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Human Development

Improving Access to HIV/AIDS Medicines in Africa

*Trade-Related Aspects of Intellectual
Property Rights Flexibilities*

Patrick L. Osewe, Yvonne K. Nkrumah,
and Emmanuel K. Sackey

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Contents

<i>Acknowledgments</i>	<i>viii</i>
<i>Abbreviations and Acronyms</i>	<i>x</i>
<i>Overview</i>	<i>xii</i>
Chapter 1	Introduction
	1
	The International Debate on TRIPS Flexibility
	2
	Scope and Methodology of the Study
	5
	Notes
	6
Chapter 2	Overview of the TRIPS Agreement and Flexibilities
	9
	Implementation of the TRIPS Flexibilities
	10
	Exemptions from Patentability
	12
	Transition Periods

	13
	Compulsory Licensing and the Regional Trade Option
	15
	Exhaustion of Rights and Parallel Importation
	20
	Limits on Test Data Protection
	21
	Bolar Exception
	22
	Implementation Challenges
	22
	Notes
	25
Chapter 3	Local Production: Experiences in Four African Countries
	27
	Zimbabwe: Varichem
	29
	Kenya: Cosmos
	32
	South Africa: Aspen
	35
	Ghana: Danadams
	39
	Local Production of ARVs in Perspective
	42
	Notes
	44
Chapter 4	Conclusions and Recommendations
	47
	Conclusions
	47
	Recommendations
	49
Appendix A	HIV/AIDS Medicines under Patent in Sub-Saharan Africa

51**Appendix B List of Persons Interviewed****53****Bibliography****57****Figures**

- 3.1 Percentage of ARVs Purchased by Government of Ghana from Danadams and Other Firms 2005
41
- 3.2 Comparison of Prices for Local and Imported Generic ARVs in Ghana, 2005
42

Tables

- 2.1 TRIPS Flexibilities That Facilitate Protection of Public Health
11
- 3.1 Key Socioeconomic Indicators
28
- 3.2 Varichem's ARV Production Line
30
- 3.3 Cosmos's ARV Production Line
34
- 3.4 Supply of ARVs to the South Africa Department of Health
38
- 3.5 Danadams's ARV Production Line
40

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Abbreviations and Acronyms

AIDS	acquired immunodeficiency syndrome
API	active pharmaceutical ingredient
ARCT	African Regional Centre for Technology
ARIPO	African Regional Intellectual Property Organization
ART	antiretroviral therapy
ARV	antiretroviral
BI	Boehringer Ingelheim
COMESA	Common Market for Eastern and Southern Africa
Decision	Decision of the WTO General Council of August 30, 2003
Declaration	Doha Ministerial Declaration on the TRIPS Agreement and Public Health
DFID	U.K. Department for International Development
ECDS	Eastern Caribbean Drug Service
ECOWAS	Economic Community of West African States
FDA	Food and Drug Administration
GATT	General Agreement on Tariffs and Trade
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
GMP	good manufacturing practice
GSK	GlaxoSmithKline

HIV	human immunodeficiency virus
IP	intellectual property
IPR	intellectual property right
KSh	Kenyan shilling
KCAEM	Kenya Coalition for Access to Essential Medicines
LDC	least-developed country
MEDS	Mission for Essential Drugs and Supplies
MSD	Merck Sharp & Dohme
MSF	Médecins Sans Frontières (Doctors without Borders)
mg	milligrams
ml	milliliters
NGO	nongovernmental organization
OAPI	Organisation Africaine de la Propriété Intellectuelle (African Intellectual Property Organization)
RTA	regional trade area
SADC	Southern African Development Community
SSA	Sub-Saharan Africa
TB	tuberculosis
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNDP	United Nations Development Programme
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

All dollar amounts are U.S. dollars (US\$) unless otherwise indicated.

Overview

This study analyzes the extent to which countries in Sub-Saharan Africa (SSA) have been able to utilize flexibilities in the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) to improve affordable access to medicines for HIV/AIDS. It also examines the option of local manufacture of antiretroviral medications, based on the experiences of four countries, and evaluates challenges to the sustainability of this option in the Sub-Saharan African context.

The study first reviews the involvement of countries in the SSA region in the evolution of the debates within the World Trade Organization (WTO) regarding access to medicines and the protection of public health. The TRIPS Agreement of April 15, 1994; the Doha Ministerial Declaration of November 14, 2001 (the Declaration); and the WTO General Council Decision of August 30, 2003 (the Decision), all provided the framework for interpretation of the TRIPS flexibilities, reflecting the input of African countries.

The TRIPS flexibilities that can be used to enhance access to HIV/AIDS medications include exemptions from patentability, transition periods, compulsory licensing, exhaustion of rights and parallel importation, limits on test data protection, and the Bolar exception. For each one, this study notes the requirements and permissions under the terms of the

TRIPS Agreement, as confirmed and interpreted in the context of the Declaration and the Decision.

The prevailing SSA intellectual property rights (IPRs) regime is examined in relation to these permissibility criteria to ascertain if and how countries are utilizing the TRIPS flexibilities to improve their access to HIV/AIDS medicines. Bearing in mind the close linkage between the legal instruments of international and regional institutions and the domestic laws of their member countries,¹ this examination is done primarily in relation to the two regional intellectual property (IP) organizations, the Organisation Africaine de la Propriété Intellectuelle (OAPI, or the African Intellectual Property Organization) and the African Regional Intellectual Property Organization (ARIPO). Obstacles to implementing the TRIPS flexibilities are centered mainly on (a) lack of awareness on the part of political leaders, (b) lack of political will, and (c) lack of efficient administrative structures and procedures that would allow for efficient coordination and decision making.

The production of HIV/AIDS medicines is not only research and technology based but also patent controlled and capital intensive, and these pose steep challenges to African countries that have ventured into this area. The study analyzes the cases of Zimbabwe, Kenya, South Africa, and Ghana to shed light on the factors that favor or hinder sustainable local production of antiretroviral (ARV) medications.

Several key findings form the basis for the study's recommendations. A central observation is that under the auspices of ARIPO and OAPI (and earlier, the World Intellectual Property Organization [WIPO]), most African countries (including least developed countries [LDCs]) already provide patent protection for pharmaceutical products, even though the Declaration stipulates that LDCs do not have to provide such protection until 2016, at the earliest.

In general, national coordination systems on IP issues are weak or non-existent in most countries in SSA. There is also a notable lack of reliable information on the patent status of ARV medicines at both the national and regional levels. In sum, the comprehension, implementation, and utilization of the TRIPS flexibilities are uneven and incomplete and need to be stepped up.

Although technical personnel in the various countries in the region are generally aware of the TRIPS flexibilities and their potential for promoting access to medicines, the same cannot be said of the political leadership. This shortcoming is crucial insofar as decision making on using the TRIPS flexibilities rests with political leaders. They need to understand and appreciate the policy space the flexibilities offer.

Against a backdrop of widespread and persistent poverty, the high cost of addressing the devastating effects of HIV/AIDS has created a sense of national and regional desperation and crisis. This has shifted the focus away from using the TRIPS flexibilities as a priority tool for increasing the long-term availability of affordable medicines. Instead, the focus is on the aid programs offered by both the research-based pharmaceutical companies and international donors, which are seen as yielding immediate, if not very substantial, results. Disincentives to using the TRIPS flexibilities include the cumbersome local administrative processes required for implementing a compulsory license, which are then further complicated by the Decision's requirements. The early experiences of some countries with compulsory licensing have been somewhat discouraging.

Although the exhaustion of rights is incorporated into the domestic legislation of most countries, only a few countries (including Kenya, South Africa, Zimbabwe, and Ghana) allow for the international level of exhaustion of rights, which provides the most flexibility. OAPI member countries have exhaustion of rights only at the regional level, and other countries such as Botswana and Nigeria have it at the national level. This raises doubts as to how effective the incorporation of such provisions into domestic legislation can be. Few countries in the region make use of the flexibility on the extent of protection of test data.

Another valuable flexibility involves determining the criteria for patentability based on what constitutes novelty. However, countries of the region have few provisions in their domestic patent laws that would allow them to utilize this flexibility to increase the availability of affordable medicines. This flexibility could be applied to prevent patents for new uses of known or previously patented medicines in SSA, as is the case in the Andean Community.² Neither ARIPO nor OAPI has any recorded case of denying a patent application based on application of this flexibility.

In the case of the Decision, most countries have not incorporated any provisions into their domestic legislation that specifically target the beneficial utilization of the innovations that the Decision brought into the TRIPS Agreement. It appears that most countries in the region procure their first-line treatment for HIV/AIDS from India, where most of these medicines are not patented. This accounts in part for the inaction on incorporating the provisions of the Decision into their domestic legislation. Other factors contributing to a reluctance to act include the rather complex nature of the system created by the Decision.

With respect to local production of HIV/AIDS medicines, country experiences in Ghana, Kenya, and Zimbabwe reveal major challenges: the high cost of bioequivalence tests for each product, required for

prequalification by the World Health Organization (WHO); the high cost of active pharmaceutical ingredients (APIs) when purchased in small quantities; and the inadequate market share and lack of economies of scale. The latter, in turn, are related to an inability to supply under the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) when manufacturers lack WHO prequalification for their products. These factors have rendered local production unsustainable in the medium to long term. Although South Africa shares some of these challenges, it is the only SSA country that has a generic manufacturing company with WHO prequalification for some of its ARV products. It also has a well-developed long-term strategy that includes the manufacture of active ingredients for its products, thereby ensuring sustainability in production.

Based on these findings, the study makes five major recommendations:

1. ARIPO and OAPI should provide technical assistance to their member countries by commissioning studies to examine the individual patent laws of the countries (in the case of ARIPO) and the Bangui Agreement (in the case of OAPI) to ensure the inclusion of provisions that maximize the benefits of the TRIPS flexibilities.
2. ARIPO and OAPI should work with development partners to establish a reliable database on ARV patent status to strengthen information flow and facilitate the utilization of the TRIPS flexibilities.
3. Development partners such as the World Bank (the Bank), WTO, and WHO should be encouraged to support programs that
 - Create political will by sensitizing the political leadership of SSA countries, as well as regional economic groupings, about the policy options offered by the TRIPS flexibilities;
 - Develop and disseminate a simplified interpretation of the TRIPS Agreement, the Declaration, and the Decision, with analyses of the options available and the role of the various stakeholders;
 - Support capacity building at the country level for the effective implementation of the TRIPS flexibilities;
 - Provide guidelines and technical assistance to local pharmaceutical manufacturing companies on the requirements for WHO prequalification and on how to avoid delays in the application process; and
 - Strengthen the regional trade areas (RTAs) to maximize economies of scale in the production and procurement of HIV/AIDS medicines by harmonizing treatment protocols, medicine registration requirements, and procurement practices.

4. Both ARIPO and OAPI should amend their legal instruments to specifically exclude new and second uses of known medicines from patentability.
5. Local pharmaceutical companies should seek to form strategic partnerships with well-established pharmaceutical companies through win-win voluntary licensing agreements and other mutually beneficial arrangements like joint ventures to enhance sustainable medium- and long-term local production.

Notes

1. Nigeria and South Africa are two major countries that are featured in the study but do not belong to either ARIPO or OAPI.
2. The General Secretariat of the Andean Community, by Resolution No. 406 of 2000, ruled that Peru did not comply with the community juridical order when it granted a patent for this second use, and ordered its revocation. The ruling was based on article 16 of Decision 344, the legislation then applicable to industrial property (now article 21 of Decision 486), which reads: "Patented products and processes, included in the state of the art pursuant to Article 2 hereunder, shall not be the subject matter of a new patent for the simple reason of their being attributed a use other than the one originally contemplated by the original patent." In other developed societies, such as the United States and Germany, the grant of these patents is expressly allowed. The Patent European Convention, by contrast, does not legislate on the matter, but the member countries grant such patents anyway. This means that patents for second uses are granted where this practice is expressly allowed, or at least where the law does not regulate it (which is not the case of the Andean Community, where the legislation expressly prohibits it). See <http://www.managingip.com/Article.aspx?ArticleID=1256267>.

CHAPTER 1

Introduction

In the contemporary global trading system, developing countries continue to face complex challenges in implementing some of the international agreements that were negotiated during the Uruguay Round of the General Agreement on Tariffs and Trade (GATT).¹ These difficulties derive primarily from these countries' weak economies, high levels of poverty, and low overall trading and industrial capacity, and they have far-reaching implications for the socioeconomic development and sustainability of these societies. In particular, the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement continues to present a number of obstacles, above all to the countries in Sub-Saharan Africa (SSA), related to procurement of pharmaceutical products.

Under the TRIPS Agreement, current and future members of the WTO must adopt and enforce, through domestic legislation, nondiscriminatory minimum standards prescribed for the protection of intellectual property rights (IPRs). Most countries of SSA are members of the World Trade Organization (WTO) and are therefore required to meet this obligation under the TRIPS Agreement. In the specific area of IPR protection for pharmaceutical products and processes, the overriding challenge for these countries is to interpret and implement the obligations, rights, and flexibilities under the TRIPS Agreement in ways that

are internationally acceptable, yet still protect public health by ensuring access to high-quality, affordable medicines. Pharmaceutical products are a major means by which the health care services industry delivers therapy to fight disease and enhance the quality of life; as such, they are indispensable to any health system. Access to vital, high-quality medicines can be seen as a basic human right and indeed as a matter of life and death for whole communities, particularly in Africa.

The HIV/AIDS pandemic is decimating populations worldwide at alarming rates—nowhere more rapidly than in SSA. According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), SSA has slightly more than 10 percent of the world's population, but is home to more than 60 percent of all people living with HIV in the world.² The global responses to the pandemic include efforts at prevention, testing, and provision of both appropriate medication and health care. HIV/AIDS has no known cure, but for persons who are already infected with the virus, the use of antiretroviral (ARV) medications and other HIV/AIDS medicines under strict medical instructions and/or supervision can prolong their lives. This has raised widespread concern about the need to make these lifesaving medicines not only available but also affordable. Those without access to treatment will progressively deteriorate and almost certainly die.

Providing access to affordable HIV/AIDS medicines, particularly in SSA, has been a multifaceted challenge. Complicating factors include poverty and inadequate funding, a lack of appropriate chemical industry capacity, poor social and medical infrastructure and amenities, inadequate legislation, and the existence of patents on ARVs. Although patent protection is by no means the only barrier to access, patents play a significant or even a determinant role in limiting access to affordable HIV/AIDS medicines because they grant the patent holder a monopoly on a pharmaceutical product and its production process for a number of years. This curtails competition by giving the patent holder freedom to set prices. These prices in many instances have been unaffordable to persons who need the medicines in developing countries, particularly in SSA.³

The International Debate on TRIPS Flexibility

The impact of patents on public health first came to international attention in 1998 when President Nelson Mandela signed the South African Medicines and Related Substances Control Amendment Act (Act 90) of 1997. This act sought to create a legal framework within which to increase the availability of lower-cost medicines in the country. It was,

however, opposed by the Pharmaceutical Manufacturers' Association of South Africa. Together with 39 transnational pharmaceutical industries, the association filed a lawsuit against the government of South Africa in the High Court in Pretoria, alleging that the changes in the law violated the TRIPS Agreement. The court initially ordered the suspension of the amendment while the case was pending.⁴ The main components of Act 90 that the industry questioned were (a) generic substitution for drugs with expired patents, (b) establishment of a committee to regulate and ensure transparency in medicine pricing, (c) incorporation of international exhaustion of rights (parallel importation), and (d) establishment of an international competitive bidding system to ensure provision of medicines for the country.

The conflict attracted many actors, both locally and internationally. On the one hand, the United States and the European Union supported the pharmaceutical companies and threatened trade sanctions against South Africa if it did not revoke the amendment. On the other hand, representatives of nongovernmental organizations (NGOs) involved in an international campaign to secure access to medicines argued that Act 90 was entirely consistent with the TRIPS Agreement provisions. The NGOs were successful in mobilizing international public opinion in their favor and the United States government eventually changed its position on the matter.⁵ By April 2001, after three years of intense court hearings, the plaintiffs had failed to provide technical arguments to show that the amendment violated the TRIPS Agreement. They had also lost government support from the United States and Europe in the dispute, and intense international pressure was building up against them. They were therefore obliged to withdraw the lawsuit.

The South African case turned out to be groundbreaking in fostering international debate and civil society activism on the public health implications of the TRIPS Agreement. By February 2001, the European Union had adopted the Action Programme to Accelerate the Fight Against HIV/AIDS. In June 2001, the United Nations Special Session on HIV/AIDS (Special Session) produced a Declaration of Commitment on HIV/AIDS that urged countries to "cooperate constructively in strengthening pharmaceutical policies and practices, including those applicable to generic drugs and IP regimes, to further promote innovation and the development of domestic industries consistent with international law."⁶ Also, during the Special Session, the United States withdrew its WTO case against Brazil's use of compulsory license.⁷

Before the Special Session, in April 2001, the African Group of the WTO had brought up the need to include the issue of access to medicines in

the TRIPS Council agenda. The HIV/AIDS pandemic was already devastating SSA, with more than 25 million people in the region believed to be infected. In the Special Session, the African Group formulated a proposal urging WTO member states to issue a special declaration affirming that none of the TRIPS Agreement provisions should impede member states from taking the necessary measures to protect public health.⁸

In September 2001, the African Group, with support from 19 other member states, presented a draft of a Ministerial Declaration on the TRIPS Agreement and Public Health, which in essence reinforced the April proposal by the African Group. The developed countries, led by the United States, presented an alternative draft that emphasized the importance of IP protection for research and development and the need to limit use of the TRIPS flexibilities to special situations of crisis or national emergency. The WTO Ministerial Conference on the TRIPS Agreement and Public Health considered these drafts during its sessions in Doha, Qatar, in November. These discussions resulted in the Doha Ministerial Declaration of November 14, 2001 (the Declaration), which significantly reflects the African Group's position on interpretation of the TRIPS Agreement in relation to public health. The subsequent WTO General Council Decision of August 30, 2003 (the Decision), on the impasse reflected in paragraph 6 of the Declaration also draws from the contribution made by the African Group to the drafting of the text presented to the General Council.

The Doha Declaration and the Decision largely settled the disagreement between the developing- and developed-country members of the WTO as to the proper interpretation of the provisions of the TRIPS Agreement. Generally, the Declaration upheld the right of member states to adopt a flexible interpretation of the TRIPS Agreement's provisions, through a waiver of article 31(f), to ensure the protection of public health. The specific concerns of the developing countries, with regard to the issue of compulsory licensing and parallel importation, were addressed by affirming the freedom of member states to determine the grounds upon which to grant compulsory licenses, their right to determine what constitutes a national emergency or circumstances of extreme urgency, and their freedom to determine which regime of exhaustion of IPRs they would establish. The Declaration also extended to at least 2016 the transition period within which least developed countries (LDCs) are required to provide IP protection for pharmaceutical products and processes, as well as test data protection (paragraph 7).

The restriction in article 31(f) of the TRIPS Agreement that required production under a compulsory license to be predominantly for the domestic market was subjected to decision by the WTO General Council. The Decision in essence decreed an interim waiver of the article 31(f) limitation, allowing medicines produced under a compulsory license to be exported to countries with insufficient or no manufacturing capacity under specified procedural terms and conditions. The Decision provides the basis for an amendment to the TRIPS Agreement that is yet to be ratified by the required number of members in accordance with the rules of the WTO. The Decision, however, remains in force until the required ratification is done (WTO 2005).

The Declaration and Decision place the issue of access to affordable medicines in a new light, requiring appropriate implementation strategies by developing countries to benefit from the TRIPS flexibilities. However, accessible and affordable HIV/AIDS medicines still remain a major challenge in SSA, five years after the Declaration and two years after the Decision, despite an ongoing global effort to shape an appropriate response to the HIV/AIDS pandemic. It is therefore necessary to review the capacity of countries in the SSA region to utilize the TRIPS flexibilities and identify the prevailing administrative and implementation challenges. Toward this end, the Bank and African Regional Intellectual Property Organization (ARIPO) have commissioned this study to assess the utilization of the TRIPS flexibilities and make recommendations aimed at improving access to affordable HIV/AIDS medicines in the African region.

Scope and Methodology of the Study

The study begins with an overview of the TRIPS Agreement and its flexibilities, delineating the legal requirements of the TRIPS Agreement regarding their use. It then examines the challenges entailed in the beneficial interpretation and implementation of the TRIPS Agreement at both the national and regional levels under the auspices of ARIPO and African Intellectual Property Organization (OAPI). The next section reviews the domestic ARV production experiences of Zimbabwe, Kenya, South Africa, and Ghana with an eye for evaluating the option of sustainable local production. The final section then draws conclusions and makes recommendations.

The study is based on existing literature and on interaction with various key players and resource persons in government institutions, the private sector, and civil society groups, especially NGOs at the

national level. Information was gathered from officials of the regional patent institutions, OAPI and ARIPO, along with official documents of these institutions. International organizations involved in HIV/AIDS work in SSA also provided input.

The study was conducted under considerable time and logistical constraints, making it difficult to meet and interview all the persons that the authors wished to consult during travel across the African continent. Another limitation was the lack of an easily accessible database on ARVs and other HIV/AIDS medicines being used in Africa, their patent status, and their relative prices. National drug procurement bodies were often reluctant to divulge information on prices and quantities of medicines obtained.

Notes

1. The Uruguay Round of trade negotiations lasted from 1986 to 1994. It culminated in establishing a rule-based global trading system with respect to tariff and nontariff barriers, agriculture and textiles, services and IPR, and trade dispute settlement under a newly formed WTO in 1995. For an extensive discussion of the Uruguay Round, see http://www.wto.org/english/thewto_e/whatis_e/tif_e/fact5_e.htm.
2. As of 2005, the estimated global population with HIV/AIDS infection was 40.3 million, of which an estimated 25.8 million cases were in SSA. Of an estimated 3.1 million deaths from AIDS globally in 2005, 2.4 million were in SSA (UNAIDS and WHO 2005).
3. Dr. Eric Goemaere, a Médecins Sans Frontières (MSF) physician working in South Africa, says, "I am revolted when I hear claims that patent rights do not constitute a barrier to treatment here in South Africa. I have seen young women and men die from AIDS-related brain tumors provoking unbearable headaches. I have seen children covered with scars due to AIDS-related dermatitis, unable to sleep for the pain. I knew that all of them could have been helped with ART, but the cost of the patented drugs was the only barrier" (Boulet, Garrison, and 't Hoen 2004, 24).
4. Ibid. Arguing in favor of the legislation, civil society groups called public attention to the number of people who died of AIDS during the suspension of the amendment because they could not afford to pay for treatment. In all, 400,000 people were reported to have died.
5. <http://www.parliament.uk/post/pn160.pdf>. In December 1999, after numerous protests, the United States government withdrew South Africa from the U.S. Trade Representative's Special 301 Watch List, which names countries that have violated trade rules. For a detailed discussion on U.S.–South Africa bilateral

- trade dispute over the Medicines Act, see <http://www.cptech.org/ip/health/sa/olderdocuments.html>.
6. Article 55 of the Declaration of Commitment on HIV/AIDS. See <http://www.un.org/ga/aids/docs/aress262.pdf>.
 7. The United States withdrew its case against Brazil in the WTO Dispute Settlement Body after intense international pressure from NGO activists. They argued that a decision against Brazil could negatively impact the continuity of that country's national AIDS program, which guaranteed universal access to care for people with HIV/AIDS (Law 9.313/96). Although this victory came at the expense of the signing of a bilateral agreement with the United States, Brazil succeeded in relying on article 5(2) of the 1967 Paris Convention to enhance its local ARV industry. This article states that each signatory country can adopt legislative measures, such as compulsory licensing, to prevent abuses resulting from exercising exclusive rights conferred by the patent, which may include the lack of local exploitation.
 8. http://www.wto.org/english/tratop_e/trips_e/counciljun01_e.htm.

CHAPTER 2

Overview of the TRIPS Agreement and Flexibilities

The TRIPS Agreement requires all current and future members of the WTO to adopt and enforce, through domestic legislation, nondiscriminatory minimum standards prescribed by the TRIPS Agreement for the protection of IPRs, including patents for pharmaceutical products. Article 7 of the TRIPS Agreement, however, requires that the enforcement of IPRs promote both innovation and the transfer and dissemination of technological knowledge in a manner conducive to socioeconomic welfare and to a balance between the rights and obligations of producers and users. This basic nature of the TRIPS Agreement, seeking to ensure a balance between the rights of IPR holders on the one hand and consumers on the other, is reinforced by the principles stated in article 8. This article allows WTO member states, in formulating or amending their IP-related laws and regulations, to adopt measures necessary to protect public health and promote the public interest in sectors vital to their socioeconomic and technological development.

Among specific obligations, article 27 requires member states to provide patent protection for all inventions, whether products or processes, in all fields of technology. There are, however, provisions under the article for exemption from patentability. Article 28 confers extensive rights on the patent holder, including exclusive marketing rights for the entire patent

duration (subject to the provisions of article 30). Article 33 provides that the minimum period of patent protection from the filing date shall be 20 years. Another obligation that has a direct impact on access to medicines is the requirement in article 39.3 that member states protect undisclosed test data against unfair commercial use.

The combined effects of the permissible flexibility in interpreting the provisions of the TRIPS Agreement and the specified limitations to the obligations under the TRIPS Agreement form the basis of what are often referred to as the “TRIPS flexibilities.” In the specific area of public health, paragraph 4 of the Declaration reiterates that the TRIPS Agreement can and should be interpreted and implemented in a manner that supports members’ right to protect public health, particularly by ensuring access to medicines for all. The Declaration (in paragraph 5) also clarifies the permissible interpretation of certain provisions of the TRIPS Agreement. These include the right to grant compulsory licenses, the freedom to determine the grounds upon which such licenses are granted, the right to determine what constitutes a national emergency and circumstances of extreme urgency, and the freedom of member states to choose which regime of exhaustion of IPRs they will establish. (See table 2.1 for both the time-based and substantive flexibilities that derive from the TRIPS Agreement, the Declaration, and the Decision and that provide policy options for ensuring access to medicines.)

Implementation of the TRIPS Flexibilities

The TRIPS flexibilities can be seen as the balancing criteria that developing countries were able to achieve to address their specific concerns over patent protection and access to medicines during related negotiations within the WTO. However, any analysis of the usefulness of the flexibilities in protecting public health must take into account the ability of developing-country member states of the WTO to implement them. This study therefore critically examines each of the flexibilities listed in table 2.1 and evaluates its implementation within SSA to enhance access to HIV/AIDS medicines in the region.

The two regional patent systems, ARIPO and OAPI, play pivotal roles in determining how their member states deal with IP issues, including utilization of the TRIPS flexibilities. ARIPO’s members include 16 mainly anglophone African states, while OAPI has 16 francophone members.¹ Several large economies in SSA, notably Nigeria and South Africa, do not belong to either system.

Table 2.1. TRIPS Flexibilities That Facilitate Protection of Public Health

<i>Flexibility</i>	<i>TRIPS article</i>	<i>Remarks</i>
Exemptions from patentability	27.1 27.3(b)	Need to interpret “novelty” in domestic legislation in a manner that excludes new and second uses of medicines
Transition period to adapt national legislation to the TRIPS Agreement	65 66	Deadlines from January 1995: a. Developed countries: 1 year, until January 1996 b. Developing countries: 5 years, until January 2000 c. LDCs: 11 years, until January 2006
Transition period to recognize patents	65.4	a. Developing countries have an additional five years (until 2005) to recognize patents in technological sectors not protected before the TRIPS Agreement (for example, patent protection for pharmaceutical products and processes) b. Pharmaceutical products and processes: transition period for LDCs extended to January 1, 2016
Compulsory licensing	31 (Other Use without Authorization of the Right Holder)	Allows exploitation of patented object through government authorization without right holder’s consent
Parallel imports or exhaustion of patent rights at regional and/or international levels	6 (Exhaustion of Rights)	Allows importation and resale in a country without consent of the patent holder of a patented product put on the market of the exporting country by the patent holder or in another legitimate manner
Limits on data protection	39.3 (Protection Limited to “Unfair Commercial Use” Only)	Need to incorporate in domestic legislation the right of pharmaceutical regulatory authorities to rely on available data to assess efficacy and toxicity of new entrant drugs with similar bioequivalence
Bolar exception (early working provision)	30 (Exception to Rights Conferred)	Allows testing and establishment of the bioequivalence of a generic version before expiry of the patent; also for purposes of research and experimentation

Source: Author’s compilation.

Note: These flexibilities are taken from the entire WTO legal framework. They include the TRIPS Agreement, the Declaration, and the Decision.

Exemptions from Patentability

Eligibility for patentability is a very important prerequisite for the initiation of action to protect the patent of any invention, including a pharmaceutical product. Article 27.1 of the TRIPS Agreement stipulates that a patent shall be available for any invention, whether product or process, if it is “new,” involves an inventive step, and is capable of industrial application. The Agreement itself does not specify what constitutes “new” or how the requirement of novelty should be met. Legally, member countries, according to paragraph 4 of the Declaration, have the opportunity and indeed the obligation to interpret and implement the provisions of article 27.1 with respect to the patentability of the “new use” of medicines in a manner that seeks to protect public health and ensure access to medicines. It would thus be legally sound to interpret and implement the novelty requirement by exempting from patentability the new use of any known pharmaceutical product, including HIV/AIDS medicines. However, where domestic legislation or regional legal instruments do not specifically preclude granting such new- and second-use patents, applications are likely to be processed without the required critical analysis and granted, albeit with serious implications for access to medicines.

In SSA, neither the domestic laws of the individual countries nor the legal instruments of OAPI and ARIPO address the issue of non-patentability of new and second uses of medicines. This creates the risk that patents will be granted for new and second uses. When a patent application is filed directly at ARIPO and OAPI, the examination of the patentability criteria of a product that is the subject of a patent application is the sole responsibility of the regional organization. In the case of ARIPO countries, for instance, it is ARIPO that examines the application as to substance (for patents) and decides whether a patent can be granted. However, member states that have the capacity to examine the substance can examine applications that are filed at their offices and are based on the applicable national patent law for patentability. In any case, a member state reserves the right to refuse to ratify a patent granted by ARIPO, thus making the patent nonoperational in its own territory. The decision on patentability of the product in question lies with ARIPO.

With OAPI, the situation is even more stringent and centralized, as stipulated in articles 2(2), 8(1), and 8(2) of the Bangui Agreement.² The Bangui Agreement is the law governing industrial property rights in each of the member states of OAPI, and member countries rely on it as the legal framework within which to operate their individual patent systems. For the member countries, therefore, the Bangui Agreement is national law.

Consequently, once a patent is granted by OAPI, it automatically applies in all member states. As is the case with ARIPO, the decision on patentability of a product that is the subject of an application rests with OAPI.

Both OAPI and ARIPO operate within the ARIPO-OAPI-ARCT-WIPO Quadripartite Agreement, which also involves the African Regional Centre for Technology (ARCT) and WIPO. It appears that under this framework, both OAPI and ARIPO function as *de facto* registration agencies for patents filed and granted in the developed countries without recourse to any meticulous examination of such patents with regard to new and second uses of existing pharmaceutical products. A related concern is that in contrast to the prevailing situation in SSA, patent challenges are very frequent in the developed world and sometimes result in the withdrawal of granted patents. Under the current system, patents can be withdrawn in the developed world, yet remain in effect within OAPI and ARIPO. To take advantage of the flexibility provided under article 27.1 of the TRIPS Agreement, therefore, it would be advisable to specifically exclude new uses from patentability in the legal instruments of both organizations, as well as in the domestic legislation of SSA countries.

Transition Periods

By virtue of the Doha Declaration, LDCs now have until the end of 2016 to become TRIPS-compliant with respect to patent protection for pharmaceutical products. This flexibility has tremendous potential for enhancing access to HIV/AIDS medicines in SSA, but it appears that African countries are not taking optimal advantage of the opportunity.

Thirty-four of the world's 50 LDCs are in SSA. The extension to 2016 provided by the Declaration could therefore be understood as mainly for the benefit of the SSA region. The reality of the situation, however, is that because of their membership in WIPO, ARIPO, and OAPI, most of these countries have had patent laws that predate the TRIPS Agreement and are less liberal than the requirements of the Declaration and the Decision.

The Bangui Agreement, for example, was last revised in 1999 and does not conform to the Declaration and the Decision. Under this agreement, which is the national patent law of its member countries, all the member states, including the LDCs, are compelled to offer patent protection for pharmaceutical products with OAPI-approved patents. The gravity of the problem becomes clear when one considers that, of the total OAPI membership of 16 countries, all but three (Cameroon, Côte d'Ivoire, and Gabon) are LDCs.

In the case of ARIPO, although member states have their individual IP laws, there is a trend toward filing most patent applications at the regional level and designating affected countries in such applications. Although this is convenient and cost-effective, the tendency is to include countries that, under the TRIPS Agreement, the Declaration, and the Decision, should not be providing patent protection for pharmaceutical products in the first place. The absence of a regularly updated database on member countries and the weakness of the notification system within the organization have contributed to this lapse. A case in point is Ghana, which did not have patent protection for pharmaceutical products before 1992, but during that period was designated as territory to be covered under a patent that ARIPO granted to Pfizer Pharmaceuticals for Zithromax. Although Ghana was notified of the grant by ARIPO, it did not make any objection within the time required. The patent holder, ARIPO, and other interested third parties therefore erroneously believed that there was a valid patent in force in Ghana, although the grant was void from the beginning.³

The regional bodies, both OAPI and ARIPO, could improve access to medicines in the SSA region by amending their respective legal instruments to take into account the transitional provisions by specifically excluding their LDC member states from patent applications for pharmaceutical products. In doing this, both OAPI and ARIPO should also provide technical assistance to their member countries and help them deal effectively with the rights that have accrued to holders of existing patents.

Across the SSA region, amendments to domestic IP laws at the country level have been generally slow. The LDC countries in the region that should benefit from the transitional provisions have yet to amend their domestic legislation to enable them to take advantage of this flexibility. A case in point is that of Malawi, an LDC member of ARIPO, which has not yet amended its law to reflect its LDC status. In effecting its anti-retroviral therapy (ART) rollout program, the government of Malawi invoked paragraph 7 of the Doha Declaration to take advantage of the 2016 extension for procurement of the fixed-dose combination drug Triomune, which is produced by Cipla, an Indian generic company. Two components of the combination, however, had been patented in Malawi before the Declaration, and no changes were made to the national law to suspend or cancel those patents. Although the products were subsequently supplied to Malawi without an objection from the patent holders, this was absolutely at the discretion of the patent holders.

The difficulty for LDCs caught up in this situation is how to incorporate this flexibility into domestic legislation within a legal framework that ensures harmony with the rights that have already accrued to holders of existing pharmaceutical patents. To create certainty in the application of this flexibility, LDC members should seek technical assistance through the regional organizations to address this issue of accrued rights. Efforts to discuss the situation with the holders of the existing patents on an individual country basis may also be helpful.

Compulsory Licensing and the Regional Trade Option

Compulsory licensing (as provided in article 31) enables a competent government authority to license the use of an invention to a third party or government agency without the consent of the patent holder under grounds to be determined by the country interested in utilizing the flexibility. The patent holder is subsequently informed, however, and adequate remuneration is paid. Compulsory licensing can also be an effective flexibility for checking anticompetitive practices, depending on how it is employed. The conditions stipulated in the TRIPS Agreement for issuance of a compulsory license include promotion of the public interest, national emergency or extreme urgency, public noncommercial use, refusal by the patent holder to deal within a reasonable time, dependent patents, and remedying of anticompetitive practices so declared by a judicial or administrative process. By the rules of the TRIPS Agreement, the provisions in domestic legislation for the use of a compulsory license need to ensure that the compulsory license provisions are not unnecessarily restrictive, prohibitive, and burdensome.

The Decision allows medicines produced under a compulsory license to be exported to member countries with insufficient or no manufacturing capacity under certain terms and conditions. The Decision is essentially an interim waiver of the article 31(f) limitation on exports of medicines produced under a compulsory license and of article 31(h), which deals with payment of compensation for issuing a compulsory license. It is important to note that a WTO waiver means essentially that a member shall not initiate a complaint against another member if the latter acts under the terms of the adopted waiver. However, to the extent that national laws are not aligned with the waiver, the patent owner could invoke provisions in national laws to prevent acquisition of the generic version of a patented medicine under a compulsory license. The effective utilization of the Decision, therefore, would depend on the extent to which national laws allow the waiver.

Domestic legislation of most countries in Africa has provided for compulsory licensing on public health grounds, and some countries in the region have had occasion to resort to the use of compulsory licensing. Although the ARIPO legal instruments are rather liberal on compulsory licensing, the OAPI legal instruments are quite restrictive.

South Africa, which does not belong to either of the two regional bodies, has a unique system. This includes a strong regime for dealing with anticompetitive practices combined with provisions for compulsory licensing. Together these create an effective synergy to encourage negotiated voluntary licenses and an eventual lowering of prices. Under article 31(k) of the TRIPS Agreement, when a judicial or administrative process has determined a practice to be anticompetitive, a member state is allowed to use compulsory licensing to remedy the situation. However, most countries in the region do not yet have an adequate regulatory framework that can identify and address anticompetitive practices (TWN 2003, 95). In such cases, it would be advisable to draw up an illustrative (non-exhaustive) list of practices that may be anticompetitive for the purpose of guiding a compulsory license application. This may take the form of administrative guidelines or directives (TWN 2003, 95). The South African experience in this area is well worth studying as a guide for other countries in the subregion.

It must be stated, however, that the South Africa Patents Act of 1978 is an example of a patent law with restrictive compulsory licensing provisions. Sections 4 and 78, which deal with state acquisition of patents, require some form of negotiation between the state and the patent holder. Article 31 does not require such negotiation as a prerequisite for issuing a government-use order in cases of emergency or extreme urgency. Though section 4 includes measures to be taken should the parties fail to reach an agreement, the commissioner is still required to hear the patent holder before acquisition by the state. Clearly, this requirement goes beyond the obligations imposed by the TRIPS Agreement, becoming an example of "TRIPS-plus" and threatening to cause delays during emergencies. This accounts, in part, for the fact that South Africa to date has not issued a compulsory license.

In 2002, the government of Zimbabwe declared an HIV/AIDS emergency for a period of six months and issued a government-use order for the production and import of ARVs, based on the provisions of chapter 26.03 of its Patents Act of 1996 (as amended in 2002). The order enabled Varichem Pharmaceuticals, a local company, to manufacture generic versions of selected ARVs at a cheaper price. Before the declaration was

issued, the average monthly cost of first-line treatment was estimated at \$30 to \$50, which was unaffordable in the local market. Varichem's generic version of the combination medicine made of lamivudine and zidovudine, called Varivar, sold at a little more than \$15 for a month's supply, about half the price of the nongeneric drug.

In 2005, the government of Ghana issued a government-use order to selected generic pharmaceutical companies in India, allowing Ghana to import generic versions of selected ARVs patented by GlaxoSmithKline (GSK). Subsequently, the cost of the ARVs, \$495 for a year's treatment, fell there by more than 50 percent, to \$235.⁴

The government of Mozambique attempted in 2004 to locally manufacture the fixed-dose combination of lamivudine, stavudine, and nevirapine under a compulsory license issued to Pharco Mozambique, a local company. The effort, however, had to be shelved because of the high price of active pharmaceutical ingredients (APIs), which rendered the production economically unviable.

OAPI presents a different approach to the use of compulsory licensing. Although article 17 of the Bangui Agreement states that "in the case of discrepancies between the provisions of the TRIPS Agreement or its Annexes and those of international conventions to which the member states are parties, the latter shall prevail," this agreement remains essentially inconsistent and noncompliant with the TRIPS Agreement, the Declaration, and the Decision in the areas of compulsory licensing, government use, and parallel importation. For instance, in the area of compulsory licensing for government use, the Bangui Agreement requires member governments to enter into a prior negotiation with the patent holder for a voluntary license. A compulsory license can be granted only upon proof of the patent holder's refusal to deal with the state on reasonable commercial terms and conditions. This is clearly TRIPS-plus and contrary to article 31(b) of the TRIPS Agreement, which waives such prior negotiation in cases of emergency. This may explain why no compulsory license has ever been issued by any member of OAPI since the organization came into being. It could be inferred that OAPI's intent is to restrict the use of compulsory licensing to attract technology transfer and investment in the pharmaceutical sector. To date, however, there is no evidence of any such investment in the OAPI region, and the pharmaceutical industry there remains in its infancy.

A common gap in the legislation of countries in the region is the lack of a clear provision for determining the level of "adequate remuneration" to be paid upon the issuance of a compulsory license. Moreover, there

are no specific provisions in the laws of the region's countries for a waiver of the payment of royalties by the importing country, as envisaged by the Decision. The rule is that when a medicine is imported from a country in which it is not patented, the obligation to pay compensation for the issuance of a compulsory license lies with the importing country. However, when the medicine is patented in both the exporting and importing countries, the payment of compensation by the importing country is waived in accordance with the Decision. Guidelines for the determination and payment of royalties will be very helpful in facilitating their administration, as well as increasing predictability and transparency. (The Canadian export royalty guidelines may provide a useful model. These guidelines use a sliding scale of 0.02 to 4.0 percent of the price of the generic product, based upon the country's rank in the Human Development Index of the United Nations. For most countries in the Economic Community of West African States (ECOWAS), for instance, the rate is less than 1 percent.

It would be useful to clarify in national laws the various circumstances under which an importing country would be required to waive payment of royalties. This is essential because most countries in the region lack production capacity and rely on imports to meet their requirements for HIV/AIDS medicines.

Most countries in the region have relatively small markets and low purchasing power. Individually, they do not offer viable and profitable markets for pharmaceutical products. Thus, they have difficulty in attracting generic industries, which seek economies of scale that can ensure both low prices for medicines and profits to investors. Consequently, most countries in the region buy their ARVs from India. But as patients begin to require the use of second-line medicines, which are most likely to be patented in India, the option of compulsory license in combination with the regional trade area (RTA) option available under the Decision becomes more attractive.

The Decision allows a recognized RTA to be categorized as a single domestic market under the TRIPS Agreement. When an RTA becomes the "domestic market," this creates the possibility of bulk purchases and economies of scale that could result in cheaper prices. The text of the Decision also explicitly defines "eligible importing Members" as members who have insufficient manufacturing capacity and meet all the conditions under article 31 of the TRIPS Agreement. Another condition for qualification stipulated in the Decision is that 50 percent of the membership of the RTA should be LDCs. The RTA is further required to institute

measures to safeguard against the risk of reexport of medicines to countries that do not qualify. This is to counter the likelihood that medicines destined for poor countries will be reexported to the developed countries.

The Indian Patents Act of 1970 has been amended to align it with India's obligations under the TRIPS Agreement. It also has provisions that enable India to issue a compulsory license solely for export in accordance with the Decision, provided that the importing country also issues a compulsory license. Thus, an RTA could issue a compulsory license for imports from India.

Arguably, pooled or bulk procurement could serve as a cost-containment strategy for the RTAs, if effectively managed. Internationally, there are many examples of best practices in pooled procurement resulting in significant savings. The Eastern Caribbean Drug Service (ECDS)—now called the “Pharmaceutical Procurement Service”—was set up in 1996. Before its establishment, individual countries managed their own procurement processes, with wide price differentials. ECDS set up a system to pool needs, selectively and competitively manage the bidding process, guarantee payment, and (most important) monitor supply and quality. In the first year of its operation, ECDS managed to lower pharmaceutical expenditure by an impressive 44 percent on average (MSH and WHO 1997).

The option is of particular interest in the case of ECOWAS, the West African economic community, because more than 80 percent of its members are LDCs.⁵ ECOWAS only needs to marshal the political will to assert its recognition as an RTA (in line with the terms of article XXIV of GATT) to derive benefits from its large market, economies of scale, and stronger bargaining power under the RTA option. In the effort to enhance access to HIV/AIDS medicines, the ECOWAS Secretariat (and indeed all other RTAs in SSA) could focus on maximizing the use of this option by first harmonizing treatment protocols for HIV/AIDS and then evolving common drug regulatory regimes and medicine procurement strategies.

The Southern African Development Community (SADC) has been discussing how to enhance access to ARVs as a block.⁶ The Common Market for Eastern and Southern Africa (COMESA) has already launched a project aimed at facilitating mutual recognition of national registration of medicines.⁷ This essentially entails an agreement among its member states that, once a product fulfills the conditions for registration in one country, it will be eligible for an abbreviated registration process in the other member states.

Exhaustion of Rights and Parallel Importation

Article 6 of the Decision provides that matters relating to exhaustion of rights shall not be subject to dispute settlement. The Doha Declaration, in paragraph 5(d), also reaffirms that countries are free to determine their own regimes for the exhaustion of patent rights without challenge. Member states can therefore opt for international, regional, or national exhaustion of patent rights. By this doctrine, the rights of the patent holder are considered exhausted or extinguished on first sale of the product anywhere in the case of international exhaustion, within the region in the case of regional exhaustion, and within the country in question in the case of national exhaustion.

Parallel importation offers benefits to developing countries by facilitating the import of patented products from countries where they are sold at lower prices into countries where the same products are sold at higher prices. It is one of the options available for use by developing countries, including African countries, to source cheaper medicines.

Before the TRIPS Agreement entered into force, the changes that were made to the preindependence patent laws of most countries in the SSA region, particularly changes made in the 1990s, were based on the WIPO Model Laws on IP and provided only for national exhaustion of rights. As countries align their laws with the TRIPS Agreement, the Decision, and the Declaration, there is a trend toward incorporating provisions that permit international exhaustion of rights. As a result, different SSA countries currently have different levels of exhaustion of rights.

For the member states of OAPI, article 8(1) (a) of the Bangui Agreement precludes international exhaustion and restricts parallel importation to the regional exhaustion regime within OAPI member countries. Its requirement that LDC members provide patent protection for pharmaceutical products and the restriction on the use of international exhaustion of rights both prevent member states from shopping around for the best price for HIV/AIDS medicines on the global market. Ghana, Kenya, South Africa, and Zimbabwe are some of the SSA countries that provide for international exhaustion of rights. Other countries, among them Botswana and Nigeria, continue to provide a narrow regime of national exhaustion of patent rights.

Botswana and Kenya provide examples of differing treatment of exhaustion of rights. Under the Botswana Industrial Property Act of 1996, the patent holder's right is deemed exhausted when the patent holder places the article on the market in Botswana. The Kenyan Industrial Property Act of 2001, by contrast, provides an international exhaustion regime.

Section 58(2) stipulates, “the rights under the patent shall not extend to acts in respect of articles which have been put on the market in Kenya or in any other country or imported into Kenya.” Regulation 37 of the Kenyan Industrial Property Regulations of 2002 further clarifies that “the limitation on the rights under a patent in Section 58(2) of the Act extends to acts in respect of articles that are imported from a country where the articles were legitimately put on the market.” NGOs operating in Kenya, such as Médecins Sans Frontières (MSF, or Doctors without Borders) and Mission for Essential Drugs and Supplies (MEDS), thus have been able to take advantage of parallel imports.

In accessing the benefits of parallel importation, the major difficulty faced by many SSA countries is that they have not adapted their domestic laws appropriately to allow for international exhaustion of rights. Therefore, they are unable to take advantage of the flexibility and shop around for cheaper medicines that may be available in other markets. Considering the HIV/AIDS disease burden and the critical need to scale up treatment in the face of scarce resources in SSA, incorporating an international exhaustion-of-rights regime into domestic patent laws could be very beneficial in promoting access to medicines.

Limits on Test Data Protection

Article 39.3 of the TRIPS Agreement allows each member to determine how to protect test data in the public interest. To interpret article 39.3 as demanding data exclusivity—rather than data protection against unfair commercial use—has the potential to block access to generic versions of new medicines. Such an interpretation would mean that until the expiration of the exclusive period, drug regulatory authorities could not use data submitted by the innovator company as a basis to assess the generic version. This could stifle initiative in production of generic versions of medicines and create a monopoly for the innovator’s product that could result in higher prices. To require generic producers to conduct trials on equivalent compounds imposes additional costs, which will be passed on to the consumer.

Most countries in Africa do not have specific provisions with respect to data protection. Where such provisions exist, the authorities protect data against disclosure to a third party for “unfair commercial use.” In Ghana, the protection provided for test data is contained in the Unfair Competition Act of 2000 and is based on the wording of article 39.3. This protection is limited to the nondisclosure of test-data information to third parties and does not preclude the use of such data for comparison in the granting of marketing approval for generic versions.

It would be useful for member states in the SSA to clearly stipulate in their domestic laws the extent of data protection in accordance with the TRIPS Agreement, with a view to strengthening the hand of national drug regulatory authorities in generic medicines registration. From a public health perspective, it is essential that countries adopt policies that ensure competition, such as limiting data protection, to permit the timely entrance of generic medicines of public health importance.

Bolar Exception

The TRIPS Agreement allows members to permit generic medicine manufacturers to undertake and complete the task of obtaining regulatory approval from national medicine regulatory authorities for their generic versions before the expiry of the patent on the original product. This flexibility, known as the “Bolar Exception,” was confirmed by the WTO dispute panel ruling involving Canada and the European Union. The ruling allows generic versions to be placed on the market almost as soon as the patent expires. This experimental-use exception is also considered as implying an early working provision.

Considering this provision’s importance to technology transfer and local manufacturing, it seems advisable to include clear and unambiguous provisions on it in national laws. Correa (2000) suggests wording along the following lines: “The patent shall have no effect with respect to any act including testing, using or making the invention solely for purposes reasonably related to the development and submission of information required under any law of (country) or of another country that regulates the manufacture, construction, use or sale of any product.”

Although the countries of the subregion have limited capacity for the production of pharmaceuticals, there is a demonstrated effort under way in Ghana, Kenya, Nigeria, South Africa, and Zimbabwe to promote the local manufacture of lifesaving medicines, including those for HIV/AIDS. The introduction of the early working system into the national laws, as has been done in South Africa and Zimbabwe,⁸ is therefore worthy of emulation as a crucial step toward the eventual production and distribution of essential medicines within SSA.

Implementation Challenges

Compulsory licensing and parallel importation are the two most commonly used flexibilities. Their effective and timely implementation requires political will and well-defined administrative structures and procedures

for coordination and decision making. This poses major challenges to countries in the SSA region in implementing these flexibilities.

The effective use of compulsory licensing as a tool for gaining access to medicines at affordable prices requires adequate technical knowledge and an efficient administrative infrastructure, both of which appear to be lacking in most countries in the region. The most significant barrier to the use of compulsory licensing in SSA is the lack of well-defined, clear, and simple administrative procedures necessary for implementation. Effective coordination of the related functions of the different state agencies involved is crucial when the issuance of a compulsory license is anticipated. For instance, although a country's patent office oversees patent applications and the granting of patents, it is the ministry of health that is responsible for determining public health needs, including the selection of required medicines. Furthermore, the trade ministry coordinates WTO activities at the country level, but the attorney general or the commissioner of patents is responsible for issuing the compulsory license.

These agencies need to work closely together in an efficient manner to ensure that the issuance of a compulsory license is timely, legal, and beneficial. Developing clear decision-making processes, with coordinated step-by-step responsibilities of various agencies, could address this difficulty and create confidence in the use of this option. The contemporary best practice within the continent for the issuance of a compulsory license is the establishment and use of a multisectoral committee involving all key players in the decision-making process.

Another challenge associated with the compulsory license option is the tedious exercise of conducting patent searches, which sometimes produce ambiguous results. A patent search is supposed to confirm the patent status of a pharmaceutical product or process and determine whether a compulsory license would be needed to legally procure a generic version. But patents are territorial and may not always be applicable in a given country. Most countries under the ARIPO and OAPI regional patent systems are designated countries under a patent application at the regional level. Once the regional office grants the application, the designated countries are to be notified, and where there is no objection, the patent protection automatically applies in those countries. Patent applicants may also make their applications at the national level. This dual level at which applications can be made and granted and the lack of effective linkage and coordination between the member states and the regional offices make patent searches difficult and sometimes unreliable.

In the case of Ghana, a patent search at ARIPO on selected ARVs was discouraging insofar as the results failed to clarify the patent status of some of the products. In its response to the search, ARIPO used ambiguous wording: “It *would appear* that those products were patented in Ghana” (emphasis added). Such uncertainty on the part of ARIPO regarding the status of medicines makes it difficult to proceed with the issuance of a compulsory license. The situation becomes even worse when results of a search conducted by the supplying company for the product, using other sources, are at variance with the results of the search conducted by the member state that wants to issue the compulsory license.

These difficulties discourage the use of this policy option when countries are in urgent need of lifesaving medicines for their people. Though the option is available, the likelihood of delay and uncertainty makes it unappealing in such circumstances. Countries that have taken advantage of this option, such as Ghana and Zimbabwe, testify to the inherent delays in the system.

The creation of a database of patented medicines in the subregion, synchronizing country and regional information, could address this challenge. Making such a database easily accessible to countries would create confidence in the procurement of affordable generic medicines by using the flexibility.

The regional trade option provided by the Decision has great potential to address the issues of accessibility and affordability if placed in the proper context and given adequate political support on a regional basis. However, taking advantage of the RTA option to reduce prices raises a number of administrative and technical difficulties. In particular, developing a regionally pooled or bulk procurement arrangement for members of the ECOWAS subregion could pose major technical and political challenges. It would entail harmonization of the procurement systems of the francophone and anglophone countries and require sufficient political will to sustain such a system for the benefit of the member states. Basic issues concerning standardization of labeling, treatment guidelines, prescribing practices, and the permissible chemical composition of medicines would require careful consideration and coordination, especially in light of the language barrier. It would be important for treatment guidelines and product labeling to conform to the different sociocultural contexts of the individual countries within the subregion to ensure optimal use.

Strategically, the option of compulsory license to import offers a better deal than local production for countries in the region. However, the

difficulty with importation under the Decision cannot be overemphasized. The complex requirements and procedures are a major reason that, to date, the Decision has not been tested.

Parallel importation, like compulsory licensing, requires administrative and institutional capacity that is lacking in most countries in Africa. If parallel importation is to be useful to countries in the region, administrative, institutional, and managerial capacity must be developed for effective implementation to ensure that substandard and counterfeit medicines do not reach markets.

Limits on data protection present the least challenge to countries in the region, because most of them do not provide for restrictive use of pharmaceutical data. The regional groups would have to resist any such introduction in the public interest, because where generic production lowers prices and increases availability of, and access to, essential medicines, it is in the public interest to limit the extent of test data protection.

Notes

1. ARIPO member states are Botswana, The Gambia, Ghana, Kenya, Lesotho, Malawi, Mozambique, Namibia, Sierra Leone, Somalia, Sudan, Swaziland, Tanzania, Uganda, Zambia, and Zimbabwe. OAPI member states are Benin, Burkina Faso, Cameroon, the Central African Republic, Chad, the Republic of Congo, Côte d'Ivoire, Equatorial Guinea, Gabon, Guinea, Guinea-Bissau, Mali, Mauritania, Niger, Senegal, and Togo.
2. Article 2(2) of the Bangui Agreement, as revised in 1999 (ARIPO 1999), states that for each of the member states of OAPI, "the Organization shall serve both as the national industrial property service within the meaning of Article 12 of the aforementioned Paris Convention and as the central patent documentation and information body." Article 8(1) states that "the Organization shall undertake the examination of patents and utility model applications according to the common procedure provided for in this Agreement and its Annexes I and II." Article 8(2) provides that OAPI "shall grant patents and register utility models and ensure their publication."
3. Interview with CEO of the Ghana Food and Drugs Board.
4. Nkrumah, Y. K. and Osewe, P. L. (2007) "TRIPS compliance and public health: opportunities and obstacles for African countries", *Int. J. Biotechnology*, Vol. 9, No. 2, pp 146.
5. ECOWAS member states are Benin, Burkina Faso, Cape Verde, Côte d'Ivoire, The Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone, and Togo.

6. SADC member states are Angola, Botswana, the Democratic Republic of Congo, Lesotho, Malawi, Mauritius, Mozambique, Namibia, Madagascar, South Africa, Swaziland, Tanzania, Zambia, and Zimbabwe.
7. COMESA member states are Burundi, the Comoros, the Democratic Republic of Congo, Djibouti, the Arab Republic of Egypt, Eritrea, Ethiopia, Kenya, Libya, Madagascar, Malawi, Mauritius, Rwanda, the Seychelles, Sudan, Swaziland, Uganda, Zambia, and Zimbabwe.
8. In South Africa, the 2002 amendments to the Patents Act of 1978 introduced Bolar provisions. In Zimbabwe, section 24(3) of the Patents Act of 1996 (as amended in 2002) allows patented products to be produced without the consent of the patentee six months before the expiry date of the patent.

CHAPTER 3

Local Production: Experiences in Four African Countries

As part of the utilization of the TRIPS flexibilities, a number of advocates have argued for the local production of ARVs as the ultimate means of enhancing access to affordable HIV/AIDS medicines in the developing world. However, production of ARVs is not only research and technology based but also patent controlled and capital intensive. All this poses a steep challenge to African countries that have ventured into this area.

Local production of pharmaceuticals in the African region has been mainly confined to the formulation of drugs in final dosage forms from imported APIs. This approach to production, however, faces significant challenges in light of the global focus on quality. Most ART rollout programs in the region rely on international funding from donors who stress affordability within the context of a strict regime of quality control, both for production processes and for products that are purchased with these funds. Producers must strike a balance between meeting international quality standards and achieving a meaningful market share that ensures viability, in spite of technology deficits and the cost implications of dependence on imported APIs.

This study examines the country experiences of Zimbabwe, Kenya, South Africa, and Ghana in the local production of ARVs in an effort to shed light on the sustainability of this option for African countries.

The socioeconomic factors shown in table 3.1 shape the context for local production of HIV/AIDS medicines in the four countries. Total expenditure on health as a percentage of gross domestic product is higher in Kenya and Zimbabwe than in Ghana and South Africa. General government expenditure on health as a percentage of total expenditure

Table 3.1. Key Socioeconomic Indicators

<i>Indicator</i>	<i>Zimbabwe</i>	<i>Kenya</i>	<i>South Africa</i>	<i>Ghana</i>
Population (<i>thousands, 2003</i>)	12,891	31,987	45,026	20,922
Average annual population growth (<i>percentage, 1993–2003</i>)	1.4	2.1	1.4	2.3
Total expenditure on health as percentage of gross domestic product (<i>2002</i>)	8.5	8.7	4.9	5.6
General government expenditure on health as percentage of total expenditure on health (<i>2002</i>)	51.6	40.6	44.0	41.0
Private expenditure on health as percentage of total expenditure on health (<i>2002</i>)	48.4	59.4	56.0	59.0
General government expenditure on health as percentage of total government expenditure (<i>2002</i>)	12.2	10.7	8.4	8.4
External resources for health as percentage of total expenditure on health (<i>2002</i>)	2.5	0.3	16.4	18.5
Social security expenditure on health as percentage of general government expenditure on health (<i>2002</i>)	0	3.8	9.2	—
Out-of-pocket expenditure on health as percentage of private expenditure on health (<i>2002</i>)	47.3	20.9	80.0	100.0
Private prepaid plans as percentage of private expenditure on health (<i>2002</i>)	38.8	77.7	6.9	0
Per capita total expenditure on health at average exchange rate (<i>US\$, 2002</i>)	118	19	206	17
Per capita government expenditure on health at average exchange rate (<i>US\$, 2002</i>)	61	8	84	7

Source: WHO 2005a.

Note: — = not available.

on health for the four countries ranges from 40.6 percent for Kenya to 51.6 percent for Zimbabwe. The disparity would appear to result from government policy on health funding.

In Ghana, Kenya, and South Africa, the private sector accounts for more than 50 percent of total expenditure on health, but not in Zimbabwe. Ghana, Kenya, and South Africa could thus be said to have a more developed private health sector than Zimbabwe. This is confirmed by the figures on out-of-pocket expenditure on health as a percentage of private expenditure on health, which are 100 percent for Ghana and 80 percent for South Africa. The figure for Zimbabwe is below 50 percent, and that of Kenya is surprisingly low at 20.9 percent. However, a look at the figures on private prepaid plans as a percentage of private expenditure on health—0 percent for Ghana, 6.9 percent for South Africa, 38.8 percent for Zimbabwe, and 77.7 percent for Kenya—explains the low out-of-pocket expenditure in Kenya.

Four companies lead local production of ARVs in the four countries: Varichem Pharmaceuticals (Private) Limited (Varichem) in Zimbabwe, Cosmos Pharmaceuticals Limited (Cosmos) in Kenya, Aspen Pharmacare Holdings Limited in South Africa, and Danadams Pharmaceuticals Limited (Danadams) in Ghana. It is interesting to note that the three companies in this sample that began local production of ARVs in 2003 and are still in production—Varichem, Cosmos, and Aspen—have experienced different levels of success.¹ The factors determining the varying results attained by these companies are the focus of this part of the study.

Zimbabwe: Varichem

Zimbabwe amended its Patents Act of 1996 in 2002 to bring it into conformity with the provisions of the TRIPS Agreement. With respect to public health, the amendment was aimed at incorporating the TRIPS flexibilities into Zimbabwe's domestic legislation to promote their beneficial utilization, including local production.² Section 34 of the Patents Act, Cap. 26:03, provides for "compulsory licensing and government use." It states that the Minister may authorize the use of a patented invention by any government department or third party "for the services of the state"³ on terms and conditions agreed to by the Minister and the patent holder. Section 35 further states that any authorization by the Minister under section 34 during a state of emergency "shall include power to make, use, exercise and vend the invention for any purpose which appears to the Minister necessary or expedient."

Sections 34 and 35 of the Patents Act create the legal basis for Zimbabwe's strategy of moving toward reliance on local production of ARVs to address the affordable access problem. In operationalizing this legislation, Zimbabwe declared a state of emergency on HIV/AIDS (with effect from January 1, 2003, to December 31, 2005), with the intent of utilizing the government-use option to improve access to ARVs. General Notice 240 of 2002, by which the Minister of Justice declared the state of emergency, permitted the state (or a person authorized in writing by the Minister) to make or use any patented drug, including any antiretroviral drugs, used in the treatment of persons suffering from HIV/AIDS or HIV/AIDS-related conditions, and/or to import any generic drugs used in the treatment of persons suffering from HIV/AIDS-related conditions.

The official gazette declaring the state of emergency was published on January 17, 2003. In a letter of authorization signed by the Minister of Justice on April 8, 2003, Varichem Pharmaceuticals (Private) Limited (Varichem), a local pharmaceutical company, was commissioned to "produce antiretroviral or HIV/AIDS-related drugs and supply three-quarters of its produced drugs to state-owned health institutions." Varichem's production line is shown in table 3.2.

Zimbabwe's ARV rollout program is funded mainly through government budgetary allocations for the public sector. This funding relies mainly on tax revenue from an HIV/AIDS gross salary levy of 3 percent on all workers. For access to affordable ARVs, the private sector relies primarily on out-of-pocket payments, private health insurance, and assistance from NGOs such as MSF and internationally organized HIV/AIDS

Table 3.2. Varichem's ARV Production Line

<i>Product</i>	<i>Pack size</i>	<i>Initial unit price (US\$)</i>	<i>Launch date</i>
Varivar ^a	60 tablets	15.35	Jul 03
Stalanev ^b	60 tablets	12.80	Oct 03
Stavudine 30 mg	60 capsules	2.60	Jun 04
Stavudine 40 mg	60 capsules	3.10	Jun 04
Lamivudine 150 mg	60 tablets	4.85	Sep 04
Nevirapine 200 mg	60 tablets	6.90	Sep 04
Zidovudine 300 mg	60 tablets	9.90	Mar 05
Indinavir 400 mg	180 tablets	69.10	Sep 05

Source: Varichem, Department of Marketing, 2005.

Note: mg = milligrams.

a. Varivar contains lamivudine 150 mg and zidovudine 300 mg.

b. Stalanev is a 3-in-1 fixed-dose combination of stavudine 30/40 mg, nevirapine 200 mg, and lamivudine 150 mg.

initiatives (notably the Global Fund). Local production was therefore expected to complement the import of generic ARVs. Local production was also targeted at the markets in neighboring countries such as Malawi, South Africa, and Zambia.

In July 2003, Varichem launched its first generic ARV product, Varivar, a combination drug comprising lamivudine 150 mg and zidovudine 300 mg. As indicated in table 3.2, by September 2005, Varichem was already manufacturing eight different ARV products. Currently, it has an installed capacity of 1.15 billion tablets and capsules. Varichem has benefited tremendously from government procurement through a special dispensation to supply ARVs to the government without going through the bid process. To date, the government of Zimbabwe has maintained its policy of supporting local manufacturing by obtaining the greater part of its supplies of ARVs from Varichem. Before the declaration was issued, the average monthly treatment cost for HIV/AIDS was estimated at \$30 to \$50, unaffordable to a large number of Zimbabweans. The Varichem generic version of the lamivudine-zidovudine combination, Varivar, sold at just over \$15 for a month's supply, about half the price for the same duration of treatment.

The first obstacle that confronted Varichem was that none of its products were prequalified by WHO.⁴ To meet WHO qualification standards, therefore, the company engaged a good manufacturing practices (GMPs) expert to conduct an audit of its plant and systems. The audit revealed that the company's plant required refurbishment to meet minimum GMP standards, at an estimated cost of \$2.5 million.⁵ The company therefore sought assistance from the United Nations Development Programme (UNDP) with a view to sourcing funds for the refurbishment and then resubmitting its product dossiers for WHO prequalification. UNDP was not able to provide the funds, however, and as of early 2007, Varichem does not yet have WHO prequalification for any of its ARV products.

The Global Fund is one of the top three AIDS program funders and has become one of the major avenues for international funding to support the availability of ARVs to those who need them. Thus, Varichem's inability to secure WHO prequalification of its products undermines its continued survival with respect to its ARV market share and therefore its ability to sustain production. This is true even though the prices for Varichem's generic ARVs (apart from Indinavir) are very competitive when compared with the prices that the Global Fund is paying for similar products from leading manufacturers such as Ranbaxy and

Cipla, not only in Zimbabwe but also in Malawi and Zambia, where Varichem-produced ARVs are registered.

Another setup challenge that Varichem had to face is the cost of conducting its *in vivo* bioequivalence trials with a company that is internationally accredited to do so.⁶ Varichem conducts these trials through an Indian clinical research organization.⁷ Over the period of production, however, the cost of these trials has risen from \$10,000 to \$15,000 to a current cost of \$20,000. This adds tremendously to the cost of production and renders Varichem less competitive.

The cost of APIs is another problem for Varichem. By arrangement with the government, Varichem's exports of ARVs were to be a major source of foreign exchange with which to import APIs for production. With the lack of a vibrant external market, however, the government has been compelled to provide the required foreign exchange for the import of APIs. The fragile nature of the Zimbabwean economy has made it impossible for the government to support the continuing foreign exchange requirements of Varichem.

In sum, although Zimbabwe correctly applied the TRIPS flexibility of compulsory licensing to promote local production and availability of ARVs, the factors outlined above have prevented the program from being successful and worthy of emulation.

It should be noted, however, that the country's ARV rollout plan has suffered from the general lack of international funding to Zimbabwe over the last few years, a dearth that appears to be politically motivated.⁸ HIV/AIDS funding from the Global Fund has also been minimal, considering the relative prevalence of the disease in Zimbabwe. Neighboring Malawi and Zambia, which have slightly lower rates of HIV/AIDS prevalence than Zimbabwe, have received more HIV/AIDS funding from the Global Fund.⁹

Kenya: Cosmos

The Industrial Property Act of 2001 substantially incorporated the TRIPS flexibilities into Kenya's domestic legislation.¹⁰ International exhaustion of rights for parallel importation and compulsory licensing are thus permitted, although the country has not had the occasion to issue a compulsory license.¹¹ The Kenya National Drug Policy also generally provides for incentives such as import duty and other tax remission to local manufacturers of pharmaceutical products and encourages the manufacture of APIs. The orientation toward local production of pharmaceutical products is captured in

this policy, which states that related patent laws are to be reviewed to ensure a balance between the need to develop local production and the requirement to respect IPRs while protecting consumers from excessively high prices of necessary medicines.

Kenya's ARV rollout program is funded mainly through government budgetary allocations, the Global Fund, and NGO assistance to the public sector. The public sector provides funding for 80 percent of the total ART requirement. Private health insurance, out-of-pocket payments, NGOs, the Clinton Foundation, the Global Fund, and the U.K. Department for International Development (DFID) all provide some funding to support the private sector effort.

Traditionally, pharmaceutical giants GSK and Boehringer Ingelheim (BI) have controlled the ARV market in Kenya. Both companies had no local ARV manufacturing facilities in Kenya and relied on the importation of their branded products for sale. There are more than 30 generic drug manufacturers in Kenya. Six of these had requested permission to manufacture some of the ARVs patented by GSK and BI, but they had considerable difficulties in meeting the conditions set by the patent holders. Cosmos therefore applied for a compulsory license under section 80 of the Industrial Property Act to manufacture ARVs in Kenya. It was during the consideration stage of this application that the two companies, GSK and BI, engaged in negotiations with Cosmos for the issuance of a voluntary license. In effect, GSK and BI granted Cosmos a voluntary license to manufacture and market lamivudine, nevirapine, zidovudine, and combinations of these drugs in Kenya and the East African region.

The strategy adopted by Kenya for local production thus centered on voluntary licensing, in contrast to Zimbabwe's strategy of compulsory licensing. Even so, Varichem and Cosmos encountered similar challenges to their efforts, apparently stemming from the same circumstances. When the government of Zimbabwe and Varichem negotiated the issuance of a compulsory license to produce ARVs locally, they expected that production would target not only the domestic market but also the whole of the COMESA market. This expectation was also in play when Cosmos negotiated the voluntary license to produce ARVs in Kenya. The grant that it eventually obtained, however, restricted it to the East African countries, thus cutting down the market share that it had hoped would make the venture viable.

Cosmos launched its first production of generic ARVs in 2003 with zidovudine 300 mg capsules, lamivudine 150 mg, nevirapine 200 mg, and a combination of lamivudine 150 mg and zidovudine 300 mg

(Lazidariv). (The company's current ARV production line is shown in table 3.3.) It is pertinent to note that the moment Cosmos started manufacturing ARVs, GSK and BI lowered their prices for those ARVs below the prices offered by Cosmos, further endangering the viability of the Kenyan company's ARV production plan.

Unlike Zimbabwe's approach, the Kenyan procurement regime does not support local industry. Cosmos does not enjoy any preferential treatment in the supply of ARVs to the government. In Kenya, when bids are invited, the persons or companies who respond get equal consideration, be they local or foreign. In 2003, Cosmos was awarded a mere 30 percent of contracts to supply ARVs to the government, and this decreased to 20 percent in 2005. The seeming lack of government support could be the result of the nature of the license under which Cosmos is manufacturing. Whereas Varichem is producing under a government-use order and hence has a ready market for its products, Cosmos is producing under a voluntary license and has to compete with like products on the market.

Like Varichem, Cosmos faced the basic problem of not having its products WHO-prequalified. It could therefore not supply ARVs under the Global Fund's arrangements. The company's sales thus were limited mainly to irregular orders by the government, mission hospitals, and some NGOs. The cost of bioequivalence tests, which rose to \$50,000 per ARV (and even higher for fixed-dose combinations), as well as the high

Table 3.3. Cosmos's ARV Production Line

<i>Product</i>	<i>Pack size</i>	<i>Price (US\$)^a</i>
Lamivudine (3TC) 150 mg (Lamirav)	60 tablets	9.20
Stavudine (d4T) 300/400 mg (Stariv)	60 capsules	3.20/4.20
Zidovudine (AZT) 100/300 mg (Zidocos)	100/60 capsules	13.60/22.70
Efavirenz (EFV) 200/600 mg (Efariv)	90/30 tablets	44.00/44.00
Nevirapine (NVP) 200 mg (Neviriv)	60 tablets	—
Fixed-dose combinations		
3TC+AZT 150:300 mg (Lazidariv)	60 tablets	32.00
3TC+AZT+NVP 30:150:200 mg (Trioriv 30)	60 tablets	26.60
3TC+AZT+NVP 30:150:200 mg (Trioriv 40)	60 tablets	27.50
dT4+3TC 30:150 mg (Turiv 30)	60 tablets	12.40
dT4+3TC 40:150 mg (Turiv 40)	60 tablets	13.30

Source: Cosmos, Department of Marketing, 2005.

Note: mg = milligrams.

— = not available.

a. At K Sh 75 to US\$1.

cost of APIs, which accounted for an estimated 50 percent of the ex-works price of ARVs, were also major financial obstacles for Cosmos. Indeed, the company's setbacks have served as lessons for another Kenyan pharmaceutical company, Universal Pharmacy (K) Limited, which has concluded arrangements for a similar voluntary license from BI and GSK, but put its plans on hold for local production of ARVs.

Furthermore, about 95 percent of the raw materials and 50 percent of the packaging materials used by Cosmos are imported. Its fixed-dose combinations are expensive and noncompetitive even when compared with those sourced through the Global Fund. Meanwhile, the Kenyan government procures most of its ARVs with the Global Fund resources and purchases only small quantities from Cosmos. Because the Global Fund is the primary source of funding for both public and private sector purchases of ARVs, Cosmos receives few orders and thus has no incentive to produce ARVs regularly. The company has become nearly dormant, manufacturing ARVs only when it has orders to supply. The company's share of the Kenyan ARV market was thus found to be only 3 percent. Cosmos is, however, still making efforts to meet WHO prequalification requirements, especially in the area of bioequivalence testing.

South Africa: Aspen

South Africa has incorporated the TRIPS flexibilities into its domestic legislation by virtue of the Patents Act of 1978 and its subsequent amendments and the Medicine and Allied Substances Control Amendment Act of 1997, satisfying the requirements for local production. Though the 1997 law may indeed be TRIPS-compliant, it is also TRIPS-plus, offering greater protection for patent owners than required by the TRIPS Agreement. The country also has vibrant provisions in its Competition Act of 1998, which have been used in the past to address the issue of ARV pricing and voluntary licensing for local production. In addition, South Africa has a very dynamic civil society that is aware of the cost of HIV/AIDS treatment and champions the cause of affordable HIV/AIDS medicines. The high prevalence of HIV/AIDS in South Africa could account in part for the active role of civil society groups in the access debate.

Although South African patent law provides for compulsory licensing, the relevant provisions could be considered TRIPS-plus because they require the agreement of the patentee (or a hearing when such agreement is lacking). Section 4 provides, "A patent shall in all respects have the like

effect against the State as it has against a Person; Provided that a Minister of State may use an invention for public purposes on such condition as may be agreed upon with the patentee, or in default of agreement, on such conditions as are determined by the commissioner on an application by or on behalf of such Minister and after hearing the patentee.” Section 78 also provides, “The Minister may on behalf of the State, acquire, on such terms and conditions as may be agreed upon, any invention or patent.”

The words “terms and conditions” in section 78 suggest some form of negotiations between the state and the patent owner, which is not a condition precedent for issuing a government-use order in cases of emergency. The wording makes it difficult to resort to these provisions in an emergency. The same is the case with section 56, which contains provisions relating to compulsory license in case of abuse of patent rights. Section 56 requires an applicant to prove that the patent is not being worked on a commercial scale or to an adequate extent and that the demand for the patented article in South Africa is not being met to an adequate extent and on reasonable terms. The terms and conditions are unduly prohibitive, because meeting any of these requirements is difficult in the light of the heavy presence of most of the multinational pharmaceutical giants in South Africa. It is not surprising, therefore, that South Africa has to date not issued a compulsory license.

The closest that South Africa came to issuing a compulsory license was in a case brought by the AIDS Law Project, a South African civil society organization. The project brought the case on behalf of several complainants to the Competition Commission of South Africa (the Commission) against BI and GSK for anticompetitive practices in their pricing of ARVs.¹² That case drew tremendous civil society outcry and ended up in negotiations. These resulted in the two companies issuing voluntary licenses to Aspen Pharmacare Holdings Limited (a South African company) and two other generic companies for the local production of generic versions of stavudine, nevirapine, lamivudine, zidovudine, and combinations thereof.¹³ The agreement between the Commission and the companies further allowed for the export of the drugs manufactured under license in South Africa to any other Sub-Saharan country, based on a royalty payment of 5 percent. When the case was heard, Aspen already had licenses from GSK and BI, but terms and conditions of the licenses were unreasonable. The settlement agreements resulted in the revision of the terms and conditions of the earlier licenses to make them reasonable. Subsequently, Aspen launched its first generic ARVs, stavudine capsules of 20 mg, 30 mg, and 40 mg, in August

2003. Aspen is one of the largest manufacturers of generic pharmaceuticals and the leading supplier of generic medicines to both the private and public sectors in South Africa.

Currently, Aspen has an installed capacity of 5.5 billion for tablets and capsules, compared to 1.15 billion for Varichem. It has prequalified all three of its stavudine products with WHO and can therefore supply them under the Global Fund arrangements. The U.S. Food and Drug Administration (FDA) has also tentatively approved its combination pack of lamivudine-zidovudine and nevirapine tablets. Three inspections of Aspen production facilities in 2005 by the FDA, the U.K. Medicines and Healthcare Products Regulatory Agency, and WHO found the plant and processes to be compliant with international standards.

As part of its vertical integration program, Aspen has also purchased an API plant in Cape Town. Together with its technology partner Matrix, it intends to begin producing APIs at this plant under a joint venture arrangement called Astrix. According to the management of Aspen, the end-state target market projection of Astrix is to manufacture APIs for supply to manufacturers of ARVs on the entire African continent. This could start with COMESA under RTA arrangements. As capacity is built, this would also serve as an incentive for the future acquisition of licenses for the production of other ARVs that Aspen is currently unable to produce.

Table 3.4 shows the orders of ARVs that Aspen received from the South African health authorities on competitive bidding. As can be seen, Aspen has managed to capture a fair share of the local South African ARV market.

On the whole, Aspen appears to have effectively taken advantage of the voluntary license to successfully build and sustain a viable local ARV manufacturing company. It has done so despite competition from the traditional producers and the need to source APIs from China and India. The company's success is primarily the result of its adoption of good business and manufacturing practices, particularly in the areas of product identification and formulation technology. Though Aspen's private sector prices may be more expensive, its public sector prices are very low. For instance, the stavudine, lamivudine, and nevirapine combination costs about 320 South African rand (R) per patient per month in the private sector, but less than R 100 per patient for ARVs sold to the state in terms of the ARV bid. The government of South Africa procures large quantities of ARVs from Aspen by reimbursing it for the cost of producing the medicines, in an arrangement similar to the one between Varichem and

Table 3.4. Supply of ARVs to the South Africa Department of Health (through August 2007)

<i>Product</i>	<i>Pack size</i>	<i>Price (US\$)</i>	<i>Quantity</i>	<i>Manufacturer</i>
Stavudine 20 mg capsule	60 capsules	3.02	84,607	Aspen
Stavudine 30 mg capsule	60 capsules	3.02	2,192,400	Aspen
Stavudine 30 mg capsule	60 capsules	3.42	939,600	Cipla
Stavudine 40 mg capsule	60 capsules	3.34	1,879,200	Aspen
Stavudine 40 mg capsule	60 capsules	3.72	1,252,800	Cipla
Zidovudine 50 mg/5 mL syrup	200 mL	3.94	2,398,500	Aspen
Zidovudine 100 mg capsule	100 capsules	17.42	216,000	GSK
Zidovudine 300 mg tablet	60 tablets	11.93	103,200	GSK
Didanosine 25 mg tablet	60 tablets	10.52	5,069	Aspen
Didanosine 50 mg tablet	60 tablets	10.06	605,750	Aspen
Didanosine 100 mg tablet	60 tablets	11.12	3,564,000	Aspen
Lamivudine 10 mg/mL syrup	240 mL	3.77	2,649,600	Aspen
Lamivudine 150 mg tablet	60 tablets	5.54	5,030,400	Aspen
Nevirapine 200 mg tablet	60 tablets	6.79	1,879,200	Aspen
Nevirapine 50 mg/5 mL syrup	240 mL	30.69	1,152,000	BI
Stavudine 1 mg/mL powder	200 mL	13.54	727,200	Bristol-Myers Squibb

Source: South Africa Department of Health 2004.

Note: mg = milligrams, mL = milliliters.

All other orders were supplied as follows: lopinavir and ritonavir preparations from Abbott; efavirenz preparations from Merck Sharp & Dohme (MSD). All prices include 14 percent value added tax and are on a delivered basis.

the Zimbabwe government. Almost all of Aspen's products have a ready market in the government sector, which also accounts for the relatively low prices offered to government.

In Cosmos, just as in Varichem, the responsibility for product identification comes from both the research and development and the marketing departments. This differs from the approach of the South African company Aspen, which has a trade-oriented strategic trade development and drug division to spearhead its product identification. In the area of formulation technology, while Varichem relies entirely on in-house skills, Cosmos uses a combination of in-house skills and limited outsourcing. Aspen, on the other hand, outsources all its formulation technology requirements. At the strategic level, therefore, it could be said that Aspen's approach to local production is based on the concept of viable trade in its product identification and competitive advantage in its formulation technology plan. This has created an enabling environment for vertical integration, with prospects for higher-capacity utilization and

eventual lowering of production costs. Both Varichem and Cosmos, however, appear to have adopted a marketing-oriented strategy based on the presumed availability of an existing market. They did not strategically focus on vertical integration of production processes for higher-capacity utilization to lower production costs as a means of capturing and maintaining their target market shares.

Although Aspen appears to have been quite successful compared with Cosmos and Varichem, the contexts are not entirely comparable. South Africa's more robust economy, its large market for ARVs, the capacity of civil society to influence public policy on ARV pricing, and the investor-friendly nature of its domestic legislation all were important factors in encouraging Aspen's success. But Aspen is not completely without problems. Its main weakness is a high conversion cost when compared with that of India. Its production processes therefore require further automation to improve efficiency and lower costs in that sphere, which could then trickle down into lower pricing for its products.

Ghana: Danadams

The Ghanaian experience with local production of ARVs centers on Danpong-Adams Pharmaceutical Industry (Ghana) Limited (Danadams), a local Ghanaian pharmaceutical company. Danadams was founded in 2004 as a joint venture between Adams Pharmaceutical (Anhui), a Chinese company, and Danpong Pharmaceuticals, a Ghanaian company, for the production of ARVs. Unlike Varichem, Cosmos, and Aspen, which have relied on a compulsory license for government use or on voluntary licenses, Danadams, in its first year of operations, focused completely on processes that would lead to acquiring regulatory approval for a selected list of ARVs. Within this first year, the company managed to acquire regulatory approval for the production of generic versions of 13 ARVs (table 3.5).

Danadams is not WHO-prequalified for the supply of ARVs, although it has very modern production facilities and processes that are GMP-compliant. Although the company is still in the process of acquiring WHO prequalification to enable it to take advantage of the ECOWAS market, it has shifted its attention to establishing contact with, and seeking voluntary licenses from, the patent holders of ARVs that are patented in Ghana. In one such application, Danadams has acquired an immunity-from-suit agreement from Bristol-Myers Squibb for the production of generic versions of stavudine and didanosine and ARVs containing either.

Table 3.5. Danadams's ARV Production Line

<i>Name of drug</i>	<i>Generic name</i>	<i>Strength</i>	<i>Registration no.</i>
Bivek caplets	Lamivudine/zidovudine	150/300 mg	FDB/SD.05-11653
Didanvek tablets	Didanosine	50 mg	FDB/SD.05-11655
Effavek capsules	Efavirenz	50 mg	FDB/SD.05-11656
Effavek capsules	Efavirenz	200 mg	FDB/SD.05-11661
Effavek caplets	Efavirenz	600 mg	FDB/SD.05-11672
Lamdek caplets	Lamivudine	150 mg	FDB/SD.05-8533
Nelfinek caplets	Nelfinavir	250 mg	FDB/SD.05-11671
Nevek caplets	Nevirapine	200 mg	FDB/SD.05-11652
Stavudek capsules	Stavudine	15 mg	FDB/SD.05-8529
Stavudek capsules	Stavudine	20 mg	FDB/SD.05-8530
Stavudek capsules	Stavudine	30 mg	FDB/SD.05-8531
Stavudek capsules	Stavudine	40 mg	FDB/SD.05-8532
Zivek caplets	Zidovudine	300 mg	FDB/SD.05-8534

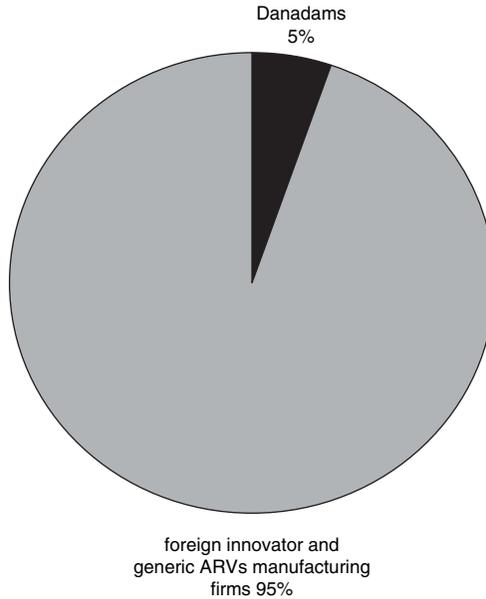
Source: Ghana Food and Drugs Board, 2005 *Drug Register*.

Note: mg = milligrams.

The Patent Act of 2003 (Act 657) provides the necessary legal framework for the issuance of a compulsory license for government use in accordance with the TRIPS Agreement. In Ghana's first experience with the issuance of such a license, the processes leading to its issuance spanned an entire year (from 2004 until 2005). The issuance of the compulsory license marked a departure from a reliance on branded ARVs and a move toward generics. During the period in which the compulsory license was being processed, stocks of ARVs decreased drastically in the country, provoking protests from civil society groups. It became necessary for the government to shop for ARVs in-country to prevent out-of-stock situations, with no time to process the relevant government-use order to cover the local production that would meet the requirement. Under an emergency procurement, the government turned to Danadams to cover the shortfall by awarding it a one-time contract for the supply of ARVs. The contract was worth \$258,926, about 5 percent of the government's expenditure on ARVs for 2005 (figure 3.1). The International Dispensary Association and other suppliers who source their products mainly from India supplied the other 95 percent.

Danadams is not WHO-prequalified, and thus the procurement from the company had to be paid for with resources from the government of Ghana and not with funds from the Global Fund. (The prices offered by Danadams in its 2005 supply to government are shown in figure 3.2.) Judging from the comparable prices that the company offered for the

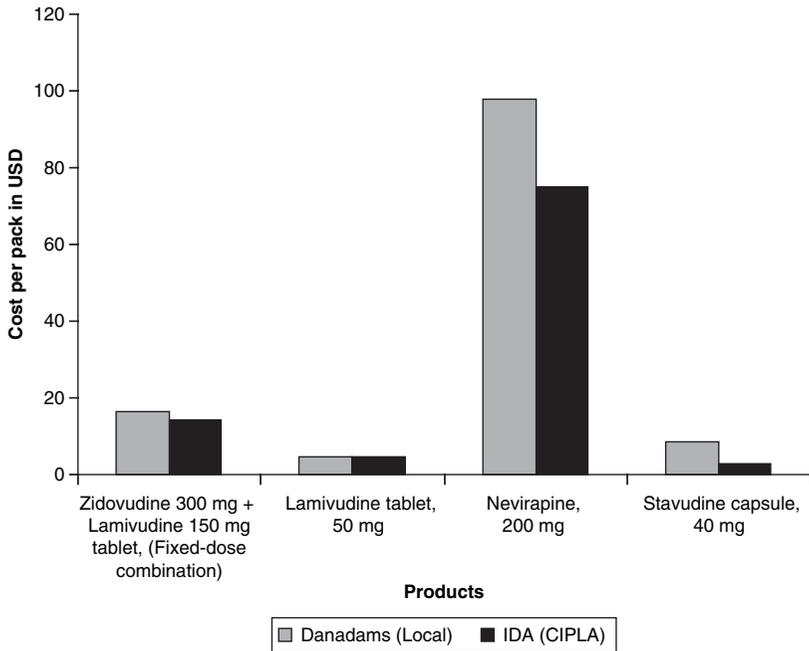
Figure 3.1. Percentage of ARVs Purchased by Government of Ghana from Danadams and Other Firms 2005



Source: Authors' calculations based on information provided by the Procurement Unit, Ministry of Health, Ghana.

fixed-dose combination (lamivudine-zidovudine) and for lamivudine, it seems likely that, given a greater market share and economies of scale, Danadams could match the prices being offered by other generic suppliers. Also, the wider margin in price for nevirapine and stavudine could be attributed to the small volumes that had to be produced to satisfy the one-time order.

In general, Danadams has encountered constraints similar to those faced by other companies in the local production of ARVs in SSA. In an interview, the chief executive of Danadams identified three major challenges: (a) the high cost of the bioequivalence tests for each product that are required for the acquisition of WHO prequalification, (b) the high cost of APIs when purchased in relatively small quantities, and (c) the inadequate market share and lack of economies of scale that result from an inability to supply under the Global Fund arrangements (this in turn the result of the absence of WHO prequalification).

Figure 3.2. Comparison of Prices for Local and Imported Generic ARVs in Ghana, 2005

Source: Procurement Unit, Ministry of Health, Ghana.

Note: mg = milligrams.

IDA = International Dispensary Association.

Local Production of ARVs in Perspective

Local production of pharmaceuticals in the African region has been mainly confined to production of medicines in final dosage forms from imported APIs. Companies face significant difficulties in their efforts to meet international quality standards, all the while capturing a critical market share that could sustain the supply of required APIs and make production economically viable.

Zimbabwe's attempt to use compulsory licensing as the means of carrying out local production encountered similar market-share and production-sustainability challenges, as did Kenya's use of voluntary licensing. In the case of South Africa, a reliance on voluntary licensing as the strategy for undertaking local production has faced fewer challenges. It would appear, however, that the higher economic and industrial capacity of South Africa, coupled with the notion of cooperation with

established pharmaceutical companies with a capacity to produce APIs locally, contributed immensely to the relative success of the South African effort.

This presents a dilemma for SSA countries seeking to improve access to HIV/AIDS medicines: they must decide whether to give priority to local production or to the building and strengthening of health delivery systems in terms of infrastructure, medicine procurement, effective drug regulatory systems, appropriate storage, and distribution. For instance, in all four countries studied, the markup in the price of ARVs for the community/retail pharmacy and wholesaler is 15–30 percent of the acquisition cost—an issue that could be addressed through appropriate distribution streamlining.

In addition, the prices of locally produced ARVs in Ghana, Kenya, and Zimbabwe do not include the extremely high cost of *in vivo* bioequivalence tests. Given that *in vivo* bioequivalence is a prerequisite for the attainment of WHO prequalification, the current prices will most likely increase sharply should these countries attempt to meet this requirement.

The following factors generally stand out as vital to the success of local production and should engage the attention of African countries planning to embark on such production:

- Availability of investment capital and profitability of the investment as a viable economic venture
- Ability to maintain installed production infrastructure and processes that satisfy the international requirements for GMPs
- Ensuring of available capacity for locally manufactured products to attain WHO prequalification before embarking on local production
- Verification that the short-, medium-, and long-term costs of supply of APIs and other raw materials conform to the need to maintain an economically viable venture
- Availability of a clear and sustainable plan for recruiting and training required technical manpower
- Ability to capture an appropriate market size that ensures competitive advantage, with the possibility of RTA-based local production that derives economies of scale from the available regional markets
- Regional cooperation to negotiate high-quality voluntary licenses that engender multiple competition, ensure access to registration data, grant permission for cross-licensing of fixed-dose combination medicines, and promote technology transfer

- Reduction of import and corporate taxes on pharmaceutical inputs and products
- Promotion of strategic partnerships between well-established pharmaceutical companies and local firms for local production through win-win voluntary licensing agreements and other mutually beneficial arrangements (such as joint ventures).

Notes

1. Danadams started business in 2005 and became the first local company to supply the government of Ghana with ARVs.
2. Kenya and Zimbabwe have been leading members of the African Group within the WTO who have advocated for a public-health-sensitive interpretation of the TRIPS Agreement.
3. “Services of the state” is so broadly defined as to take it out of a wholly health care agenda. In section 35(1), “services of the state” is supposed to include managing situations of war; securing and maintenance of supplies and services essential to life and well-being; promoting productivity of industry, commerce, and agriculture; fostering exports and reducing imports; addressing the balance of trade; ensuring the optimal use of community resources for community interests; addressing the relief of suffering; and restoring and distributing of essential supplies and services in Zimbabwe or any foreign country in grave distress as a result of war.
4. WHO prequalification has become a standard of quality assurance for generic drugs. Since 2004, it has also become crucial for recipients of assistance from the Global Fund, because it requires that grantees purchase only from pre-qualified sources. For more information on the prequalification program, see <http://mednet3.who.int/prequal>.
5. Major determinants of GMP include, among others, infrastructure and machinery, personnel qualification, manufacturing procedures, acceptable bioequivalence tests, standard of hygiene, quality of products, and documentation.
6. Bioequivalence trials can be either *in vitro* (comparative dissolution tests) or *in vivo*. While *in vitro* trials involve comparing a generic product to a brand product by laboratory dissolution tests, *in vivo* trials involve estimating the rate and extent of systemic absorption of a drug in healthy human volunteers. *In vivo* bioequivalence tests conducted by accredited clinical research organizations are a prerequisite for the attainment of WHO prequalification for ARVs.
7. In light of the inability of Varichem to attain WHO prequalification for its ARVs, it is unclear whether the clinical research organization that conducts bioequivalence tests for the company has international accreditation.

8. Western donors responded to the government's controversial land reform program by freezing aid to Zimbabwe. This led government officials to believe that delays by the Global Fund were also politically motivated. However, announcing a grant to Zimbabwe's health sector in 2005, a Global Fund spokesman said that the country's internal politics had not influenced previous Fund decisions (IRIN 2005).
9. So far, Zimbabwe had \$10.3 million approved in Round 1, and only \$4.3 million has been disbursed. Even this amount was for the UNDP to scale up disease prevention and care. Another \$35.9 million from a Round 5 approval is still outstanding, pending a decision on who should be the principal recipient. Malawi's total grant, however, is \$62.6 million; Kenya's is \$39.6 million, with a \$70 million, three-year HIV grant approved; and Zambia's is \$69.1 million.
10. Sections 58(2) and 54(1) of the Industrial Property Act of 2001 allow for parallel importation, while section 80 allows for compulsory licensing. This was after intense lobbying by civil society groups, especially the Kenya Coalition for Access to Essential Medicines (KCAEM). KCAEM is made up of international NGOs such as MSF, Health Action International, and Action Aid, along with Kenyan local NGOs such as Women Fighting AIDS in Kenya plus a number of individuals from various backgrounds.
11. Although the president of the Republic of Kenya declared HIV/AIDS a national disaster in August 1999, the declaration was never published in the *Kenya Gazette*. Analysts viewed the declaration as a move to implement compulsory licensing, which was subsequently reviewed.
12. The South African Competition Commission threatened to investigate GSK and BI for contravening the provisions of the Competition Act of 1998. The two companies pleaded for negotiations with the interested parties in lieu of the investigation. The subsequent negotiations resulted in the granting of voluntary licenses to companies that required them for the manufacture of ARVs in South Africa.
13. The other companies that benefited from the settlement agreement are the Council of Scientific and Industrial Research's (CSIR's) Bio/Chemtek (a government-private partnership) and Thembalami Pharmaceuticals (Proprietary) Limited. Thembalami is a joint venture between local group Adcock Ingram Limited and Indian pharmaceutical giant Ranbaxy Laboratories Limited. GSK issued a voluntary license to Thembalami to make generic versions of its patented medicines lamivudine and zidovudine and a combination of the two. In April 2004, BI licensed Thembalami to make generic versions of its medicine nevirapine.

CHAPTER 4

Conclusions and Recommendations

Conclusions

Based on the findings of the study, a number of conclusions can be drawn regarding implementation of the TRIPS flexibilities and the use of local production to enhance access to affordable ARVs in SSA.

Regarding implementation of the TRIPS flexibilities:

- Neither the regional legal instruments of OAPI and ARIPO nor the domestic legislation of countries in the region appropriately address the issue of nonpatentability of new and second uses of medicines. This issue must be addressed for countries to be able to take advantage of the flexibility provided in article 27(1) of the TRIPS Agreement.
- LDCs in both ARIPO and OAPI have been unable to take advantage of the provisions of the Declaration that exempt LDCs from providing patent protection until 2016. While the OAPI situation derives from provisions of binding regional legal instruments, the ARIPO problem stems from an uncertainty about how to deal with the accrued rights of existing pharmaceutical patent holders.
- Neither ARIPO nor OAPI has a regularly updated, easily accessible, and reliable database on patents. Information flow and guidance on technical matters relating to the use of the flexibilities is virtually nonexistent.

- The cumbersome processes associated with compulsory licensing have tended to make this strategy rather unappealing to countries in the region. In the case of OAPI, it would appear there is a deliberate policy orientation at the regional level to discourage the use of compulsory licensing as a means of attracting foreign investment. (Compulsory licensing for importation, for instance, is not permissible under the Bangui Agreement.)
- Although the regional trade option appears to offer great opportunities for eventually increasing access to medicines and improving public health, not much has been done under the auspices of the existing RTAs to take advantage of it.
- OAPI categorically restricts exhaustion of rights to the regional level. Non-OAPI countries in the region, however, have varied levels of exhaustion of rights. There is no concerted effort by ARIPO to promote an international exhaustion-of-rights regime among its members, even though this appears to be more beneficial than national or regional exhaustion regimes as a tool for enhancing access to medicines.
- Local legislation needs to be amended to specifically provide for the use of test data by national drug regulatory authorities to give marketing approval for generic medicines.
- Although capacity for the local production of ARVs in the region is gradually developing, only a few countries provide explicit provisions on the early working system.
- There is an absence of simple and well-defined structures, administrative procedures, and guidelines required for the efficient coordination and timely application of compulsory licensing and parallel imports.
- Although technical personnel in the various countries of the region are generally aware of the TRIPS flexibilities and their potential for promoting access to medicines, the same cannot be said of the political leadership. The use of the TRIPS flexibilities ultimately rests with these political leaders, who need to understand and appreciate the policy space that the flexibilities offer. Unfortunately, they exhibit a crucial shortcoming in this area.

Regarding local production:

- Except in South Africa, local production of pharmaceuticals in the SSA region has been mainly confined to low-end production of medicines in final dosage forms from imported APIs, rather than high-end production involving the manufacture of APIs.

- Local producers face significant challenges in meeting international quality standards and capturing a critical market share that could make production economically viable and sustainable.
- The cost of bioequivalence testing for each product, necessary for the acquisition of WHO prequalification, appears to be far beyond the budgets of most local manufacturers of ARVs and therefore contributes to their inability to attain WHO prequalification for their products.
- Local manufacturers are importing APIs in relatively small quantities at rather high prices, based on a few pending ARV orders. Greater market share would increase the volume of APIs purchased to the levels needed to obtain better negotiated prices, resulting in lower prices of the ARVs produced.
- Local manufacturers are hobbled by inadequate market share and a lack of economies of scale resulting from an inability to supply under the Global Fund arrangements because of the absence of WHO prequalification.

Recommendations

Five recommendations flow from the conclusions above.

1. The two major regional IP organizations, ARIPO and OAPI, should provide technical assistance to their member countries by commissioning special studies to examine the national patent laws (in the case of ARIPO) and the Bangui Agreement (in the case of OAPI) to ensure the inclusion of provisions that maximize the benefits of the TRIPS flexibilities and promote affordable access to HIV/AIDS medicines. The studies should address issues such as the legal implications of bringing accrued patent rights on pharmaceutical products in LDCs under the terms of the extension of the transition period to 2016; the development of simple administrative structures and procedures for the timely implementation of compulsory licenses and parallel imports of HIV/AIDS medicines; and the drafting of appropriate provisions that empower national drug regulatory authorities in their reliance on, and use of, data for the registration of generic ARVs.
2. Both ARIPO and OAPI should, under the auspices of the African Union and other development partners, establish a reliable database on ARV patent status to strengthen information flow and facilitate the utilization of the TRIPS flexibilities.

3. Development partners such as the World Bank, WTO, and WHO should be encouraged to support programs that seek to do the following:
 - Create the required political will by sensitizing the political leadership of SSA countries and the regional economic groupings (such as ECOWAS, COMESA, EAC, and SADC) on the policy options offered by the TRIPS flexibilities to improve access to HIV/AIDS medicines and how to implement them to advantage.
 - Develop and disseminate a simplified interpretation of the TRIPS Agreement, the Declaration, and the Decision, with elaborate analyses of the options available and the roles of the various stakeholders at the country level.
 - Scale up support for capacity building at the individual country level for the effective implementation of the flexibilities to ensure sustainability of the supply of HIV/AIDS medicines.
 - Provide simple guidelines and technical assistance to local pharmaceutical manufacturing companies on the requirements for WHO prequalification and how to avoid delays associated with the application process.
 - Strengthen the RTAs as focal points for maximizing the advantages of economies of scale in the production and procurement of HIV/AIDS medicines by, among other things, harmonizing treatment protocols, medicine registration requirements, and procurement practices.
4. Both ARIPO and OAPI should amend their legal instruments to specifically exclude new and second uses of known medicines from patentability.
5. Local pharmaceutical companies should seek to form strategic partnerships with well-established pharmaceutical companies through win-win voluntary licensing agreements and other mutually beneficial arrangements (such as joint ventures) to enhance sustainable local production in the medium and long terms.

APPENDIX A

HIV/AIDS Medicines under Patent in Sub-Saharan Africa

<i>Drug</i>	<i>Patent owner</i>	<i>Priority date</i>	<i>20 years expiry</i>	<i>SSA countries covered</i>
Abacavir (racemic mixture)	Wellcome (GSK)	June 27, 1988	June 26, 2009	ARIPO, South Africa
Abacavir (enantiomer)	Wellcome (GSK)	December 22, 1989	December 21, 2010	ARIPO, South Africa
Didanosine-ddl	Bristol-Myers Squibb	July 22, 1991	July 20, 2012	South Africa
Efavirenz Stocrin/ Sustiva	Merck (MSD)	August 7, 1992	August 6, 2013	South Africa
Indinavir	Merck (MSD)	November 8, 1991	November 7, 2012	South Africa
Lamivudine - 3TC (Epivir)	Merck	May 7, 1993	May 6, 2014	ARIPO, OAPI, South Africa
	IAF Biochem (GSK)	February 8, 1989	February 8, 2010	
	IAF Biochem	May 2, 1990	May 1, 2011	
Nelfinavir	Glaxo	June 3, 1991	June 2, 2012	ARIPO, South Africa
	Agouron (Roche)	October 7, 1993	October 7, 2014	
Nevirapine - Viramune	BI	November 17, 1989	November 17, 2010	ARIPO, OAPI, South Africa

(continued)

52 Improving Access to HIV/AIDS Medicines in Africa

<i>Drug</i>	<i>Patent owner</i>	<i>Priority date</i>	<i>20 years expiry</i>	<i>SSA countries covered</i>
Ritonavir + Lopinavir-Keletra	Abbott	December 29, 1992	December 28, 2013	South Africa
	Abbott	December 13, 1995	December 12, 2016	
Saquinavir	Hoffmann-La Roche	December 11, 1989	December 11, 2010	Malawi, OAPI, South Africa Zimbabwe
Stavudine-D4T	Yale University (BMS)	December 17, 1986	December 17, 2007	South Africa
Zidovudine-AZT	Glaxo Wellcome	March 16, 1985	March 16, 2006	ARIPO, South Africa
AZT+3TC (Combivir)	Glaxo Wellcome	October 31, 1996	October 29, 2017	ARIPO, OAPI, South Africa
AZT+3TC+ Abacavir (Trizivir)	Glaxo Wellcome	April 29, 1998	March 23, 2016	ARIPO, OAPI, South Africa

Source: WHO/EDM/PAR/2004. 6 *Determining the Patent Status of Essential Medicines in Developing Countries.*

APPENDIX B

List of Persons Interviewed

1. Mr. E. K. Agyarko, CEO, Food and Drugs Board, Ghana
2. Mr. Frank A. Boateng, President, Pharmaceutical Society of Ghana
3. Mr. Kwesi Poku Boateng, Danadams Pharmaceuticals Ltd.
4. Mr. Sam Boateng, Director, Procurement and Supplies, Ministry of Health, Ghana
5. Mr. Ben K. Botwe, DCE (Drugs Division), Food and Drugs Board, Ghana
6. Mr. Lloyd Chapanga, Quality Assurance Manager, Varichem, Zimbabwe
7. Dr. Andrew K. Chemwolo, Drug Regulation Division, Kenya
8. Ms. Santhani Chetty, Principal Regulatory Control Officer, Medicine Control Council, South Africa
9. Mr. Archibald T. Chinuka, GMP and Regulatory Affairs Director, Varichem, Zimbabwe
10. Mr. Christopher Chitemerere, Director, Marketing Department, Varichem, Zimbabwe
11. Mr. Denis Croze, Acting Director Advisor, Office of the Deputy Director General, Economic Development Sector, WIPO, Geneva, Switzerland
12. Ms. Delese Darko, Head, Drug Evaluation & Registration, Food and Drugs Board, Ghana

13. Mr. Paul Dhanaun, Director, Universal Corporation Limited, Kenya
14. Mr. Dunstan, Kenya Medical Research Institute (KEMRI), Kenya
15. Ms. Esme D. du Plessis, Patent Attorney, Pretoria, South Africa
16. Mr. Julian Fleet, Senior Advisor, Care and Public Policy, Social Mobilization and Information Department, UNAIDS, Geneva, Switzerland
17. Dr. Yaw Adu Gyamfi, CEO, Danadams Pharmaceuticals Ltd.
18. Ms. Martha Gyansa-Lutterodt, Program Manager, Ghana National Drugs Program
19. Mr. Rutendo Kuwana, Principal Regulatory Officer, Medicines Control Authority, Zimbabwe
20. Ms. Makarati, Legal Officer, Human Resources, Legal and Parliamentary Affairs, Ministry of Justice, Zimbabwe
21. Rev. Jonathan Martey, Head of Laboratory, Food and Drugs Board, Ghana
22. Ms. Emma Mudzura, Regulatory Officer, Medicines Control Authority, Zimbabwe
23. Dr. O. Mugurungi, Chief Coordinator, AIDS and TB Program, Ministry of Health and Child Welfare, Zimbabwe
24. Ms. B. Mutetwa, Director of International Trade, Zimbabwe
25. Mr. Macdonald Netshiterizhe, Director, Commercial Law and Policy Consumer & Corporate Regulation Division, Department of Trade and Industry, South Africa
26. Ms. Elizabeth Ng'ang'a, Senior Principal Parliamentary Counsel, Attorney-General's Chambers, State Law Office, Kenya
27. Ms. Ngumo, Deputy Director, Kenya Medical Research Institute (KEMRI), Kenya
28. Mr. Stavros Nicolaou, Senior Executive, Strategic Trade Development Department, Aspen, South Africa
29. Mr. Eric Norenberg, International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), Geneva, Switzerland
30. Mr. Abel Nyagwa, Public Relations Officer, National AIDS Control Council, Kenya
31. Ms. Josephine Nyakatawa, Ministry of Industry and International Trade, Zimbabwe
32. Dr. Amanda Ombeva, Project Officer, HIV/AIDS, Kenya Medical Supplies Agency (KEMSA), Kenya
33. Mr. Geoffrey Onyeama, Director, Economic Development Bureau for Africa, WIPO, Geneva, Switzerland
34. Mr. Gaurang Patel, Director, Cosmos, Kenya

35. Mr. M. Nuno Pires de Carvalho, Director Advisor, Legislation for Public Policy and Economic Development Sector, WIPO, Geneva, Switzerland
36. Mr. Maxwell Ranga, Director, Human Resources, Legal and Parliamentary Affairs, Ministry of Justice, Zimbabwe
37. Dr. Giorgio Roscigno, CEO, Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland
38. Mr. Joseph Tamakloe, Principal State Attorney, registrar General's Department
39. Dr. Isaiah K. Tanui, Deputy Program Manager, TB/HIV Collaboration, Kenya
40. Dr. Wanyanga, Executive Director of Pharmaceutical Limited and former General Manager, Regulatory Affairs, Cosmos, Kenya
41. Ms. Jayashree Watal, Counselor, Intellectual Property Division, WTO, Geneva, Switzerland
42. Ms. Françoise Wege, Senior Counselor, WIPO, Geneva, Switzerland
43. Dr. J. K. Yano, Legal Officer, Pharmacy and Poisons Board, Kenya

Bibliography

- ARIPO. 1982. "Protocol on Patents and Industrial Designs within the Framework of the African Regional Intellectual Property Organization (ARIPO)." Harare, Zimbabwe, December 10. Amended several times, 1987–2004. ARIPO, Harare, Zimbabwe. http://www.aripo.org/Documents/Protocols/harare_agreement.pdf.
- Berger, J. M. 2004. "Advancing Public Health by Other Means: Using Competition Policy to Mitigate the Impact of Patent Protection." Paper presented at the International Centre for Trade and Sustainable Development (ICTSD) and the United Nations Conference on Trade and Development (UNCTAD) Dialogue on Ensuring Policy Options for Affordable Access to Essential Medicines, Bellagio, Italy, October 12–16. http://www.iprsonline.org/unctadictsd/dialogue/2004-06-29/2004-06-29_berger.pdf.
- Booker, S., and A. Colgan. 2005. "People with HIV/AIDS Lose as Drug Companies Gain." *Third World Resurgence* 184 (December): 5–6.
- Boulet, P., C. Garrison, and E. 't Hoen. 2004. "Drug Patents under the Spotlight: Sharing Practical Knowledge about Pharmaceutical Patents." Médecins Sans Frontières, Geneva. <http://www.accessmed-msf.org/resources/key-publications/key-publication-detail/article/drug-patents-under-the-spotlight-sharing-practical-knowledge-about-pharmaceutical-patents/>.
- Cohen, J. C., M. Gyansa-Lutterodt, and K. Torpey. 2003. "Increasing Access to Medicines: An Assessment and Policy Options for Ghana." 25. DFID (U.K. Department for International Development), London.

- Cohen J. C., M. Gyansa-Lutterodt, K. Torpey, L. C. Esmail, and G. Kurokawa. 2005. "TRIPS, the Doha Declaration, and Increasing Access to Medicines: Policy Options for Ghana." *Globalization and Health* 1: 17. <http://www.globalizationandhealth.com/content/1/1/17>.
- Correa, C. M. 1998. *Implementing the TRIPS Agreement: General Context and Implications for Developing Countries*. Penang, Malaysia: Third World Network.
- . 2000. *Integrating Public Health Concerns into Patent Legislation in Developing Countries*. Geneva: South Centre. <http://www.southcentre.org/publications/publichealth/toc.htm>.
- Criat, B., J. Dumoulin, Y. A. Flori, T. Barnett, Y. Souteyrand, and J. P. Moatti. 2003. "Patents, Generic Drugs and the Markets for Antiretrovirals." 27–37. http://scholar.google.com/scholar?hl=en&lr=&q=cache:1zXmxmBhcsJ:www.univ-paris13.fr/CEPN/Intro_partie1.pdf.
- Fink, C. 2003. "Implementing the Doha Mandate on TRIPS and Public Health." Trade Note 5, World Bank, Washington, DC. <http://old.developmentgateway.org/download/191422/TradeNote5.pdf>.
- IRIN (Integrated Regional Information Networks). 2005. "Zimbabwe: New Global Fund Grant Approval Long Overdue: NGOs." October 7. <http://www.aegis.org/news/irin/2005/IR051022.html>.
- Kanaga, R. 2006. "General Council Approves 'Permanent Solution' on TRIPS and Health." *Third World Economics: Trends and Analysis* 369: 16–31.
- Khor, M. 2003. "Rethinking IPRs and the TRIPS Agreement." Paper, Third World Network, Penang, Malaysia.
- Madeley, J. 1996. *Trade and the Poor: The Impact of International Trade on Developing Countries*. London: Intermediate Technology Publications.
- Moore, M. 2001. "Yes, Drugs for the Poor—and Patents as Well." *International Herald Tribune* (February 22). <http://www.ihf.com/articles/2001/02/22/edmoore.t.php>.
- MSF (Médecins Sans Frontières). 2001. "Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases." Report from the Campaign for Access to Essential Medicines and the Drugs for Neglected Diseases Working Group, MSF, Geneva. http://www.accessmed-msf.org/fileadmin/user_upload/medinnov_accesspatents/fatal%20imbalance.pdf.
- MSF. 2005. "Amendment to WTO TRIPS Agreement Makes Access to Affordable Medicines Even More Bleak." Press release, December 5, MSF, Geneva. <http://www.accessmed-msf.org/media-room/press-releases/press-release-detail/article/amendment-to-wto-trips-agreement-makes-access-to-affordable-medicines-even-more-bleak/>.

- MSH (Management Sciences for Health) and WHO. 1997. *Managing Drug Supply: The Selection, Procurement, Distribution, and Use of Pharmaceuticals*, 2nd ed., ed. J. D. Quick. Bloomfield, CT: Kumarian Press.
- Musungu, S. F., and C. Oh. 2005. "The Use of Flexibilities in TRIPS by Developing Countries: Can They Promote Access to Medicines?" Study 4C, commissioned by the Commission on Intellectual Property Rights, Innovation, and Public Health (CIPIH), Geneva. <http://www.who.int/intellectualproperty/studies/TRIPSFLEXI.pdf>.
- Musungu, S. F., S. Villanueva, and R. Blasetti. 2004. *Utilizing TRIPS Flexibilities for Public Health Protection through South-South Regional Frameworks*. Geneva: South Centre. <http://www.southcentre.org/publications/flexibilities/flexibilities.pdf>.
- OAPI (African Intellectual Properties Organization). 1999. "Agreement Revising the Bangui Agreement of March 2, 1977, on the Creation of an African Intellectual Property Organization." Bangui, Central African Republic, February 24. http://www.oapi.wipo.net/doc/en/bangui_agreement.pdf.
- Reichmann, J. H., and C. Hasenzahl. 2003. "Non-voluntary Licensing of Patented Innovations: Historical Perspective, Legal Framework under TRIPS, and an Overview of the Practice in Canada and the USA." ICTSD and UNCTAD, Geneva. http://www.ictsd.org/pubs/ictsd_series/iprs/CS_reichman_hasenzahl.pdf.
- South Africa Department of Health. 2004. "HIV/AIDS Care, Management, and Treatment Plan for Period ending 31 August 2007." Contract RT71-2004.
- South Centre and CIEL (Centre for International Environmental Law). 2005. "The 6 December 2005 TRIPS Amendment and Public Health at the WTO." *Intellectual Property Quarterly Update* (fourth quarter): 1–6. Geneva. http://www.ciel.org/Publications/IP_Update_4Q05.pdf.
- TWN (Third World Network). 2003. *Manual on Good Practices in Public-Health-Sensitive Policy Measures and Patent Laws*. 95. Penang, Malaysia: TWN.
- UNAIDS (Joint United Nations Programme on HIV/AIDS) and WHO. 2005. "AIDS Epidemic Update: December 2005: Special Report on HIV Prevention." UNAIDS/WHO, Geneva. http://www.unaids.org/epi/2005/doc/EPIupdate2005_pdf_en/epi-update2005_en.pdf.
- UNCHR (United Nations Commission on Human Rights). 2003. "Economic, Social and Cultural Rights: The Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health." Report of the Special Rapporteur, Paul Hunt, submitted in accordance with Commission Resolution 2002/31, February 13, Geneva. <http://www.unhchr.ch/Huridocda/Huridoca.nsf/0/9854302995c2c86fc1256cec005a18d7>.

- UNCTAD (United Nations Conference on Trade and Development). 2002. "UN-Recognized Categories of Countries Receiving Special Attention from UNCTAD." Geneva. <http://www.unctad.org/Templates/webflyer.asp?docid=5972&intItemID=3641&lang=1>.
- Velasquez, G., and P. Boulet. 1999. "Globalization and Access to Drugs: Perspectives on the WTO/TRIPS Agreement." Revised. DAP 7, WHO/DAP/98.9, WHO, Geneva.
- WHO (World Health Organization). 2004. *Determining the Patent Status of Essential Medicines in Developing Countries*.
- . 2005a. *The World Health Report 2005: Make Every Mother and Child Count*. Geneva: WHO. http://www.who.int/whr/2005/whr2005_en.pdf.
- . 2005b. "Access to Medicines: Intellectual Property Protection: Impact on Public Health." *Drug Information* 19 (3): 236–41. <http://www.who.int/medicines/areas/policy/AccessstoMedicinesIPP.pdf>.
- . 2006. "Global Framework on Essential Health Research and Development." Agenda item 4.10, EB117.R13, Fifty-Ninth World Health Assembly, 117th Session, January 27, Geneva. http://www.who.int/gb/ebwha/pdf_files/EB117/B117_R13-en.pdf.
- WTO (World Trade Organization). 1994. "Agreement on Trade-Related Aspects of Intellectual Property Rights." Annex 1C of the Marrakesh Agreement, 319–51, WTO, Geneva. http://www.wto.org/english/docs_e/legal_e/27-trips.pdf.
- . 2001. "Declaration on the TRIPS Agreement and Public Health." Adopted November 14, WTO, Geneva. http://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm.
- . 2002a. "Extension of the Transition Period under Article 66.1 of the TRIPS Agreement for Least-Developed Country Members for Certain Obligations with Respect to Pharmaceutical Products." June 27, WTO, Geneva. http://www.wto.org/english/tratop_e/trips_e/art66_1_e.htm.
- . 2002b. "Least-Developed Country Members: Obligations under Article 70.9 of the TRIPS Agreement with Respect to Pharmaceutical Products." July 8, WTO, Geneva. http://www.wto.org/english/tratop_e/trips_e/art70_9_e.htm#fnt1.
- . 2003. "Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health." August 30, WTO, Geneva. http://www.wto.org/english/tratop_e/trips_e/implem_para6_e.htm.
- . 2005. "Hong Kong Ministerial Declaration." December 18, WTO, Geneva. http://www.wto.org/english/thewto_e/minist_e/min05_e/final_text_e.htm#public_health.

Index

A

Abacavir, 51
access to treatment, 2, 13
 affordable medicines, 5
 complicating factors, 2
Act 90. *See* Medicines and Related
 Substances Control Amendment Act
Action Programme to Accelerate the Fight
 Against HIV/AIDS, 3
administrative procedures, 22, 23
African Group, 4, 44n.2
African Intellectual Property Organization
 (OAPI), 10, 12–13, 14, 17, 20, 25n.1,
 47, 48, 49, 50
 compulsory licensing, 16
 patent searches, 23
African Regional Centre for Technology
 (ARCT), 13
African Regional Intellectual Property
 Organization (ARIPO), 10, 12–13,
 13, 14, 47, 50
 compulsory licensing, 16
 patent searches, 23–24
Agyarko, E. K., 53
antiretroviral (ARV) medications
 combination, 36, 37

 export, 15
 factors for success, 43–44
 Kenya, 42
 new and second uses, patentability, 12
 production, local, 27–45
 South Africa, 36, 37, 38, 42–43
 Sub-Saharan Africa, 51–52
 Zimbabwe, 42
 see also access to care; pricing
API. *See* pharmaceutical ingredients, active
Aspen Pharmacare Holding Limited, 29,
 35–39
 South Africa, 37
Astrix, 37
AZT+3TC, 52
AZT+3TC+Abacavir, 52

B

Bangui Agreement, 12–13, 17, 20,
 25n.2
BI. *See* Boehringer Ingelheim
bidding, competitive, 3, 37
Bio/Chemtek, 45n.13
bioequivalence tests, 32, 34, 41, 43,
 44n.6, 49

Bivek, Ghana, 40
 Boateng, Frank A., 53
 Boateng, Kwesi Poku, 53
 Boateng, Sam, 53
 Boehringer Ingelheim (BI), 33, 34, 36,
45n.12
 Bolar Exception, 11, 22
 Botswana, 20–21
 Botwe, Ben K., 53
 Brazil, *7n.7*

C

capacity building, 43, 50
 Chapanga, Lloyd, 53
 Chemwolo, Andrew K., 53
 Chetty, Santhani, 53
 China, 39
 Chitemerere, Christopher, 53
 Chiuka, Archibald T., 53
 Combivir, 52
 commercial use, unfair, 21
 Common Market for Eastern and Southern
 Africa (COMESA), 19, *26n.5*, 33
 competition, 2
 anticompetitive practices, 16, 36
 competitive bidding, 3, 37
 Competition Act of 1998, 35, *45n.12*
 compulsory licensing. *See* licensing
 conclusions, 47–49
 cooperation, regional, 43
 Cosmos Pharmaceuticals Limited, 29,
 32–35
 product line, 34
 costs, 17–18
 manufacturing, 32
 patient's, 31, 35
 production, 34–35
 South Africa, 39
 Zimbabwe, 31
 Croze, Denis, 53

D

Danadams Pharmaceuticals Limited, 29,
 39–42, *44n.1*
 challenges, 41
 production line, 40
 Danpong Pharmaceuticals, 39
 Darko, Delese, 53
 databases, patented medicines, 24

data protection, 21–22
 limits, 25
 Decision. *See* World Trade Organization
 General Council Decision
 decision-making processes, 23
 Declaration of Commitment on
 HIV/AIDS (the Declaration), 3, 4, 5,
 7n.6, 10, 13, 14
 Dhanaun, Paul, 54
 Didanosine, 38, 51
 Didanvek, 40
 dosage forms, 27
 drug formulation, 27, 38
 Dunstan, Mr., 54
 du Plessis, Esme, 54

E

Eastern Caribbean Drug Service (ECDS), 19
 Economic Community of West African
 States (ECOWAS), 18, 19, 24, *25n.3*
 Efariv, 34
 Efavirenz, 34, 51
 Effavek, 40
 emergencies. *See* national emergencies
 Eпивir, 51
 European Union, 3
 exhaustion of rights, 10, 20–21, 32, 48
 see also importation, parallel

F

Fleet, Julian, 54
 funding, 31, 32, 33

G

General Agreement on Tariffs and Trade
 (GATT), implementation, 1
 generics, 3, 16–17, 22, *44n.4*
 Ghana, 39, 42
 Kenya, 33
 South Africa, 36–37
 Zimbabwe, 31
 Ghana, 17, 21, 24, 40
 ARV production, 27–29, 39–43
 government expenditure on ARV, 41
 socioeconomic indicators, 28
 GlaxoSmithKline (GSK), 17, 33, 34, 36,
45n.12

Global Fund, 31–32, *44n.4*

Kenya, 34

South Africa, 37

Zimbabwe, *45n.8*

Goemaere, Eric, *6n.3*

good manufacturing practices (GMPs),
31, *44n.5*

Ghana, 39

South Africa, 37–38

GSK. *See* GlaxoSmithKline

Gyamfi, Yaw Adu, 54

Gyansa-Lutterodt, Martha, 54

H

HIV/AIDS

incidence, 2, 4, *6n.2*

mortality, *6n.4*

I

importation, parallel, 3, 4, 20–21, 22,
25, 32

see also exhaustion of rights

India, 18–19

Indian Patents Act of 1970, 19

Indinavir, 30, 51

Industrial Property Act, 20, 31–32,
45n.10

infrastructure, 43

intellectual property (IP), 1, 9

protection, 4

see also African Intellectual Property
Organization; importation, parallel;
legislation; Trade-Related Aspects of
Intellectual Property Rights (TRIPS)
Agreement

interviewees, 53–55

investment capital and profitability, 43

K

Keletra, 52

Kenya, 20–21, *45nn.10,11*

ARV production, 27–29, 32–35

Industrial Property Act of 2001,
20–21

National Drug Policy, 32–33

socioeconomic indicators, 28

Kuwana, Rutendo, 54

L

Lamdek, Ghana, 40

Lamivudine, 17, 30, 31, 33, 34, 36, 37,
41, 51

Lazidariv, 33–34

legislation, 2–3, *7n.7*, 9, 12, 13, 14–15, 16,
20–22, 35–36, 47, 48, 50

Botswana, 20–21

Competition Act, 35, *45n.12*

India, 19

Industrial Property Act, 20–21, 31–32,
45n.10

Kenya, 20–21

Medicine and Allied Substances Control
Amendment Act of 1997, 35

Patents Act, 16–17, *26n.6*, *26n.6*,
29–30, 40

regional, 17–18

South Africa, 16, *26n.6*, 35–36

Unfair Competition Act of 2000, 21

United States, 3, *6n.5*, *7n.7*

WIPO Model Laws, 20

Zimbabwe, 16–17

licensing, 10, 34

compensation for, 18

compulsory, 4, 5, 10, 15–19, 22, 23,
24–25, 32, 48

Ghana, 40

Kenya, 32

South Africa, 36, 37, 42–43

voluntary, 33, 41–43

Zimbabwe, 32

M

Makarati, Ms., 54

Malawi, 14

Mandela, Nelson, 2

manpower, 43, 48

market share, 18, 27, 33, 43, 49

Ghana, 39, 41

South Africa, 38–39

Zimbabwe, 32

Martey, Jonathan, 54

Matrix, 37

Medicine and Allied Substances Control
Amendment Act of 1997, 2–3, 35

medicines. *See* antiretroviral medications

Mozambique, 17

Mudzura, Emma, 54

Mugurungi, O., 54

Mutetwa, B., 54

N

national emergencies, 10, 16, 30, 36, 40
 Nelfinavir, 51
 Nelfinek, 40
 Netshiterizhe, Macdonald, 54
 Nevek, 40
 Nevirapine, 30, 33, 34, 36, 37, 38
 Nevirapine-Viramune, 51
 Neviriv, 34
 Ng'ang'a, Elizabeth, 54
 Ngumo, Ms., 54
 Nicolaou, Stavros, 54
 Norenberg, Eric, 54
 Nyagwa, Abel, 54
 Nyakatawa, Josephine, 54

O

OAPI. *See* African Intellectual Property Organization
 Ombeva, Amanda, 54
 Onyeama, Geoffrey, 54

P

parallel importation. *See* importation, parallel
 partnerships, 44, 50
 Patel, Gaurang, 54
 patent holders, discretion, 14
 patents, 2–3
 eligibility, 12
 exemptions, 9–10, 11, 12–13
 laws, 13, 49
 medicine database, 24
 period, 10
 pharmaceuticals, 14
 protection, 2, 9–10, 14, 20
 rights, 6*n*.3
 rights, exhaustion of, 10, 20–21, 32, 48
 searches, 23
 systems, 10
 patentability, 12
 exemptions from, 11, 12–13
 new use, 12
 patented medicines in SSA, 51–52
 Patents Act, 16, 26*n*.6, 29–30, 40
 personnel, technical, 43, 48

Pfizer Pharmaceuticals, 14
 pharmaceutical industries, 2–3
 pharmaceutical ingredients, active (API), 41, 43, 48, 49
 costs, 43
 Kenya, 32–33
 South Africa, 37
 Zimbabwe, 32
 Pharmaceutical Manufacturers' Association of South Africa, 2–3
 Pharmaceutical Procurement Service, 19
 pharmaceutical products, 2, 14, 20
 Pires de Carvalho, M. Nuno, 55
 pricing, 3, 34, 42, 43
 private sector, 29, 33
 procurement, 19, 34
 production, local, 27–45
 see also pharmaceutical ingredients, active
 product labeling, 24

Q

qualification standard, Zimbabwe, 31
 quality, 27

R

Ranbaxy Laboratories, 45*n*.13
 Ranga, Maxwell, 55
 recommendations, 49–50
 regime of exhaustion, 10, 32, 48
 see also importation, parallel
 regional trade area (RTA), 18–19, 24, 50
 regional trade option, 15–19
 remuneration, 17–18
 Ritonavir + Lopinavir, 52
 Roscigno, Giorgio, 55
 royalties, 18, 36

S

Saquinavir, 52
 services of the state, 44*n*.3
 socioeconomic indicators, 28
 South Africa, 45*n*.12
 ARV production, 27–29, 32–35
 compulsory licensing, 16

Medicines and Related Substances
 Control Amendment Act
 (Act 90), 2–3
 Patents Act, 16, 26*n.6*
 socioeconomic indicators, 28
 Southern African Development
 Community (SADC), 19, 25*n.4*
 Special Session on HIV/AIDS, 3–4
 Stalanev, 30
 Stariv, 34
 Stavudek, 40
 Stavudine (d4T), 30, 34, 36, 37,
 38, 52
 Stocrin/Sustiva, 51
 study scope and methodology, 5–6
 Sub-Saharan Africa (SSA)
 ARV medications, 51–52
 HIV/AIDS incidence, 2
 Tamakloe, Joseph, 55
 Tanui, Isaiah K., 55
 taxes, 44
 test data, protection limits, 21–22
 Thembalami Pharmaceuticals, 45*n.13*
 trade, regional, 48
 Trade-Related Aspects of Intellectual
 Property Rights (TRIPS) Agreement,
 1–2, 9–10
 Bolar Exception, 11, 22
 compliance, 13
 compulsory licensing, 11
 exemptions from patentability, 11
 interpretation, 50
 limits on data protection, 11
 obligations, 9–10
 parallel imports, 11
 transition periods, 11, 13–15
 TRIPS flexibility, 2–5, 10–26, 47–48, 49
 facilitating protection of public
 health, 11
 implementation, 10–22
 implementation challenges, 22–25
 Kenya, 32
 South Africa, 35
 Zimbabwe, 32
 TRIPS-plus, 16, 17, 35–36
 waiver, 15
 transparency, 3
 treatment guidelines, 24
 Triomune, 14
 Trivoriv, 34
 Trizivir, 52

U

Unfair Competition Act of
 2000, 21
 United Nations, 3
 United States, 3, 6*n.5*, 7*n.7*

V

Varichem Pharmaceuticals, 16–17, 29–32,
 33, 37, 44*n.7*
 production line, 30
 Varivar, 17, 30, 31

W

Wanyanga, Dr., 55
 Watal, Jayashree, 55
 Wege, Françoise, 55
 World Health Organization (WHO)
 prequalification, 31,
 44*m.4*, 7, 50
 World Intellectual Property Organization
 (WIPO), 13
 Model Laws, 20
 World Trade Organization (WTO),
 1, 3–4, 10
 General Council Decision
 (the Decision), 4, 5, 14, 15,
 18–19, 24
 Uruguay Round, 6*n.1*

Y

Yano, J. K., 55

Z

Zidocos, 34
 Zidovudine (AZT), 17, 30, 31, 33, 34, 36,
 37, 38, 41, 52
 Zimbabwe, 4, 16–17, 44*n.3*,
 45*m.8,9*
 ARV production, 27–29, 29–32
 Patents Act of 1996, 16–17
 socioeconomic indicators, 28
 Zinkev, 40
 Zithromax, 14

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Providing access to affordable, good quality HIV/AIDS medicines remains a challenge in Sub-Saharan Africa. Although patent protection is by no means the only barrier to access, it has significant implications for accessibility. Experiences from a number of countries show that local production of HIV/AIDS medicines depends not only on research and technology, but also on highly regulated patents and intensive capital investment. These factors pose major challenges to African countries that have ventured into this undertaking. The Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) requires all World Trade Organization members to adopt certain minimum standards for the protection of intellectual property rights, including the rights of pharmaceutical product patent holders. *Improving Access to HIV/AIDS Medicines in Africa* analyzes the extent to which countries in Sub-Saharan Africa have been able to use flexibilities in the agreement to improve access to affordable antiretroviral (ARV) medicines. It also examines the option of local manufacture of ARV medicines—based on the experiences of Ghana, Kenya, South Africa, and Zimbabwe—and it evaluates factors that favor or hinder sustainable local production. Finally, the book makes recommendations on how countries in the region can use the TRIPS flexibilities to improve access to life-saving medicines.



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