

Aspen Pharmacare*

by Stu Woolman and Courtenay Sprague

In the late 1990s, in the context of the South African government's reactionary public health policy and a conservative investment climate, Stephen Saad, Aspen Pharmacare's chief executive officer, saw the opportunity to supply the South African market with brand name, generic and over-the-counter HIV and TB medication at affordable prices and at a profit. The Aspen case reveals a number of potentially replicable business responses to the problem of providing affordable medicines in a developing country. First, Aspen recognized that the costs of building a large-scale manufacturing plant would be more than off-set by the profits to be secured from the public and private demand for antiretroviral (ARV) drugs in South Africa and the rest of the continent. Second, Aspen convinced the state to provide incentives to build a plant sufficiently large to meet South Africa's growing need. Third, Aspen's ability to negotiate voluntary licenses with multinational drug companies allows drugs under patent to be distributed at significantly reduced prices. This strategy avoids putting South Africa in the politically uncomfortable position of breaking foreign patents and the legally undesirable position of weakening the state's own intellectual property regime. Finally, Aspen's joint ventures with Indian generic manufacturers provide some assurance it will continue to possess an uninterrupted supply of the active pharmaceutical ingredients (APIs) required to manufacture ARVs.

Introduction

In a conservative investment climate, Stephen Saad saw opportunity. In a revanchist health policy environment, Stephen Saad saw need. The opportunity: to build a major pharmaceutical manufacturer capable of supplying the South African market with brand name, generic and over-the-counter medicines at affordable prices. The need: to supply South Africans with the essential medicines required for the treatment of life-threatening diseases such as HIV/AIDS and tuberculosis. Through a series of well-planned deals and calculated risks, the greatest being the 2.4 billion rand (\$320 million) acquisition of SA Druggists, Saad turned Aspen Pharmacare into the largest producer of tablets and capsules in Africa. By building the largest manufacturing plant in the country, Saad put Aspen Pharmacare in a position to supply South Africa's national antiretroviral treatment program with approximately 60% of its current requirements.

Five and a half million South Africans are infected with HIV/AIDS and more than 600,000 individuals will require immediate access to life-extending antiretrovirals each year for at least the coming decade.¹

*Stu Woolman is Associate Professor, School of Law, University of Pretoria; Research Associate, Centre for Human Rights, University of Pretoria, South Africa; Research Associate, South African Institute for Advanced Constitutional, Public, International and Human Rights Law. Courtenay Sprague is Lecturer, Graduate School of Business Administration, University of the Witwatersrand (Wits), South Africa and Doctoral Candidate, Development Studies, Wits.

As is well-known, the South African Government could be doing more: only an estimated 21% of people living with the human immunodeficiency virus who require antiretroviral therapy (ART) have access to such treatment in public clinics and hospitals.² Unless the roll-out of the national ART program expands significantly, 3.5 million South Africans will die of AIDS-related infections by 2010, according to current projections.³

The Government has started to move in the right direction. In 2004, it initiated a long-anticipated, free national antiretroviral treatment (ART) program for its HIV-infected population.⁴ However, delays in the implementation of the ART program have been widespread. The South African Department of Health, pressed by the threat of legal action by national activist organizations, declared, in March 2004, that they would need to purchase an emergency supply of antiretrovirals (ARVs) as a stop-gap measure until the formal public sector tender process for drug procurement was concluded. In May 2004, despite the emergency supply, drug shortages continued to be well-documented. Commentators observed that the South African Government was in the unenviable position of possessing “some generic medicines — sitting with the Medicines Control Council [South African equivalent of the US Federal Drug Administration] for more than a year awaiting registration” — while still being obliged “to purchase [ARVs] from brand name sources” at substantially higher prices.⁵

As the South African Department of Health has acknowledged, the solution to this dire situation — a free, sustainable, universal ART program — depends upon both lower

Ten personal interviews were conducted with Aspen Pharmacare, South African government officials, the CSIR and individual academics and researchers from the University of KwaZulu-Natal, the University of the Witwatersrand, and Ashira Consulting.

¹ See P. Barker and F. Venter, “Setting District-Based Annual Targets for HAART and PMTCT – a First Step in Planning Effective Intervention for the HIV/AIDS Epidemic” *South African Medical Journal*, 97 (10) (2007): 916–17. According to the Department of Health, which relies on the Actuarial Society of South Africa (2000) model, ‘it is estimated that by then [2009] about 1.4 million people will require ARV therapy’: Government of the Republic of South Africa, ‘Department of Health Operational Plan for Comprehensive HIV and AIDS Care, Management and Treatment for South Africa’, (2003), available at <http://www.info.gov.za/otherdocs/2003/aidsplan.pdf>

² World Health Organisation, “Summary Country Profile for HIV/AIDS Treatment Scale-Up” (June 2005)(data as of end-2004), available at <http://www.who.int/3by5/countryprofiles/en>. Even people outside of South Africa are quite familiar with the politics surrounding access to ART in South Africa. As Salon.com, the popular US website, observes: “the South African government’s slow response to the AIDS crisis South Africa’s hesitations and missteps on the issue are well-chronicled.” “The AIDS Drug Warrior” Salon.com (18 June 2001), available from <http://www.salon.com>.

³ On the actuarial science that underpins these projections, see Bureau for Economic Research *The Impact of HIV/AIDS on Selected Business Sectors in South Africa, 2005* (Stellenbosch University October 2005) 11-12, citing Rob Dorrington and estimates projected by the Actuarial Association of South Africa (ASSA2002) Model. Dorrington states: “By 2010, despite interventions and treatments, we estimate that nearly 3.5 million South Africans will have died of HIV/AIDS related causes.” See <http://www.assa.co.za>. See also *Joint WHO/UNAIDS Fact Sheet N°283* (January 2005). South Africa must also confront a growing tuberculosis (TB) epidemic, including multi-drug and extreme drug resistant TB. Indeed, TB and HIV co-infection is complicating treatment for both diseases. See Médecins Sans Frontières (MSF) “The TB/HIV Time Bomb: A Dual Epidemic Explodes in South Africa” available from <http://www.msf.org>.

⁴ Government of the Republic of South Africa, Department of Health. 2003. *Operational Plan for Comprehensive HIV and AIDS Care, Management and Treatment for South Africa*, available from <http://www.info.gov.za/otherdocs/2003/aidsplan.pdf>.

⁵ “Antiretroviral Sources of Supply May not be Able to Meet Popular Demand” available from <http://www.redribbon.co.za>.

drug prices and an uninterrupted local supply of ARVs. Companies such as Aspen Pharmacare have recognized that the government's best hope for meeting public health needs over the long-term rests on the state's ability to nurture the country's nascent generic drugs industry. (Such an industry could also supply drugs to other African countries at affordable prices.) While observing that the creation of such an industry posed an immense challenge for both government and big business, *The Economist* noted that Aspen Pharmacare provides a model for local generic firms and is currently "doing the most to supply the market with . . . generic drugs."⁶

Unequal Access to Medicines

The health revolution in industrialized countries over the last 30 years can be measured in increased life expectancy — an additional four months over each calendar year⁷ — and the near-eradication of treatable diseases such as malaria and tuberculosis (TB). However, a majority of the world's population — 80% — resides in the developing world and they have not enjoyed the benefits of the health revolution. For example, a girl born today in Sierra Leone can expect to live almost 50 fewer years than a girl born in Japan.⁸ Children in Southern Africa now have a shorter life expectancy than their grandparents.⁹ To make matters worse, many people in the developing world routinely fall ill and die from diseases for which available treatment exists.¹⁰

The Millennium Development Goals (MDGs) recognizes that differences in life expectancy rates between the developing and developed world turns, in part, on access to essential medicines to treat an array of preventable and treatable diseases. Millennium Development Goal (MDG) 8, Target 17 is "[to] provide access to affordable drugs in

⁶ *The Economist*, "Aspen's upward Slope: Can South Africa's Top Generics Manufacturer become a Global Giant?" 6 October 2005.

⁷ See World Health Organisation (WHO), *World Health Report 2006* and *World Health Report 2000*. See also, Médecins sans Frontières (MSF) *Fatal Imbalance* 2001.

⁸ Jennifer Ruger, "Health and Social Justice" *Lancet* 364 (2004):1075-1080.

⁹ François Dabis and Ehounou René Ekpini, "HIV-1/AIDS and Maternal and Child Health in Africa" *Lancet* 359 (2002): 2097-2104. In South Africa, rates of life expectancy have dropped to 48.8 years while mortality rates have risen — largely due to opportunistic infections associated with HIV/AIDS. WHO *World Health Report 2004* (Global Burden of Disease Estimates for 2002); UNDP, *Human Development Report 2005*. New York and Oxford: Oxford University Press. See also Celia Dugger, "Devastated by AIDS, Africa Sees Life Expectancy Plunge," *The New York Times*, 16 July 2004. A UNDP-French government-sponsored study of annual average rates of change in life expectancy at birth during four decades revealed a "massive loss of life expectancy caused in sub-Saharan Africa in the 1990s by the HIV/AIDS pandemic." Giovanni Andrea Cornia and Leonardo Menchini, "The Pace and Distribution of Health Improvements during the Last 40 Years: Some Preliminary Results." Paper presented at UNDP-French Government Sponsored Forum on Human Development, 17-19 January 2005. Wines, drawing on data released from *Statistics South Africa*, reported: "South Africa's government reported...that annual deaths increased 57 percent from 1997 to 2003, with common AIDS-related diseases like tuberculosis and pneumonia fueling much of the rise." Michael Wines "AIDS-Linked Death Data Stir Political Storm in South Africa" *New York Times* (19 February 2005). For a comprehensive discussion of the impact of HIV/AIDS on mortality and morbidity rates in sub-Saharan Africa, see Dean T. Jamison, Richard G. Feachem, Malegapuru W. Makgoba, Eduard R. Bos, Florence K. Baingana, Karen J. Hofman and Khama O. Rogo, eds., *Disease and Mortality in Sub-Saharan Africa* (second edition). Washington, DC: World Bank, 2006.

¹⁰ MSF 2001 *op cit*. See also Lincoln Chen and Giovanni Berlinguer "Health Equity in a Globalizing World" in Timothy Evans, ed., *Challenging Inequities to Health: From Ethics to Action*, Oxford: Oxford University Press, 2001.

developing countries... in cooperation with pharmaceutical companies".¹¹ Millennium Development Goal 6 takes specific aim at combating HIV/AIDS, malaria and other diseases.

Access to essential medicines for HIV/AIDS, in particular, should lead to a decrease in morbidity and mortality rates in the developing world. But as Jim Yong Kim, the former director of the HIV/AIDS Division at the WHO, warns: "Expanding AIDS treatment is the most complex public health challenge the world has ever faced."¹² Given the complexity of the problem, how are governments, international organizations, civil society and pharmaceutical companies to engineer a significant reversal in current health outcomes?

Recent developments in the southern hemisphere suggest that public-private partnerships of varying kinds can create sustainable ART programs in developing countries. With appropriate government incentives, voluntary licenses and technology transfers from multinationals, generic pharmaceutical manufacturers located in developing countries could become low-cost producers of the life-extending drugs that HIV-infected individuals require. Indeed, Aspen Pharmacare has, with some support from the South African government, followed this model. Aspen has been so successful, it is not hard to imagine that the company could soon possess a meaningful comparative advantage as a producer of ARVs — leveraging that advantage to become a supplier of low-cost pharmaceuticals to HIV-infected individuals (for whom treatment is indicated) throughout the African continent. Aspen faces a number of sizable hurdles before it achieves such a goal.

Aspen Pharmacare

Stephen Saad, the CEO of Aspen Pharmacare, is a pharmaceutical entrepreneur. At the age of 29, he sold his shares in the pharmaceutical group, Covan Zurich, to Adcock Ingram for 20 million rands (US\$2.85 million).¹³ In 1997, the trio of Saad, Aspen Deputy CEO Gus Attridge and Steve Surllese created Aspen. It began as a small business, in the port city of Durban, worth approximately 50 million rands (\$6.6 million). Based on a series of weighted risks, including taking on 2.5 million rands (roughly \$330,000) in debt to grow the company, Saad identified a number of niche opportunities for Aspen.

The greatest risk, however, was Aspen's hostile 1999 takeover of the underperforming yet heavyweight SA Druggists.¹⁴ The price tag was 2.4 billion rands (\$320 million). Based upon its short but successful track record, Aspen was able to raise the necessary capital from investors. A skeptical market assumed that Aspen would simply strip the company of its assets. And they were not far from the mark. As Saad admits: "One of the plans we had was to sell off the manufacturing business. But I realised we would be selling the heart and lungs."¹⁵ Instead, Aspen sold SA Druggists'

¹¹ See <http://mdgs.un.org/unsd/mdg/Host.aspx?Content=Indicators/OfficialList.htm>.

¹² Sharon Lafraniere "Poor Lands Treating Far more AIDS Patients" *New York Times* (27 January 2005).

¹³ The exchange rate used throughout this article is ZAR 7.5 to USD 1.

¹⁴ Although the pharmaceutical industry is highly regulated and has high barriers to entry, SA Druggists' credibility with doctors and pharmacists and its well-established brands offset these potential costs of doing business. Interview with Stavros Nicolaou, 15 December 2006

¹⁵ Shoks Mzolo and Stuart Theobald "Generic Drugs: A Chance at Life" *Financial Mail* (South Africa), 17 November 2006.

non-core operations and invested more heavily in pharmaceutical manufacturing. It made significant investments in new facilities, while upgrading existing pharmaceutical manufacturing sites: four in South Africa and one in India. These sites house a total of nine manufacturing facilities. A tenth plant has recently been completed. One of these manufacturing plants, in Port Elizabeth, is both the largest on the African continent and the leading producer of tablets and capsules in Africa.¹⁶

Photo 1 An Aspen Plant



Source: Aspen Pharmacare, <http://www.aspenpharma.com>

Growing at an average rate of 40% per year, the company quickly established itself as a leading South African drug company.¹⁷ In August 2005, the Aspen Group announced annual revenues of 2.9 billion rands (\$386 million) and net profits of 494 million rands (\$66 million). Aspen's success correlates with an increase in the production of — and the demand for — generic medicines.

Generic Drugs and Voluntary Licenses

A generic drug is a pharmaceutical product that is usually intended to be interchangeable with an innovator product (a proprietary or brand name product). It is generally, but not always, manufactured without a license from the innovator company. It is generally, but not always, marketed after the patent on the original product expires. More importantly for our purposes: generic drugs are much cheaper to purchase than branded drugs.

The use of generic drugs offers one possible solution to the problem of access to medicines for the treatment of HIV/AIDS and an array of other intractable infectious and tropical diseases in developing countries. As the WHO explains:

Because of their low price, generic drugs are often the only medicines that the poorest can access. The Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement does not prevent governments from requiring accurate labelling or allowing generic substitution. Indeed, it is argued that competition

¹⁶ The Aspen company background is also based on interviews with Stavros Nicolaou (Aspen Pharmacare), 28 February 2006; 19 July 2006; and, 15 December 2006.

¹⁷ Aspen first developed a brand-name based upon the quality and the affordability of its products. The Group's product line extends from branded, generic, over-the-counter, fast moving consumer goods, to personal care, nutritional and nutraceutical products: penicillin, oral contraceptives, hormonals, fast-moving consumer goods (FMCG), complementary medicines, cosmetics, capsules, creams, ointments, lotions, powders, liquids and tinctures.

between drug companies and generic producers has been more effective than negotiations with drug companies in reducing the cost of drugs, in particular those used to treat HIV/AIDS.¹⁸

The South African Department of Trade and Industry recognized these benefits and introduced a public policy initiative, the Strategic Investment Programme (SIP), to induce Aspen to invest R200 million (\$27 million) in a manufacturing facility in Port Elizabeth capable of producing — amongst other medicines — significant amounts of generic ARVs. On the back of that investment, and the ‘promise’ of a mass ART program in South Africa, Aspen has secured voluntary licenses from a significant number of multinational patent-holders to produce a broad array of ARVs.¹⁹

These voluntary license agreements contain, as a rule, 0 to 5% royalty charges, backward technology transfers, and assistance with respect to both the manufacture and the distribution of the drug. GlaxoSmithKline, which has signed seven voluntary licensing agreements for ARVs in Africa (five in South Africa and two in Kenya) outlines the pharmaceutical company’s perspective on voluntary licenses as follows:

Voluntary licences (VL) enable local manufacturers to produce and sell generic versions of our products. A decision to grant a VL depends on a number of factors including the severity of the HIV/AIDS epidemic in that country, local healthcare provision and the economic and manufacturing environment. . . . Selecting the most appropriate licensee is key. We need to be sure that the manufacturer will be able to provide a long-term supply of good-quality medicines and will implement safeguards to prevent the diversion of medicines to wealthier markets.²⁰

One might well wonder why a multinational pharmaceutical company would agree to ‘give-away’ its patented processes for the manufacture of drug that continues to be extremely profitable. However, a genuine pecuniary interest attaches to well-enforced voluntary licenses and makes them highly attractive to pharmaceutical companies. The licenses ensure better resource allocation in the markets where pharmaceutical companies derive the better part of their profits: Europe, North America and parts of Asia. Voluntary licenses eliminate the production and the marketing of high cost drugs in regions that will show little or no meaningful profit. At the same time, the voluntary license eliminates the need for multinationals — and various states — to police the grey markets in drugs that inevitably occur when purchasers of brand name pharmaceuticals in developing countries who benefit from differential pricing attempt to resell the brand name product in markets in the developed world. Voluntary licenses to generic manufacturers in developing countries eliminate such arbitrage and safeguard more lucrative markets.

The ultimate benefits of voluntary licenses are shared. In 2001, before South African companies started producing ARV generics, the cost of ARVs to the patient was more than 3,000 rands per month (\$400). Today, Aspen Pharmacare can supply triple combination therapy to the South African government at 90 rands — or \$12 — per

¹⁸ See <http://www.who.int/trade/glossary/story034/en/>

¹⁹ Interviews with Stavros Nicolaou (Aspen Pharmacare), 28 February 2006; 19 July 2006; and, 15 December 2006.

²⁰ GSK (GlaxoSmithKline) *Corporate Social Responsibility Report 2005*.

patient, per month.²¹

HOW GENERICS AND PATENTED PRODUCTS COMPARE

This is what a visit to the local chemist showed

PATENTS	GENERICS
Antiretrovirals Retrovir 250g - R294,12 (Glaxo)	Zidovudine 250g - R110,10 (Aspen)
Diabetes drugs Glucophage 850g x 60 - R35,49 (Merck)	Metformin 85g x 60 - R35,49 (Sandoz)
Sprained ankle Voltaren Gt 50mg - R39,48 (Novartis)	Panamor AT 50mg - R8,19 (Novartis)
Bronchitis Fieomez syrup 200ml - R30,45 (Pfizer)	Adco Linctopent 200ml - R26,60 (Adcock)

SOURCE: FM RESEARCH

Sources: *Financial Mail* 17 November 2006; FM Research (South Africa) 2006.

Access to Medicines through Voluntary Licenses

The access and supply surrounding low cost generic medicines is a political battle – not just a problem of resource allocation to be solved by market efficiencies. It is fiercely contested on national and international fronts. A brief history of this charged environment further reflects just how remarkable Aspen’s achievements are.²²

In 2001, the Government of the Republic of South Africa was at loggerheads with foreign multinational and local pharmaceutical companies over patent rights. The dispute ultimately took the form of a suit by the Pharmaceutical Manufacturers’ Association of South Africa —filed on behalf of 39 drug companies — to prevent the Medicines and Related Substances Control Amendment Act (Medicines Act) from taking effect.²³ The applicants contended that the Medicines Act contravened both the South African Constitution and the TRIPS Agreement.²⁴ The gravamen of their complaint was that the Act granted the Minister of Health unlimited discretion to ignore the country’s patent laws. Shortly after the trial began in March 2001, it became clear that the section of the Medicines Act at the center of the dispute was modeled on a draft legal text prepared by the World Intellectual Property Organization (WIPO) Committee of Experts. Given WIPO’s involvement, and WIPO’s role in TRIPS enforcement, it became impossible for the drug companies to argue that the Medicines Act violated TRIPS.²⁵ In April 2001, due to their weak legal position, and the strong international support for South Africa’s attempt to provide cheaper medicines to meet a public health epidemic, the companies dropped the suit. While the suit ultimately set no legal precedent, the outcome tilted the

²¹ Figures from Shoks Mzolo and Stuart Theobald, “Generic Drugs: A Chance at Life” *Financial Mail* (South Africa), 17 November 2006.

²² See Courtenay Sprague and Stu Woolman, “Moral Luck: Exploiting South Africa’s Policy Environment for an Effective National Antiretroviral Treatment Programme” *South African Journal on Human Rights* 22 (part 3) 2006: 337-379.

²³ See Government of the Republic of South Africa, Dept of Health, “Briefing Document, Defending the Medicines Control Amendment Act,” 2 March 2001.

²⁴ Case No 4183/98 (Witwatersrand High Court, filed 18 February 1998).

²⁵ See Ellen t’Hoen ‘TRIPS, Pharmaceutical Patents and Access to Essential Medicines: Seattle, Doha and Beyond’ (2003) International AIDS Economics Network, <http://www.iaen.org/papers/>.

balance of power back, ever so slightly, toward the developing countries' rights to access essential medicines.²⁶

By 2002, with the price of ARV drugs still unaffordable for the majority of South Africans, the Treatment Action Campaign (TAC) lodged a complaint with the Competition Tribunal. The complaint asserted that a proposed merger between Glaxo Wellcome and Smithkline Beecham would so increase the new company's South African market share as to inevitably lead to monopoly-like prices for a significant number of ARVs. The Competition Tribunal rejected this contention. The Tribunal's concerns were largely allayed by the agreement of the merging parties to issue voluntary licenses for several drugs: antiemetic Kytril; anti-viral Famciclovir; and antibiotics Polysporin, Cicatrin and Neosporin.²⁷ In the settlement agreements with Boehringer Ingelheim and GlaxoSmithKline (GSK), several existing voluntary licensing agreements with Aspen for ARVs were given extended reach. The licenses permitted both the production and the sale of nevirapine, zidovudine (AZT) and lamivudine (commonly known as 3TC) within South Africa and for export to 47 countries in Africa for a royalty of no more than five per cent of net sales.²⁸ By signing these voluntary licenses, both GSK and Boehringer Ingelheim had agreed not to seek enforcement of their patents on the African continent. These agreements demonstrated that voluntary licenses can — in the right environment — be profitably exploited in the service of a free, universal ART program for the treatment of HIV/AIDS.

The ongoing legal disputes between the South African government, civil society and the pharmaceutical manufacturers often mask the manner in which voluntary licenses from established multinationals to existing local generic manufacturers defy traditional notions of how development objectives should be attained. They demonstrate, instead, the potential for businesses to meet significant development and public health challenges while still achieving a profit. For example, Aspen Pharmacare is currently producing significant amounts of first and second line ARVs, as well as multi-drug resistant (MDR) tuberculosis drugs, under voluntary licenses with Eli Lilly, GlaxoSmithKline, Gilead Sciences, Boehringer Ingelheim, Bristol-Myers Squibb, F. Hoffmann-La Roche Ltd., and Merck Sharpe & Dohme. The public record demonstrates that Aspen alone has voluntary licenses to produce the following 13 TB and HIV/AIDS drugs: Nevirapine; Efavirenz (Stocrin)²⁹; Atazanavir; Tenofovir; Tenofovir+Emcitrabine (combination drug); Lamivudine (3TC); Zidovudine; Lamivudine+Zidovudine; Stavudine; Didanosine; Saquinavir; Capreomycin and Cycloserine. Aspen has recently reached agreement on additional voluntary licenses.

²⁶ As Petchesky notes, "The success of Brazil and South Africa in challenging US and corporate rigidities on patents," together with the ever-tenacious transnational health and human rights NGOs, "gave a green light to developing country coalitions to move aggressively on the matter of access to medicines" at the 2001 Doha Round in Qatar. Rosalind Pollack Petchesky, *Global Prescriptions Gendering Health and Human Rights*. New York: Zed Books, 2003, p. 104.

²⁷ See *Glaxo Wellcome and Smithkline Beecham v Competition Commission Case No 58/AM/May* (28 July 2000).

²⁸ See *Hazel Tau Competition Commission Case No 2002 Sep 226*.

²⁹ The brand name in South Africa is Stocrin; in Europe and other locations it is Sustiva.

Photo 2 Research and Development at Aspen



Source: Aspen Pharmacare <http://www.aspenpharma.com>

These agreements are not aberrations: 93 per cent of Aspen's requests for voluntary licenses have been granted.³⁰ Given the growing TB epidemic in South Africa, the specter of multi-drug and extreme drug resistant TB, and the complications associated with the treatment of HIV and TB co-infection, the recent manufacturing, supply and distribution agreement between Aspen and Lupin Ltd of India to produce first and second line TB drugs complements Aspen's aforementioned voluntary licenses for ARVs.³¹

Aspen now has 11 AIDS drugs in its stable.³² And it expects that stable to grow.³³ In March 2005, the Company announced that it had increased its AIDS drugs production by 30% since late last year to cope with demand. While about 50% of Aspen's local AIDS drugs sales were to the private sector, Saad predicted significant increases in public-sector volumes as more government clinics and hospitals started treating patients. Aspen also anticipates significant growth across the continent: Nigeria and Uganda have already placed orders. However, regulatory hurdles in African countries had delayed PEPFAR orders.³⁴ Indeed, Aspen Senior Executive and Head of Strategic Trade, Stavros Nicolaou, cautioned that "supplying both African governments and PEPFAR projects is still in its infancy" and that many of the Aspen generics are still in the process of being registered in various African countries.³⁵

Barriers to Long-Term Success

Aspen's first challenge is to convince the South African government that tax relief and investments should be continued.³⁶ Aspen's second challenge involves increasing

³⁰ Interview with Stavros Nicolaou, 19 July 2006.

³¹ See "Big Boost for Fight against TB" *Fin24*, 26 September 2005.

³² Aspen's success has not gone unnoticed. Aspen was the world's first pharmaceutical manufacturer to be granted US Food and Drug Administration (FDA) approval for the manufacture of co-packed generic anti-retrovirals (ARVs) manufactured at its world class oral solid dose (OSD) facility. The Clinton Foundation chose Aspen as the first company in the southern hemisphere to manufacture generic ARVs for their program. It did so, as Stavros Nicolaou notes, because it was impressed by the manner in which Aspen had positioned itself in the marketplace. Interview with Stavros Nicolaou (Aspen Pharmacare), 15 December 2006.

³³ "Antiretroviral medicines are becoming a bigger and bigger part of our production — we could never have foreseen this growth," Stephen Saad said." Tamar Kahn "Aspen to Focus on AIDS Drugs Market across 15 Countries" *Business Day*, 23 August 2005.

³⁴ Kahn, *op cit*.

³⁵ *Ibid*.

³⁶ In the government's 2005 report on South Africa's progress in achieving the MDGs, in response to target 17 (In cooperation with pharmaceutical companies, provide access to affordable drugs in developing countries), the government states: "Measurement of target not available for South Africa (free primary health care for all)". While the national policy may embrace the provision of essential medicines for the

production in a way that meets current demand for the full set of first and second line ARVs. Aspen's third challenge — a marker of its success — is the presence of new competitors who threaten the company's market share. Amongst Aspen's chief local competitors in the ARV generics market are Adcock-Ingram, Sonke Pharmaceuticals (Pty) Ltd., and Cipla-Medpro, a joint venture between Cipla Ltd of India and Medpro Pharmaceutica, a South African generic pharmaceutical company. Adcock Ingram, a South African subsidiary of Tiger Brands, and the second largest generics' producer in the country, plans to enter the ARV market with a unique single tablet, triple-combination therapy.³⁷ However, according to some analysts, economies of scale, partnerships with northern multinational pharmaceutical companies, a market for generic drugs in sub-Saharan Africa, FDA approval and black empowerment initiatives³⁸ (an absolute imperative for doing business in post-apartheid South Africa) suggest that Aspen has a good chance of remaining the market leader.³⁹

Aspen's fourth challenge — and a challenge to all generic ARV manufacturers — is to ensure ongoing access to the active pharmaceutical ingredients (APIs) necessary to produce ARVs. As we have documented elsewhere, most generic manufacturers are currently dependent upon generic manufacturers of APIs in India, China and other countries in Asia.⁴⁰ Should the epidemic become a national health priority in India or China — domestic demand for APIs may exhaust the existing supply. (The Chinese response to HIV has evolved in recent years; however, the Chinese have been criticized for “failure to respond to the HIV/AIDS threat and for systematic suppression of information about the size of the problem.”⁴¹) Generic manufacturers from other nations would be left out in the cold. Aspen has attempted to insulate itself from the vagaries of API availability by

South African population, this is not yet universal, nor is it accessible to many poor people, particularly for vulnerable populations such as pregnant women and HIV-infected children. According to UNICEF South Africa, each day 260 children are born infected with HIV in South Africa. This is equivalent to 94,900 children newly-infected with HIV each year. Without ARVs most of these children will die by their second birthday. In a report by South African civil society to the United Nations, Mellors documents that “very few children (10%) are accessing ARV treatment”. See Shaun Mellors, *Monitoring the Implementation of the UNGASS Declaration of Commitment: Country Report South Africa* (civil society shadow report). International Council of AIDS Service Organizations [no date provided]. HIV-related diseases are now responsible for 40% of child mortality cases in South Africa; rendering AIDS the largest killer of children under five in the nation. See UNICEF South Africa, *Impact on Children: Paediatric Testing and Treatment*, 2006. Available from <http://www.unicef.org/southafrica>.

³⁷ Tiger Brands' 2005 Annual Report outlines its intentions:

“Given that the HIV and Aids pandemic is widespread globally and expected to grow in the next five to ten years, there is clearly a viable market for ARV drugs, which will be volume driven. Worldwide there are about 40 million people currently infected with the virus. There are 25,4 million people infected in sub-Saharan Africa, with six million of these residing within our borders. Adcock Ingram aims to be a key player in the ARV market.... [and] plans to formulate and strengthen key relationships and partnerships, to facilitate entry into the ARV market, are being implemented.”

Available from www.tigerbrands.co.za/Investor/InvestorCentre/2005Results/AnnualReport/downloads/pdf

³⁸ Aspen chose not to close its factories under Saad's leadership but instead expanded manufacturing from 30% into 100% of its core business. This decision flowed in large part from consultation with and cooperation from the trade unions. Indeed, the trade unions now hold almost 17% of Aspen's shares. Aspen new manufacturing operations, in particular, its new plant in Port Elizabeth are responsible for the creation of approximately 1400 new jobs in the Eastern Cape (one of South Africa's poorest provinces.)

³⁹ *Financial Mail op cit*, p. 38.

⁴⁰ See Courtenay Sprague and Stu Woolman, *op cit*.

⁴¹ Therese Hesketh, “HIV/AIDS in China: The Numbers Problem” *Lancet* 369 (2008): 621-623.

purchasing the largest fine chemicals manufacturer in South Africa and by initiating joint ventures with two Indian manufacturers of APIs – Lupin and Matrix.⁴²

Aspen's fifth challenge is to negotiate the uncertainty surrounding the enforcement of international and domestic intellectual property regimes. Thus far, Aspen has avoided confrontation with both governments and multinationals by securing voluntary licenses and tech transfers for the better part of its ARV product line. However, IP — and especially TRIPS-related — questions hover over the generic APIs produced by India and China. For example, now that India has passed IP legislation intended to make the nation TRIPS-compliant, non-Indian manufacturers must ask whether their access to Indian APIs will be deleteriously affected. Aspen's co-operative approach to its relationships with both government and multinationals should serve it well in future negotiations.

Innovation and Replicability

This analysis of Aspen Pharmacare reveals at least five potentially replicable business responses to the problem of providing affordable ARVs, as part of a sustainable national ART program within a developing country context. First, Aspen recognized that the costs of building a large-scale manufacturing plant would be more than off-set by the profits to be secured from the public and private demand for ARVs in South Africa and the rest of the continent. Second, Aspen convinced the state to provide various forms of incentives to build a plant sufficiently large to meet South Africa's growing need for affordable, generic ARVs. Third, Aspen's ability to negotiate voluntary licenses with multinational drug companies allows drugs under patent to be distributed at significantly reduced prices and should enable the state to reach a larger number of individuals with HIV/AIDS (provided that other key dimensions, such as health systems and health personnel, are functioning well). Fourth, Aspen's knack for securing voluntary licenses avoids putting South Africa in the politically uncomfortable position of breaking foreign patents and the legally undesirable position of weakening the state's own intellectual property regime. Fifth, Aspen's joint ventures with Indian generic manufacturers Matrix and Lupin provides some assurance it will continue to possess an uninterrupted supply of the active pharmaceutical ingredients (APIs) required to manufacture ARVs.

A DFID study of generic pharmaceutical companies suggests that Aspen's business model could be replicated in other developing countries with the requisite levels of infrastructure, access to active pharmaceutical ingredients, skilled human capital, existing manufacturing plants, and appropriate government incentives.⁴³ (It must be noted that many African countries do not yet possess those necessary features.) The DFID study also supports the authors' claim that South Africa requires a state-sponsored socio-industrial policy that will create additional incentives for private investment in infrastructure, manufacturing and advanced training.

⁴² Stavros Nicolaou states that these joint ventures create a "strategic stockpile" of APIs for Aspen. Interview with Stavros Nicolaou (Aspen Pharmacare), 15 December 2006.

⁴³ See DFID *Leveraging the Private Sector for Public Health Objectives* (2004). The DFID study, which was particularly concerned with domestic production in sub-Saharan Africa, concentrated on the following factors: quality; geographical accessibility; physical availability; acceptability; affordability; the feasibility of domestic production of medicines to combat TB and malaria, as well as HIV/AIDS; government strategy; and the domestic market.

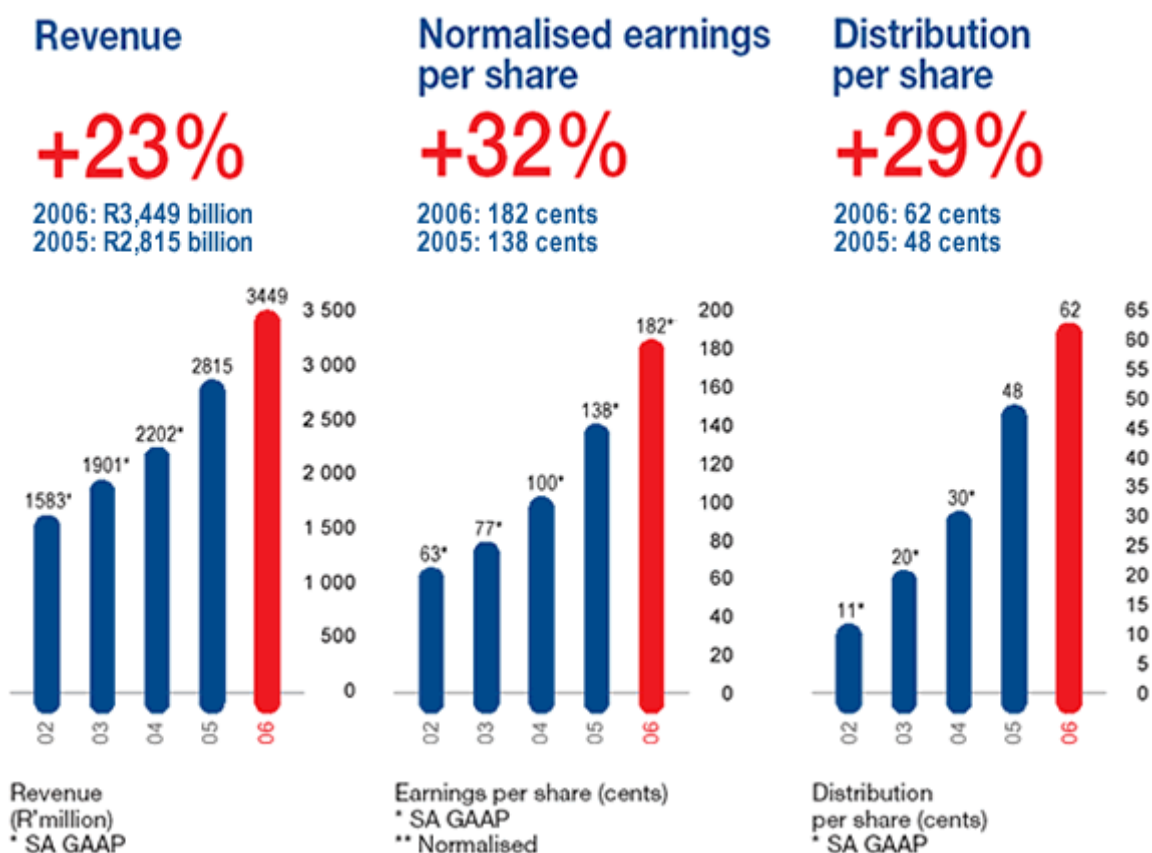
References

- Bureau for Economic Research (2005). *The Impact of HIV/AIDS on Selected Business Sectors in South Africa*, (October 2005), available from <http://www.assa.co.za>.
- Case No 4183/98 (Witwatersrand High Court, filed 18 February 1998).
- Chen, L., and G. Berlinguer (2001). "Health Equity in a Globalizing World" In Evans, T., M. Whitehead, F. Diderichsen, A. Bhuiya and M. Wirth (2001). *Challenging Inequities to Health: From Ethics to Action*. Oxford: Oxford University Press.
- Cornia, G. A., and L. Menchini (2005). "The Pace and Distribution of Health Improvements during the Last 40 Years: Some Preliminary Results." Paper presented at UNDP-French Government Sponsored Forum on Human Development (17-19 January 2005).
- Dabis, F., and E.R. Ekpini (2002). "HIV-1/AIDS and Maternal and Child Health in Africa" *Lancet* 359, 2097–2104.
- Department for International Development (DFID)(2004a). Health Systems Resource Centre. Access to Medicines in Under-Served Markets: What are the Implications of Changes in Intellectual Property Rights, Trade and Drug Registration Policy? London: DFID. Available from <http://www.eldis.org>.
- DFID (2004b). Processes and Issues for Improving Access to Medicines: The Evidence Base for Domestic Production and Greater Access to Medicines. London: DFID. Available from <http://www.eldis.org>.
- DFID (2004c). Leveraging the Private Sector for Public Health Objectives. London: DFID. Available from <http://www.eldis.org>.
- DFID (2004d). Increasing Access to Essential Medicines in the Developing World: UK Government Policy and Plans.
- Dugger, C. (2004). "Devastated by AIDS, Africa Sees Life Expectancy Plunge," *The New York Times*, 16 July 2004.
- GlaxoSmithKline (2005). *Corporate Social Responsibility Report 2005*.
- Glaxo Wellcome and Smithkline Beecham v Competition Commission Case No 58/AM/May (28 July 2000).
- Government of the Republic of South Africa, Dept of Health (2001). "Briefing Document, Defending the Medicines Control Amendment Act" (2 March 2001).
- Government of the Republic of South Africa, Department of Health (2003). *Operational Plan for Comprehensive HIV and AIDS Care, Management and Treatment for South Africa*, available from <http://www.info.gov.za/otherdocs/2003/aidsplan.pdf>.
- Hazel Tau Competition Commission Case No 2002 Sep 226.
- Jamison, D., R. Feachem, M. Makgoba, E. Bos, F. Baingana, K. Hofman and K. Rogo, eds (2006). *Disease and Mortality in Sub-Saharan Africa* (second edition). Washington, DC: World Bank.
- Kahn, T. (2005). "Aspen to Focus on AIDS Drugs Market across 15 Countries" *Business Day* (South Africa), 23 August 2005.
- Lafraniere, S. (2005). "Poor Lands Treating Far more AIDS Patients" *New York Times* 27 January 2005.
- Lucchini, S., B. Cisse, S. Duran, M. de Cenival, C. Comiti, M. Gaudry and JP Moatti.

- (2003). Decrease in Prices of Antiretroviral Drugs for Developing Countries: from Political Philanthropy” to Regulated Markets? Available from <http://www.iaen.org/papers>.
- Médecins Sans Frontières (MSF)[no date provided]. “The TB/HIV Time Bomb: A Dual Epidemic Explodes in South Africa” available from <http://www.msf.org>.
- MSF (2001). *Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases*. Geneva: MSF Access to Essential Medicines Campaign and the Drugs for Neglected Diseases Working Group.
- Mellors, S. [no date provided]. *Monitoring the Implementation of the UNGASS Declaration of Commitment: Country Report South Africa*. Toronto: International Council of AIDS Service Organizations.
- Mzolo, S., and S. Theobald (2006) “Generic Drugs: A Chance at Life” *Financial Mail* (South Africa), 17 November 2006.
- Petchesky, RP. (2003). *Global Prescriptions Gendering Health and Human Rights*. New York: Zed Books.
- Ruger, J. (2004). “Health and Social Justice” *Lancet* 364 (2004), 1075-1080.
- Smart, T. “Antiretroviral Sources of Supply May Not be Able to Meet Popular Demand” available from <http://www.redribbon.co.za>.
- Sprague, C. and S. Woolman. “Moral Luck: Exploiting South Africa’s Policy Environment for an Effective National Antiretroviral Treatment Programme” *South African Journal on Human Rights* 22 (part 3) 2006, 337-379.
- “The AIDS Drug Warrior” Salon.com, 18 June 2001, available from <http://www.salon.com>.
- Tiger Brands’ 2005 Annual Report, available from www.tigerbrands.co.za/Investor/InvestorCentre/2005Results/AnnualReport/downloads/pdf.
- The Economist*, “Aspen’s upward Slope: Can South Africa's Top Generics Manufacturer Become a Global Giant?” 6 October 2005.
- t’Hoen, E. “TRIPS, Pharmaceutical Patents and Access to Essential Medicines: Seattle, Doha and Beyond” (2003) International AIDS Economics Network, <http://www.iaen.org/papers/>.
- United Nations Development Program (UNDP). Millennium Development Goals and Indicators, available from <http://mdgs.un.org/unsd/mdg/Host.aspx?Content=Indicators/OfficialList.htm>.
- UNDP (2005). *Human Development Report 2005*. New York and Oxford: Oxford University Press.
- United Nations Children’s Fund (UNICEF) South Africa (2006). *Impact on Children: Paediatric Testing and Treatment*. Available from <http://www.unicef.org/southafrica>.
- United Nations Joint Programme on AIDS (UNAIDS-WHO (2005). *Joint WHO/UNAIDS Fact Sheet N°283* (January 2005).
- Wines, Michael. “AIDS-Linked Death Data Stir Political Storm in South Africa” *New York Times* 19 February 2005.
- World Health Organisation (WHO) (2006). *World Health Report 2006*. Geneva: WHO.
- WHO (2005). “Summary Country Profile for HIV/AIDS Treatment Scale-Up” (June 2005)(data at end-2004), available from

<http://www.who.int/3by5/countryprofiles/en>, accessed 15 August 2006.
WHO (2004). *World Health Report 2004* (Global Burden of Disease Estimates for 2002).
Geneva: WHO.
WHO (2000). *World Health Report 2000*. Geneva: WHO.

Exhibit 1 Aspen's Financial Highlights 2006

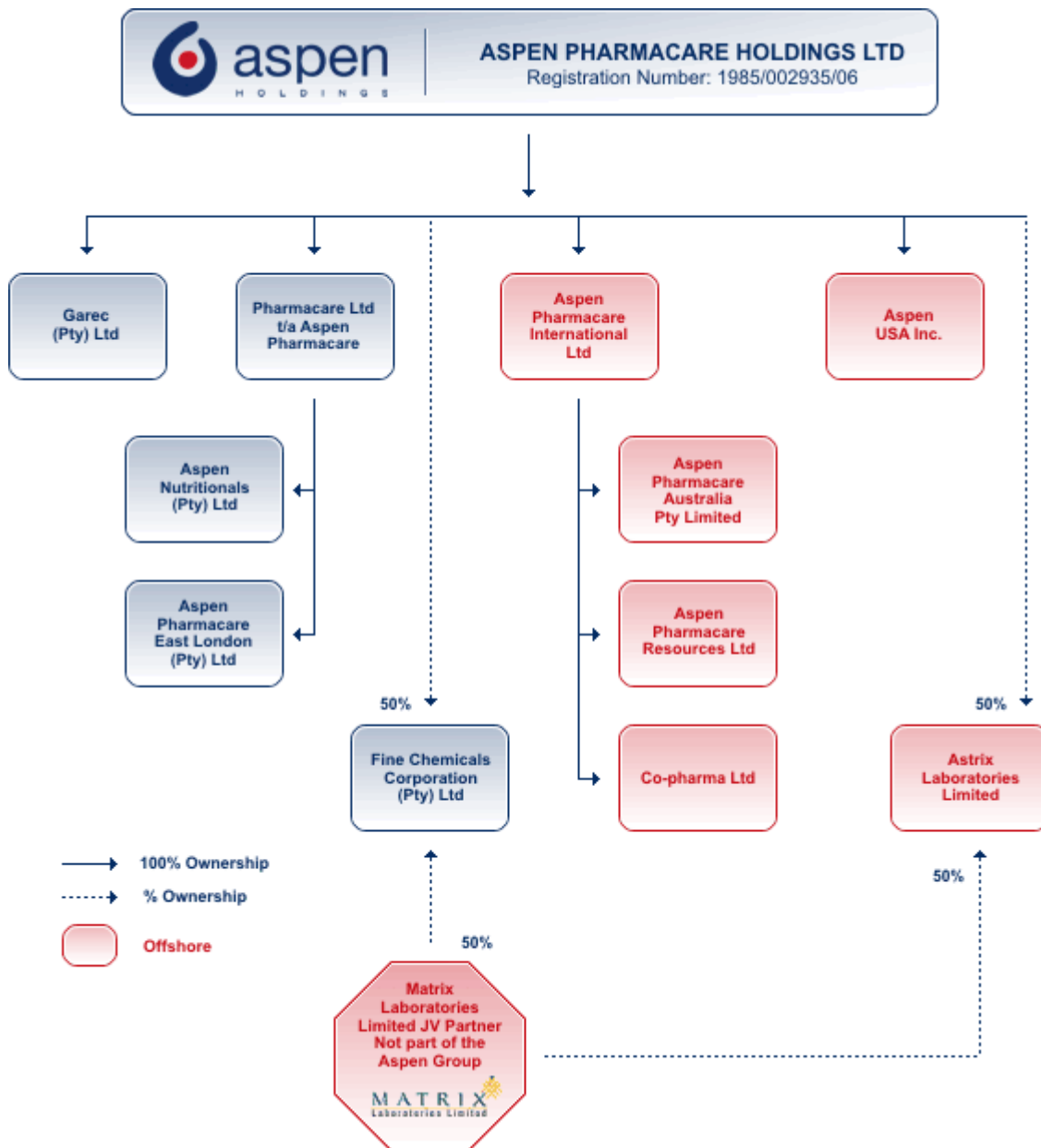


	30 June 2006 R'million	30 June 2005 R'million	Change %	Compound growth*
Group summary				
Revenue	3 449,3	2 814,6	23	22
Normalised operating profit	1 004,1	782,9	28	26
Normalised profit after tax	626,6	468,9	34	29
Net cash from operating activities	402,4	652,8	(38)	15
Ordinary share performance				
Earnings per share – basic (cents)	185,4	54,7	239	31
Headline earnings per share (cents)	185,5	55,4	235	31
Normalised earnings per share (cents)	182,1	137,6	32	31
Distribution per share (cents)	62,0	48,0	29	54
Operating cash flow per share (cents)	116,9	191,7	(39)	15

* Compound growth represents five-year compound annual growth, calculated for the period 2002 to 2006.

Source: Aspen Annual Report 2006, available from
http://www.aspenpharma.com/Annrep_2006/financial_highlights.htm

Exhibit 2 Aspen Organogram



Source: <http://www.aspenpharma.com>.