the character of the purchase transaction. That is why it is important that governments pay attention to including TRIPS Agreement flexibilities in their national legal framework; that is, to allow for actions that are important to protecting public health.

### ***Least developed WTO member countries***

Least developed countries are likely to face the greatest budgetary constraints in purchasing HIV/AIDS-related medicines and supplies. Several least developed countries have high rates of HIV-infection, and even with external financial support, it is extremely important that they obtain

medicines at low prices.<sup>15</sup> Many ARVs are available from originators for least developed countries at special prices, and might be cheaper than generics. But if a government wants to buy generics, and if it is concerned that the originator(s) would enforce its patent(s), the following paragraphs explain how it may exercise its rights to buy generics. Some originators may voluntarily waive their enforcement rights.

Many least developed countries have legislation to grant patent protection, and almost all least developed countries have at least some legislation to grant trademark and copyright protection. Legislation in some least developed countries may provide for protection of data submitted for regulatory purposes.

The TRIPS Agreement took into account the special and differential interests of least developed WTO members in several ways, and the Ministerial Declaration on the TRIPS Agreement and Public Health accorded further special treatment for least developed countries. Least developed countries were initially allowed until January 1, 2006, to apply the provisions of the TRIPS Agreement (other than provisions relating to national and most favored nation treatment that applied to all members after one year) (Art. 66.1, TRIPS Agreement). While developing members were also allowed certain transitional exceptions from TRIPS obligations, these members were not permitted to reduce protection already in place during those transitional periods.<sup>16</sup> Least developed countries were not, however, subject to the prohibition against reducing existing levels of protection.<sup>17</sup> The allowance for least developed countries through January 1, 2006 applies to all forms of intellectual property rights.

As discussed earlier, decisions made by the TRIPS Council pursuant to paragraph 7 of the Declaration on the TRIPS Agreement and Public

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<sup>15</sup> It is important that medicines are of assured quality. Procedures relating to quality assurance are discussed elsewhere in this Technical Guide. In this section, attention is only on intellectual property rights. There is no inherent correlation between intellectual property rights and quality in the sense that generic producers are capable of producing medicines of quality equal to that of intellectual property rights holders.

<sup>16</sup> Article 65.5 provides: "A Member availing itself of a transitional period under paragraphs 1, 2, 3 or 4 shall ensure that any changes in its laws, regulations and practice made during that period do not result in a lesser degree of consistency with the provisions of this Agreement."

<sup>17</sup> Article 66 defines the exception for least developed countries, and does not incorporate by reference or otherwise the prohibition against reducing levels of protection set out in Article 65.5. While there is a provision on the protection of existing subject matter in Article 70.2, that Article does not apply to least developed countries per the terms of Article 66.1.

Health allow least developed countries until January 1, 2016, to implement or enforce pharmaceutical product patent and data protection.

Under the TRIPS Agreement the effect of the various allowances in favor of least developed countries is that national authorities are free to reduce or eliminate protection for trademarks and copyrights at least until January 1, 2006.<sup>18</sup> And they may elect not to implement or enforce pharmaceutical product patent and data protection until at least January 1, 2016. All these actions are consistent with the TRIPS Agreement obligations of least developed countries.<sup>19</sup>

The fact that national decisions not to implement or to “disapply” intellectual property rights may be taken without violating TRIPS obligations still leaves it to the national authorities of each least developed country to take steps in the national legislative, administrative, or judicial framework.

While authority to disapply the above-mentioned TRIPS provisions does not need to be granted until the time it is exercised, and it may even be possible to grant it “after the fact,” as in most legal matters, by acting in advance the government can save itself and its procurement authorities from the potential delay and expense involved in legal battles with intellectual property rights holders—and from potential political pressure from the home governments of intellectual property rights holders.

Because the political and constitutional arrangements in each country are somewhat different, it is difficult to offer general guidance on the specific steps least developed country governments should take to pave the way for avoiding intellectual property rights–based obstacles to procuring generic medicines and supplies. If the executive and parliament (or legislature) cooperate in adopting a grant of authority for the procurement authority to disapply intellectual property rights in order to promote and protect public health, this should in most or all least

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<sup>18</sup> Consistent with their national treatment and most favored nation obligations under Articles 3–5, TRIPS Agreement.

<sup>19</sup> Least developed countries might initially appear to be acting inconsistently with the terms of the Paris or Berne Convention by, for example, interfering with a patent right, but Paris and Berne obligations outside the TRIPS context are not enforceable by trade sanctions. In any case, actions by governments in favor of least developed countries at the WTO should be understood to allow for the same exceptions to Paris and Berne Convention obligations under general principles of equity. Otherwise, the actions by the same governments at the WTO would be undertaken in manifest bad faith.

developed countries be adequate to accomplish the objective. Other procedures are certainly possible and acceptable.<sup>20</sup> The government should, however, avoid discriminating among intellectual property rights holders of different nationalities so as to comply with TRIPS Agreement national and most favored nation treatment requirements.

## Developing WTO member countries

The situation for developing member legislation and regulation is more complicated than that for least developed country authorities because of the applicability of TRIPS Agreement rules.

The procurement authority may choose to purchase locally or to import an ARV or other medicine directly from the patent holder or its authorized distributor. In such circumstances, intellectual property rights should not constitute an obstacle because the patent holder is expressly or by implication consenting to the sale and use of the medicine under its

### Box B.1 Parallel importing

*Exhaustion of rights.* When patented medicines are placed on the market in exporting countries B–E, the patent right is exhausted in importing country A. The procurement authority in country A is free to import from the lower-priced markets—exporting countries B and E.



<sup>20</sup> Action by the executive or parliament alone may well be adequate (depending on the constitutional arrangement), and the courts might have authority to act on their own to disapply patent protection taking into account TRIPS Agreement principles.

patent. Even here, however, caution must be exercised. Recall that patents are granted and are independent for each country (or region). When a patent holder sells a medicine in one country, it gives up its right to further control the use or resale of the medicine in that country (the principle of “national exhaustion of rights”), including the right to resell the product for export. But if the patent holder holds a “parallel patent” in an importing member country, it might seek to block importation into that other country based on its locally held patent in that other country.

The procurement authority may find that it is purchasing medicines from a patent holder in an exporting country, rather than locally. If medicines are purchased from the holder of parallel patents in the exporting and importing member, the procurement authority should obtain an express promise from the seller (holder of the parallel patent) that it will not attempt to invoke its patent in the importing country. This promise may be in the form of the patent holder’s acknowledgment that it is selling the medicines for import into the purchaser’s country. A court in the importing country may decide that by selling the product for export the patent holder implicitly waived any right to invoke its parallel patent in the importing country. But the importer will avoid potential legal costs by obtaining an express acknowledgment in advance.

The country into which medicines are brought may also adopt a rule of “international exhaustion” of patents (and other intellectual property rights). Under international exhaustion, the lawful sale of an intellectual property rights–protected medicine in any country causes the intellectual property rights holder to give up control over further movement of the medicine regardless of national border. The economic theory behind this rule is that the holder is given one opportunity to exploit the value of its intellectual property rights in the medicine (or other product), not multiple opportunities as the medicine moves in international trade. The TRIPS Agreement, as explicitly confirmed by the Doha Declaration, allows WTO member countries to adopt a rule of international exhaustion.

If a developing member does so, the first sale by the patent holder or its authorized representative in an exporting member will exhaust any parallel intellectual property rights in the importing country<sup>21</sup>—and intellec-

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<sup>21</sup> There is some debate about whether a medicine (or other product) sold under “compulsory license” (see definition below) in an exporting country will exhaust a patent in an importing

### **Box B.2 Parallel imports in South Africa—under the rule of international exhaustion**

South Africa has adopted legislation (Section 15C of the Medicines and Related Substances Control Amendment Act, No. 90 of 1997) pursuant to which its Minister of Health (through the Medicines Control Council) has issued regulations that establish the conditions for the parallel importation of medicines into the country. In addition to the regulations, the Council has issued a Guideline for Parallel Importation of Medicines in South Africa.

The regulations provide that: “parallel importation” means the importation into the Republic of a medicine protected under patent and/or registered in the Republic that has been put onto the market outside the Republic by or with the consent of such patent holder.

The regulations and guideline provide procedures under which a parallel importer must obtain a permit to undertake importation. These procedures are intended to ensure that parallel import medicines are duly approved and registered by the Department of Health, and that the parallel importer will comply with requirements ordinarily imposed on vendors of medicine in South Africa, such as using an approved storage facility and having in place a recall procedure. The guideline also establishes that, “The parallel importer may use the proprietary name approved in South Africa as well as any trade marks applicable to the medicine in order to ensure the public health interests.”

Assume that the procurement authority in South Africa seeks to purchase an anti-infective medicine used to treat opportunistic infections associated with HIV/AIDS and that medicine is under patent in South Africa and Thailand. The anti-infective is sold by the patent holder’s authorized distributor in Thailand to wholesale purchasers at \$1.00 per capsule. The same anti-infective is sold by the patent holder’s authorized distributor in South Africa to wholesale purchasers at \$2.50 per capsule. The procurement authority in South Africa can purchase the anti-infective from a wholesaler in Thailand and import it. The patent holder in South Africa will not be able to block the importation based on its local patent because its patent rights are “exhausted” when the medicine is first sold in Thailand.

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country. The theory behind “nonexhaustion” would be that the patent holder did not “consent” to the sale, and so has not had the chance to exploit the value of the patent. The theory behind “exhaustion” in these circumstances is that the patent holder receives “adequate remuneration” in the exporting country and does in fact receive an economic return. The discussion in this section will be updated as the legal situation surrounding exhaustion and its relationship to compulsory licensing becomes clarified through practice.

tual property rights may not be used to block the importation. Products imported under a rule of international exhaustion are often referred to as “parallel imports.” Parallel import medicines are typically purchased from a party other than the patent holder—for example, from a medicine wholesaler that initially purchased from the patent holder in the “first sale.” By its first sale to the wholesaler, the patent holder “exhausts” its right to prevent the wholesaler from reselling the medicine and any right of the patent holder to block importation into a country with a rule of international exhaustion.

“Differential” or “equity” pricing refers to selling medicines at lower prices in beneficiary markets while maintaining higher prices for the same medicines in nonbeneficiary markets. It is perceived as a way of allowing innovating companies to recover research and development costs in higher income markets, while making medicines more affordable in lower income markets.

Procurement authorities purchasing and importing medicines under preferential pricing arrangements may be asked by patent holders for contractual commitments not to re-export or permit the re-export of medicines. This is requested so that “arbitraders” will not be allowed to purchase and resell the medicines in wealthier markets, thereby depriving the intended beneficiaries of access to the low-priced medicines and undercutting the economic return from the patent in the wealthier markets. While it is reasonable to provide a contractual commitment not to re-export preferentially priced medicines, the procurement authority should be careful not to make commitments that exceed its internal control capacity. If commitments are made, resources will need to be allocated to fulfilling them.

The law of a developing country should ordinarily permit enforcement of a contract that includes a commitment not to re-export in the same manner as other contractual commitments.

It is sometimes thought that a rule of international exhaustion allowing for parallel imports is inconsistent with preferential pricing of medicines. The suggestion is that patent holders fearing parallel importation of low-price medicines into wealthier markets will refrain from supplying low-price medicines. But rules that prohibit the importation of preferentially priced medicines are already in place in most if not all of the major developed country markets. And if authorities cooperate in preventing the re-export of preferentially priced products, parallel importation should

not be an obstacle to preferential pricing arrangements. If this does become a problem, governments may have to increase their cooperative efforts to control the movement of preferentially priced medicines.

### ***Compulsory licensing and government use***

Most or all countries—developed and developing—allow the government to make use of patented inventions for public purposes with fewer bureaucratic obstacles than apply to the private sector. The procurement authority may find it useful to invoke this authority in obtaining HIV/AIDS medicines. There remains an obligation to pay the patent holder “adequate remuneration in the circumstances of each case, taking into account the economic value of the authorization.” The remuneration may be determined after the fact.

To overcome obstacles that may be presented by patents, developing country governments and their procurement authorities can secure access to HIV/AIDS-related medicines, including ARVs, through a “compulsory license” or “government use” authorization. Recall that a patent is a government grant that permits its holder to exclude third parties from the market for a product, such as an HIV/AIDS-related medicine. A “compulsory license” is an authorization by the government to itself or to a third party to use the patent without the permission of the patent holder. A compulsory license authorizing the government to use the patent for its own purposes is also referred to as a “government use” authorization (in British terminology, “Crown use”). The term “compulsory licensing” is used here to refer to compulsory licensing and government use authorization, unless expressly indicated otherwise.

The legal concept of compulsory licensing is long embedded in international patent law. The patent system involves a tradeoff between the interests of society in encouraging new invention (and disclosure) and the interests of society in promoting competitive markets, access to products, and affordable prices. Since the earliest discussions of an international patent system, it was recognized that governments would encounter circumstances in which social interests in access and affordability would override longer term interests in encouraging invention (by granting exclusive rights to patent holders). It was also recognized that the government would be entitled to use or authorize the use of the patent without

the consent of the patent holder. The law of every country allows for some form of compulsory licensing of patents.<sup>22</sup>

Important HIV/AIDS medicines or supplies are covered by one or more patents in many countries. If the procurement authority wishes to procure a bioequivalent medicine (a generic version) from a party other than the patent holder or its authorized distributor, including by importing the medicine, it may need to authorize procurement under a compulsory license. The TRIPS Agreement, in Article 31, authorizes every government to grant compulsory licenses without restriction as to purpose. This authority was confirmed in paragraph 5(b) of the Doha Declaration.<sup>23</sup> Article 31 establishes certain procedural and substantive requirements regarding compulsory licensing. For government procurement authorities dealing with HIV/AIDS medicines, the procedural requirements are minimized in important ways. Note that the procurement authority is not required to use these “fast track” options, and may decide to seek a voluntary license, waiver of enforcement, or price concessions from the patent holder prior to granting a compulsory license. The special rules, in any case, provide assurance that the procurement authority can act rapidly when the situation calls for it.

Under Article 31(b) of the TRIPS Agreement, a party seeking a compulsory license must first have sought a license from the patent holder “on reasonable commercial terms and conditions and [indicate] that such efforts have not been successful within a reasonable period of time.” But government procurement authorities do not need to comply with this precondition in respect of HIV/AIDS medicines, on two separate grounds:

First, the precondition may be waived for national emergency or other circumstances of extreme urgency. And the Doha Declaration has expressly recognized that “HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency.”<sup>24</sup> To take advantage of the right to waive the precondition under these circumstances, the government does not need to

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<sup>22</sup> We are not aware of any country the law of which does not allow for compulsory licensing or government use in some form. Even if the patent law does not expressly incorporate such a provision, the sovereign authority of the state to take private property for government purposes (with such compensation as may be provided for under constitutional principles) will allow at least for government use.

<sup>23</sup> See text at note 9 above.

<sup>24</sup> Declaration, para. 5(c), note 12 above.

“declare” a general national emergency under legislation or constitutional authority that may allow it to suspend a citizen’s rights on a temporary basis. It is legally sufficient that the national health authority state that a compulsory license be granted because of a national health emergency or an extremely urgent public health circumstance. It is highly unlikely that any patent holder or foreign government would seek to challenge the validity of such a statement in the HIV/AIDS context, particularly in view of the Doha Declaration.

Second, the precondition may also be waived “in cases of public non-commercial use.” The precise meaning or limit of “public non-commercial use” is not spelled out in the TRIPS Agreement, leaving developing countries to interpret the term in good faith. It is clear, however, that a government procurement authority purchasing HIV/AIDS medicines for distribution through public clinics and without seeking to make a commercial profit from such distribution, will be engaging in “public non-commercial use.” If members of the public are required to bear all or a portion of the cost of the medicines either directly or through health insurance, this should not affect the public noncommercial character of the transaction as long as the government was not seeking to profit from the arrangement (that is, if the arrangement is essentially revenue neutral). There may well be further flexibility inherent in the “public non-commercial use” language of the TRIPS Agreement.<sup>25</sup>

The situation for HIV/AIDS is expressly recognized in the Doha Declaration. The HIV/AIDS pandemic is a national emergency and circumstance of extreme urgency in every developing country confronting it. From a practical standpoint, it may be easiest and most efficient for a government and its procurement authority to rely on the ground of national

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<sup>25</sup> There are many ways that the terms “public non-commercial use” may be defined in good faith. The term “public” could refer to use by a government, as opposed to private entity. The term “public” may refer also to the purpose of the use, that is, use for “public” benefit. A private entity could be charged with exploiting a patent for the benefit of the public.

“Noncommercial use” may be defined either in relation to the nature of the transaction, or in relation to the purpose of the use. On the nature of the transaction, “noncommercial” may be understood as “not-for-profit” use. A commercial enterprise does not ordinarily enter the market without intending to earn a profit. Regarding the purpose of the use, “noncommercial” may refer to the supply of public institutions that are not functioning as commercial enterprises. The supply of a public hospital operating on a nonprofit basis may be a “noncommercial” use of the patent.

“Public noncommercial use” is a flexible concept, leaving governments considerable flexibility in granting compulsory licenses without requiring commercial negotiations in advance.

emergency or extreme urgency as the basis for a waiver under TRIPS Article 31(b). For HIV/AIDS, the ground of public noncommercial use may work just as well in view of the pandemic and urgent need to address it. But if patent holders should fear that the public noncommercial use grounds may be used by procurement authorities “down the road” in more nuanced circumstances, some patent holders might choose to challenge its use even for HIV/AIDS as a “matter of legal principle,” thereby inviting delays.

To sum up, a government may issue a compulsory license to its procurement authority to acquire generic HIV/AIDS medicines, including by import, despite the presence of a local patent by stating that it is doing so to address a national emergency or circumstance of extreme urgency. As a matter of general practice, it is preferable that national patent or public health laws or regulations expressly provide a basis for such action. But if such laws or regulations are not in place, this does not prevent a government from taking this action. Inherent in the sovereignty of every government is the right to protect the public interest in a national emergency or circumstance of extreme urgency, and the government does not need to refer to specific national legislation to exercise this authority. Nothing in the TRIPS Agreement requires that the steps a government takes in these circumstances be laid out in advance.

Article 31(h) of the TRIPS Agreement requires that “the right holder shall be paid adequate remuneration in the circumstances of each case, taking into account the economic value of the authorization.” The TRIPS Agreement does not attempt to define “adequate remuneration,” leaving it to each government to determine this amount in good faith. The government does not need to determine this amount in advance of granting the compulsory license, and its legislation may specifically refuse to allow a patent holder the right to seek an injunction to block the granting of a license for government use.<sup>26</sup>

When a compulsory license is granted for procurement of a generic version of an HIV/AIDS medicine or supply, the government will be dealing with the circumstance of attempting to maximize the quantity of

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<sup>26</sup> Article 44:2, TRIPS Agreement, provides in relevant part: “Notwithstanding the other provisions of this Part and provided that the provisions of Part II specifically addressing use by governments, or by third parties authorized by a government, without the authorization of the right holder are complied with, Members may limit the remedies available against such use to payment of remuneration in accordance with subparagraph (h) of Article 31.”

medicines it can procure, and with the highest level of public interest at stake. Under these circumstances, the government may be justified in limiting “adequate remuneration” to the patent holder to a low royalty based on the purchase price of the generic medicines.

Article 31 of the TRIPS Agreement includes other procedural and substantive requirements for granting compulsory licenses. Because national legislation and regulations have been, or will be, revised to take into account these requirements, the procurement authority should be able to ascertain the requirements of national law. Certainly, however, implementation of the TRIPS Agreement is an ongoing process. And as developing members gain experience, they will be evaluating their laws and regulations to determine whether they adequately account for the public interest.<sup>27</sup>

Government use and compulsory licensing are the principal means enabling procurement authorities to overcome patent barriers to obtaining lower priced generic medicines and related supplies. But for many developing countries the option to use such licensing is illusory. They do not have sufficient local production capacity to make needed medicines at a reasonable cost.<sup>28</sup>

The TRIPS Agreement generally allows WTO members to grant compulsory licenses and to satisfy those licenses by importing. However, there is a catch. There must be medicines lawfully available for import. In other words, even if patent barriers are overcome domestically, there may be patents in prospective exporting countries that prevent the manufacture and export of needed medicines and supplies.<sup>29</sup> This problem will become very serious after January 1, 2005, when all developing countries are required to have patent protection for pharmaceutical products in place, and when “mailbox” pipeline applications that have

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<sup>27</sup> There are a number of published sources that can be consulted for this purpose. The United Nations Conference on Trade and Development and the International Center for Trade and Sustainable Development have developed a TRIPS Resource Book that contains detailed practical information regarding the implementation of the TRIPS Agreement from the perspective of developing countries (available at [www.iprsonline.org](http://www.iprsonline.org)) The World Health Organization also has important publications on this subject. Available at [www.who.int/medicines](http://www.who.int/medicines).

<sup>28</sup> Also, a country without sufficient production capacity may have difficulty making price demands because it lacks a credible threat of taking over production.

<sup>29</sup> This is not an absolute barrier because TRIPS compulsory licensing rules only require that a “predominant” part of production be for domestic supply. So, if there is a substantial domestic market for a generic medicine in an exporting country, and a license has been granted for that market, there may be a significant supply available for export.

accumulated during the past 10 years are given effect.<sup>30</sup> The availability of newer off-patent medicines from India, as the most notable illustration, will be reduced.

The WTO addressed the problem of countries with insufficient or no capacity in the pharmaceutical sector and their inability to make effective use of compulsory licensing in “Paragraph 6” negotiations that concluded on August 30, 2003.<sup>31</sup> The result of these negotiations was a “waiver” of the provision of the TRIPS Agreement that otherwise might limit exports under compulsory license (Article 31(f)).<sup>32</sup> A procuring-importing country (except a least developed country, which is automatically eligible) needs to notify the WTO that it intends to take advantage of the waiver.<sup>33</sup> It may then request that a producer in an exporting country supply it.<sup>34</sup> The producer may be a private enterprise, or it may be the government (or a private enterprise acting on its behalf). The exporting country must grant a license authorizing use of the patent for export. When imports commence there should also be a license in the importing country (if a license is needed to overcome a domestically granted patent).<sup>35</sup>

The waiver also exempts the importing country from an obligation under Article 31(h) of the TRIPS Agreement to pay remuneration since

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<sup>30</sup> The term of a “mailbox” patent will be based on its initial filing date, so the duration will be shorter than that of a newly applied for patent.

<sup>31</sup> WTO General Council, Implementation of paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, IP/C/W/405, August 30, 2003, and The General Council Chairperson’s statement, August 30, 2003 (available at [www.wto.org](http://www.wto.org)). “Paragraph 6” refers to the paragraph of the Doha Declaration on the TRIPS Agreement and Public Health that provided the mandate for these negotiations.

<sup>32</sup> The “waiver” was adopted without prejudice to other legal rights WTO Members may have. So, for example, if Article 30 that allows exceptions to the rights of patent holders can be used by exporting countries as the basis for exports, this right has not been taken away. It was in part uncertainty concerning how Article 30 will be interpreted by the WTO Appellate Body that led to the Paragraph 6 negotiations. Also, the waiver provides that WTO Members will before the end of 2003 commence working on a formal amendment to the TRIPS Agreement that eventually will be substituted for the waiver. The terms of the amendment should be at least as favorable to procurement authorities as the waiver, so the terms described above should satisfy the TRIPS Agreement under any reasonably foreseeable circumstance.

<sup>33</sup> This may be a “one-time” notification. It is not necessary to repeat this notification each time the waiver is used. However, both the importing and the exporting countries must provide further notifications (with respect to the name of the product and certain other matters) whenever the system set out in the August 30, 2003, decision is used.

<sup>34</sup> The exporting country may be a developed or developing country.

<sup>35</sup> A least developed member may decide it will not enforce a patent, and in that case will not need to grant a license. Also, there may not be a patent in force in the importing member.

the patent holder will be compensated in the exporting country “taking into account the economic value to the importing Member of the use that has been authorized in the exporting Member.”

The August 30, 2003, decision of the General Council and the accompanying statement of the Chairperson contain further detailed provisions for its implementation.<sup>36</sup> Because the Paragraph 6 solution is new as of August 2003, there will be a start-up period as prospective exporting countries decide on the best way to implement the rules.<sup>37</sup>

## Registration and regulatory review

Medicines are typically registered by public health authorities before they are placed into use. The registration process may include the import of a sample of a generic medicine, and a local patent holder may object to the import for such registration purposes. A WTO member is permitted under Article 30 of the TRIPS Agreement to provide a limited exception to the rights of patent holders to allow third party acts involved in the registration process (a “regulatory review exception”). Such an exception may be adopted by specific legislation or regulation, or the courts may allow such an exception on their own. When the procurement authority acquires generic medicine under a government use or compulsory license, that authorization should in any case allow for registration of the medicine.

The TRIPS Agreement in Article 39.3 includes a requirement that a narrowly defined category of undisclosed test or other data submitted as a condition of marketing approval be protected against “unfair commercial use.”<sup>38</sup> The provision applies only to “pharmaceutical or agricultural chemical products that utilize new chemical entities.”

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<sup>36</sup> These provisions are explained in *Exportation of Drugs under Compulsory Licenses: The WTO Decision on Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health*, available at [www1.worldbank.org/hiv\\_aids/docs/GHAPnote10.03.03.pdf](http://www1.worldbank.org/hiv_aids/docs/GHAPnote10.03.03.pdf).

<sup>37</sup> Specific implementing legislation is not necessarily required in each prospective exporting country, for example, if its law allows for the direct application of TRIPS rules. It is, however, likely that a number of countries will elect to amend their patent law to implement the waiver.

<sup>38</sup> Article 39, TRIPS Agreement: “3. Members, when requiring, as a condition of approving the marketing of pharmaceutical or of agricultural chemical products, which utilize new chemical entities, the submission of undisclosed test or other data, the origination of which involves a considerable effort, shall protect such data against unfair commercial use. In addition, Members shall protect such data against disclosure, except where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use.”

Typically a generic pharmaceutical product, including an HIV/AIDS medicine, will be registered by local public health authorities before it is distributed to the public. It is at this stage that a patent holder may argue that the public health authorities should not be allowed to rely on test data provided by the patent holder, even if submitted by it for approval of the medicine in another country, because to do so would take unfair commercial advantage of its efforts. The patent holder may suggest that a generic producer should be required to generate an entirely new set of test data as a condition of registration, even though doing so would involve delay and duplicate efforts with no corresponding public benefit. Patent holders use data protection claims as aggressively as traditional intellectual property rights claims to attempt to block the introduction of generic medicines.

There is considerable legal controversy over the scope of the obligation that Article 39.3 of the TRIPS Agreement places on WTO members. It is clear, however, that claims to protection of data and claims to patent protection are different matters. The fact that there is a patent on a medicine does not preclude its registration as a generic.<sup>39</sup> Developing country governments should include a regulatory review exception in their approach to patents. Developing country governments should make suitable provisions in their regulatory frameworks to facilitate registration when data are used for public purposes. When a government is approving the use of a medicine for HIV/AIDS treatment in its health care system, it is not making “unfair commercial use” of originator data. It is addressing an urgent public health need.<sup>40</sup>

## Determining the patent status of HIV/AIDS medicines

To determine whether government authorization to import a generic HIV/AIDS medicine or supply medicine is required, the procurement authority needs to check whether that medicine is locally under patent in-

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<sup>39</sup> This was confirmed by a WTO dispute settlement panel in *Canada—Patent Protection of Pharmaceutical Products*, WT/DS114/R, March 17, 2000. The potential inhibiting effects of patents on medicines registration can be avoided by use of a regulatory review exception, or by authorizing acts in connection with registration in a government use or compulsory license.

<sup>40</sup> For a thoughtful discussion of this topic, see U.K. Commission on Intellectual Property Rights, *Integrating Intellectual Property Rights and Development Policy*, at 50–51 (Report of the Commission on Intellectual Property Rights, London, 2002).

country. The relevant branded medicine may not be available locally, with patent numbers listed on an information sheet, to readily indicate the situation in the local market.<sup>41</sup> Unfortunately, the procedure for determining whether a particular medicine is under patent is often difficult. Patents are not granted or listed by categories that allow for searches according to trademark, brand name, international nonproprietary name, or other medicinal classification. Often a medicine that is well known under a trademark or brand name will be protected by several linked patents, and the links will not be identified in a single patent disclosure. Pharmaceutical patent holders are not always anxious to allow their competitors to determine whether a particular molecule or formulation technology is covered by patent.

Persons who are not specialists in the technology of pharmaceuticals will find it difficult to determine the patent status of a particular medicine by, for example, examining published patents. One possible route for the procurement authority is to make a request to the national patent office to provide a report on which HIV/AIDS medicines are under patent locally and the period of patent protection. But not all national patent offices are willing or prepared to undertake this activity. Another possible method is to engage the services of a professional patent-searching firm that will prepare a report for a fee. Depending upon the complexity of the search, the fee may be substantial.

Responding to the difficulties created by this situation, some non-governmental organizations, notably Médecins Sans Frontières, have been working for several years to identify the patent situation of HIV/AIDS medicines in developing countries. It is publishing and updating lists describing the patent situation in a number of countries. But it cautions that it cannot provide information with absolute certainty for the technical reasons described above. It may not be possible to state with certainty that all of the patents linked to a particular medicine have been identified. Even so, until improvements in this situation are agreed on at the international level, the best information available may be obtained from Médecins Sans Frontières. More work is needed on identifying patents associated with medicines. This will require cooperation among public

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<sup>41</sup> When a producer lists a patent number on medicines packaging, this should indicate that the producer holds or is the licensee of the relevant patent. But this does not mean that the patent is valid, and many patents challenged in courts or administrative tribunals are found to be invalid.

health organizations, such as the World Health Organization, along with national and regional offices maintaining patent data.

## Trademarks and copyrights

The producer of generic HIV/AIDS medicine or supplies will typically avoid using the trademark or brand name of another producer, because this invites costly litigation. It is therefore unlikely that procurement authorities will find it necessary to be concerned with potential claims for trademark infringement. However, there are two possibilities to which attention should be drawn.

First, branded pharmaceuticals producers sometimes assert that the color or shape of medicine is protected as their trademark. This area of trademark law also involves a degree of controversy. Although colors may serve as trademarks, when a color serves a useful (or utilitarian) function, it is not serving as a trademark, but as an idea or method of use. If physicians, pharmacists, and patients associate a particular kind of drug with a particular color, the color serves a function allowing easy identification for health-related purposes. Very frequently, patients come to rely on the color and shape of a drug as a primary means of identification. For this reason, a developing country can defend the introduction of a comparably colored or shaped medicine on grounds that the color and shape serve a functional, as contrasted with a trademark, purpose. Moreover, Article 17 of the TRIPS Agreement allows for the limited “fair use” of trademarks, and it is certainly in the fair public interest to allow the use of colors in generic medicines when purchased and distributed by public health authorities. It is nonetheless useful to be aware of the possibility of such claims.

Second, recall the earlier discussion of parallel importation. The seller of a medicine trademarked in one country may also seek to block importation of the medicine into another country based on the independent registration of its mark. If the government permits parallel importation, the authorization should also extend to trademarks and copyrights because these intellectual property rights are also invoked by medicines producers to attempt to block the introduction of generics. Even when purchasing directly from the trademark holder or authorized distributor in an exporting country, the importing procurement authority should obtain acknowledgement that intellectual property rights will not be invoked to block

importation. A court may well decide that such authorization is an implied condition of the sale, but it is wise to avoid such complications.

Legislation and regulations in a developing member should also address the possibility that an HIV/AIDS medicine producer will assert copyright interests in physician or patient information materials. Copyright interests are subject to “fair use” under the TRIPS Agreement, Article 13, with cross reference to Berne Convention Article 9(2). When HIV/AIDS-related generic medicines are procured by public health authorities, this will constitute fair use of information materials, which in any case are not likely to be considered “expressive works” within the meaning of copyright.



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## *HIV Test Kits and Other Diagnostics*

When used correctly, HIV tests can determine if HIV is present in a person's blood. There are two main types of HIV tests:

- Antibody tests, such as ELISA, simple-rapid, and Western blot.
- Virologic tests, such as the HIV antigen test, polymerase chain reaction test, and viral culture.

### **Antibody tests**

HIV antibody tests look for antibodies against HIV; they do not detect the virus itself. When HIV enters the body, it infects white blood cells known as T4 lymphocytes, or CD4 cells. The infected person's immune system responds by producing antibodies to fight the new HIV infection. The presence of the antibodies is used to determine the presence of HIV infection. Enzyme immunoassays (EIAs) are recommended for laboratories that process large numbers of specimens daily. Rapid tests are useful in settings where EIAs are not practical and in geographic areas with limited laboratory infrastructure. The Western blot is used mainly to confirm a prior test.

## Virologic tests

Antibody tests are the most commonly used tests, but under special circumstances—in a recently infected individual, during the window period, or for a child born to an HIV-positive mother—more direct diagnostic methods may be used. Unlike antibody tests, virologic tests determine HIV infection by detecting the virus itself. Virologic tests are rarely used to diagnose HIV in developing countries since they require sophisticated laboratories. But they may be used to monitor progress of infection or response to therapy, say by measuring viral load.

HIV testing strategies vary from one country to the other depending on the estimated HIV prevalence and available technologies. Ordinarily, it is the responsibility of government regulatory bodies—ministries of health, national HIV/AIDS control programs, or national reference laboratories—to formulate the most feasible testing strategies for a country.

UNAIDS/WHO recommend using two or three different combinations of EIAs or rapid tests as a testing strategy. The first test, a screening test, should be highly sensitive to reliably detect antibodies. The second test, a confirmatory test, should be highly specific to confirm that the specimen truly contains antibodies specific to HIV.

Factors to consider in developing an HIV testing strategy include:

- Expected HIV prevalence
- Laboratory infrastructure
- Availability of refrigerators/regular electricity
- Performance of test kits
- Cost
- Impact on the delivery of health services.

Testing strategies should be designed to maximize both sensitivity and specificity for HIV antibody detection.

## Selecting HIV test kits

The selected test kits should have been evaluated by WHO and meet the requirements of at least 99 percent sensitivity and at least 99 percent specificity.<sup>1</sup>

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<sup>1</sup> UNAIDS/WHO. Operational Characteristics of Commercially Available Assays to Determine Antibodies to HIV-1 and/or HIV-2 in Human Sera. Reports 11, 12 and 13. Geneva: UNAIDS/WHO.

In addition to the performance of the HIV test kits, various operational factors influence the selection of assays:

- Laboratory infrastructure
- Access to a reference laboratory
- Desired characteristics of the test (antigen, antibody)
- Simplicity of test procedure
- Equipment necessary to perform the test
- Performance time
- Shelf life of reagents
- Price
- Storage conditions
- Technical skill of laboratory staff
- Laboratory logistics.

Countries should evaluate the accuracy and operational characteristics of HIV test kits in-country and determine the most appropriate combination and sequence of tests. While most countries will already have a national testing strategy, many may not have the capacity to evaluate test kits in-country.

If the national laboratory infrastructure lacks the capacity to perform the evaluation, then after selecting a test(s) from the UNAIDS/WHO list, a testing algorithm can be chosen based on evaluations by another independent, noncommercial source, preferably in the region.

For more detailed information on selecting a HIV testing strategy and selecting HIV test kits, please see the following:

- UNAIDS/WHO (1999). Operational characteristics of commercially available assays to determine antibodies to HIV-1 and/or HIV-2 in human sera. Reports 11, 12 and 13. Geneva: UNAIDS/WHO or visit [www.who.int/bct/Main\\_areas\\_of\\_work/BTS/HIV\\_Diagnostics/HIV\\_Test\\_Kit\\_Evaluation.htm](http://www.who.int/bct/Main_areas_of_work/BTS/HIV_Diagnostics/HIV_Test_Kit_Evaluation.htm) (Note: Addresses of manufacturers are also included at the back of these reports.)
- WHO/CDC/UNAIDS (2001) Guidelines for using HIV testing technologies in surveillance, evaluation and implementation. Geneva: UNAIDS/WHO.
- Walkowiak, H. and Gabra, M. (2002). Commodity Management in VCT Programs: A planning guide. Management Sciences for Health

(RPM Plus) and Family Health International or visit [www.msh.org/resources/online\\_reports/pdf/VCT\\_Final.pdf](http://www.msh.org/resources/online_reports/pdf/VCT_Final.pdf)

Countries should require that all laboratories (national, regional, and local) that conduct HIV testing, participate in an external quality assurance of a laboratory's procedure. In addition, they should have a functioning internal quality assurance program. All laboratories should routinely monitor and assess the quality in the preanalytical, analytical, and postanalytical phases of the testing. Details of the components to be monitored in each phase can be found in "Guidelines for Using HIV Testing Technologies in Surveillance."<sup>2</sup>

## Quantification

Before procuring HIV test kits, countries must decide how many kits and other commodities to buy. Some manufacturers and suppliers will help providers quantify their needs (on the basis of the experience with other countries and facilities) and establish delivery schedules.

HIV test kits are complicated products to manage. First, their average shelf life is a short 12 months, requiring smaller and more frequent shipments. Second, many of the kits require cold storage, limiting the number of locations where they can be stored. Third, use can vary greatly between service delivery points within a single country. And fourth, few data exist for logistics and consumption in large programs, complicating the accurate forecasting of demand.

## General principles for quantification

- Use at least two quantification methods to check your estimates.
- When quantifying needs for a new service or intervention, order extra supplies to "fill the pipeline."
- Quantification will need to consider lead time—the average time between recognizing that a commodity needs to be ordered to having it available for use. The longer the lead time is, the more safety or buffer stock will be needed to prevent stockouts between orders.

<sup>2</sup> UNAIDS/WHO *Guidelines for Using HIV Testing Technologies in Surveillance*. 2001. Geneva: UNAIDS/WHO.

- Adjust quantification estimates for losses or waste, and take into account the amount of products already in the system.
- No matter which method is used, there is usually a gap between estimated needs and available funds, and decisions will need to be made on how to adjust and reconcile the quantities needed.

Source: Walkowiak, H., and M. Gabra. VCT Toolkit: Commodity Management in VCT Programs: A Planning Guide. Family Health International/Management Sciences for Health, December 2002.

## Procurement

Whichever procurement source used, all HIV test kits must have been evaluated by WHO and meet the requirements of at least 99% sensitivity and at least 99% specificity.

Test kits can be purchased using one of the following procurement options:<sup>3</sup>

- WHO bulk HIV test kit procurement scheme
- Limited international bidding
- Direct contracting or shopping

WHO established the HIV Test Kit Bulk Procurement Scheme in 1989. The goals of the scheme are to facilitate access to high-quality test kits at a low cost through an easy purchase procedure.

There are 22 tests on the WHO Current Bulk Procurement Scheme List of Available Assays, including a greater number of simple-rapid assays than ever before. This scheme encompasses the main types of tests used to detect HIV antibodies today—EIAs, simple-rapid assays, and confirmatory assays. WHO negotiates prices for all assays in the bulk procurement scheme directly with the manufacturers, enabling it to offer a per test cost of about half that of the open market price.

After selecting HIV test kits that have been evaluated by WHO and meet the minimum requirements for specificity and sensitivity, kits may be procured from a limited number of sources through competition.

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<sup>3</sup> Market information (e.g., names of manufacturers and prices) that can be used to help countries make informed decisions is included in MSF/UNICEF/UNAIDS/WHO's publication: "Sources and Prices of Selected Medicines and Diagnostics for People Living with HIV/AIDS/ June 2003."

## Ancillary equipment and supplies

In addition to HIV test kits, the consumables needed for HIV testing may include the following:

- Automated analyzers, such as ELISA readers
- Reagents and controls for ELISA testing (if appropriate to the quality assurance strategy)
- Centrifuges
- Refrigerators
- Test tube racks
- Timers
- Consumables, such as pipettes, pipette tips, and specimen tubes
- Supplies to collect specimens, such as lancets, needles, syringes and plasters
- Disposable gloves
- Disinfectants and cleaning supplies
- Sharps disposal bins for needles and lancets as defined under the Universal Precautions strategy
- Waste disposal (biohazard) bags for blood-contaminated non-sharps, such as gauze, swabs, gloves, and testing cards.

Increased access to ARVs has also highlighted the need for appropriate and cost-effective diagnostic support. Diagnostic support is essential to monitor the progression of the disease, the effectiveness of treatment, and the development of resistance. The main measures used are CD4+/CD8+ cell counts and viral loads.

Accurate and reliable measures of CD4+/CD8+ cells help in assessing the immune system and managing the health care of persons infected with HIV. The pathogenesis of AIDS is largely attributable to the decrease in the number of CD4+/CD8+ cells. Progressive depletion is associated with an increased likelihood of severe HIV disease.

The most common method to measure CD4+/CD8+ cells is multi-platform or single-platform flow cytometry. But this is also the most complicated and expensive method. Several alternative methods require fewer reagents and may be more cost-effective.

Using highly active antiretroviral therapy (HAART) and monitoring therapy response by using viral load testing have contributed to clinical

management of persons infected with HIV. Measurements of viral load can be used to determine when ART should be initiated and to monitor treatment efficacy.

The most commonly used viral load assays are nucleic acid based. Of these, only three have been approved by the U.S. Food and Drug Administration (FDA) which means that they have undergone extensive evaluation.

- The HIV-1 reverse transcriptase polymerase chain reaction assay (Amplicor HIV-1 Monitor Test, version 1.5, Roche Diagnostic),
- In vitro nucleic amplification test for HIV-RNA (NucliSens HIV-1 QT, by Organon Tekniak),
- In vitro signal amplification nucleic acid probe assay (VERSANT HIV-1 RNA 3.0 Assay).<sup>4</sup>

Other types of nucleic acid and nonnucleic acid viral load assays may perform equally well. To make a decision about which viral load assay to use, review the information in the MSF guide.<sup>5</sup>

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<sup>4</sup> Centers for Disease Control and Prevention. (November 16, 2001). Guidelines for Laboratory Test Result Reporting of Human Immunodeficiency Virus Type 1 Ribonucleic Acid Determination. *MMWR* November 16, 2001/Vol.50/No. RR-20.

<sup>5</sup> MSF/UNICEF/UNAIDS/WHO. Sources and Prices of Selected Medicines and Diagnostics for People Living with HIV/AIDS. June, 2003.