The Compulsory License Red Herring

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International Policy Network

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Executive Summary

The global battle against HIV/AIDS and ill-health in poor countries has taken a major turn over the past decade. From being a "neglected disease" in the 1990s, spending on HIV/AIDS has been transformed, with tens of billions of dollars spent on scaling up the production and distribution of treatments. This funding has come from a combination of bilateral aid, multi-lateral organisations, public-private partnerships, philanthropists and pharmaceutical companies. It has contributed to a twelve-fold increase in the number of people receiving regular treatment. Nevertheless, many people who might benefit from treatment continue to go untreated.

To address this unmet need, some health activists argue that intellectual property rights must be weakened. In particular, they claim that the "flexibilities" in the TRIPs agreement, enabling governments to issue "compulsory licenses," are too restrictive and deter governments from employing them. Particular criticism has been reserved for the "Paragraph Six solution" – rules that allow governments in countries without local pharmaceutical manufacturing capacity to issue a compulsory license to import medicines.

The paper argues that a revision to the compulsory licensing process through the WTO is an unnecessary diversion. While it is true that few compulsory licenses have been issued in the past decade, access to medicines has increased rapidly. We argue that while there remain considerable barriers to access, these have little to do with IPRs.

IPR standards have improved in many regions – and this may actually have increased access to medicines in general and ARVs in particular. The following facts are apposite:

- 65% of first-line anti-retroviral medicines are now produced by generic manufacturers;
- many second- and third-line ARVs that are protected by patent rights are being manufactured in India and other developing countries with rights-holders consent. These agreements result in useful partnerships that transfer technology and know-how to developing economies;
- many other first-, second-, and third-line medicines protected by patent holders are being manufactured in India without the consent of rights-holders, yet these companies have to date not registered legal challenges to this production. Many of these medicines are for export, which questions the need to revisit the Paragraph Six system.
- Finally, options to promote access and to encourage sustainable downstream R&D through differential pricing are being explored by the private sector.

All of these developments suggest that increasing access has been the result of a remarkable degree of flexibility within the global IPR system.

Revisiting the debate over TRIPS flexibilities once more represents a mis-prioritisation of resources and would divert attention away from the far more important debate about improving overall access to healthcare in poor countries. Here, again, the evidence is incontrovertible: A combination of a lack of adequate healthcare personnel, porous and dilapidated infrastructure, and poor governance remain the main factors inhibiting access to better healthcare.

The Compulsory License Red Herring

Introduction

Global trade rules administered by the World Trade Organisation (WTO) have long included protection for intellectual property rights (IPRs) but also flexibilities to those rights that aim to balance innovators' requirement to earn a return on investment with the need for people in poor countries to access medicines. As such, member states reserved the right to issue compulsory licenses on patented medicines when the Trade Related aspects of IPRs (TRIPS) agreement was first accorded in 1994. The public health aspects of this right were clarified by the WTO's Doha Declaration in 2001, and then once again in August 2003.

Over the last fifteen years, these flexibilities have only rarely been used. A loose coalition of generics companies, health activists and member states is now pushing to revisit the WTO amendments that concern compulsory licenses. Partly because of this activism, the WTO still does not have the necessary majority to permanently ratify the August 2003 TRIPS Article 31(f) amendments, concerning compulsory licenses in countries that do not have domestic pharmaceutical industries.[1] The debate about TRIPS and compulsory licenses as a means to promote access to medicines is still fiery, particularly as it relates to HIV/AIDS.

One prominent generics company has described the process created by the August 2003 amendments as unworkable (see box). The Tanzanian High Commissioner to Canada, His Excellency Ombeni Sefue, said of TRIPS flexibilities in 2006: "It's not that we don't want to do [them]. It's just that we haven't because…all the bureaucratic, administrative, and legal requirements take a lot of time…The system is too complicated."[2] Health activists have also complained that it is overly bureaucratic for African governments to take advantage of TRIPS flexibilities, as they require compulsory licenses to be issued on a case by case basis.[3]

Are these concerns about flexibilities that deviate from TRIPs requirements justified? Has access to ARVs been hindered by the allegedly cumbersome nature of TRIPS flexibilities? This paper attempts to answer these questions by examining access to ARVs in lower-income countries, with particular reference to concerns about intellectual property.

The paper begins by examining rates of access to ARVs in less developed countries, and then goes on to detail some of the strategies adopted by manufacturers of medicines to increase access to their products. The paper concludes by considering other barriers to access to medicines unrelated to intellectual property.

TRIPS flexibilities and examples of their use

At the 1994 conclusion of the Uruguay Round of negotiations of the old General Agreement on Trade and Tariffs (GATT), member states agreed to formalise the global protection of intellectual property rights. The agreement, known as TRIPS requires WTO member states to provide patent holders certain exclusive but temporary rights, including the right to prevent unauthorised persons from making, using, offering for sale, or importing a patented product, or using a patented process.

The emergence of HIV/AIDS as a major health problem in developing countries in the 1990s gave rise to concerns about the adverse impact of this Agreement on public health, given that IPR protection allows rights-holders temporary exclusive manufacturing and marketing rights on patented HIV/AIDS medicines, or

anti-retroviral medicines (ARVs). The fear that this would lead to unaffordable high prices for ARVs in poor countries had already emerged in the form of legal challenges against pharmaceutical companies in South Africa, eventually ending in 2001. These concerns were taken up at the WTO during negotiations of the so-called "development" round in Doha, and resulted in the November 2001 "Doha Declaration".[4]

The Doha Declaration clarified questions pertaining to public health that were posed by the TRIPS agreement. WTO member states "recognise that intellectual property protection is important for the development of new medicines," "the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health."[5] In essence, this allows member states "flexibilities" to override intellectual property rights in certain public health circumstances, which are detailed in Article 31 in TRIPS. Governments can issue "compulsory licenses" that allow manufacturers to legally produce pharmaceutical products under patent with a minimal rate of royalty being paid back to rights-holders.

While flexibilities already built into TRIPS permitted compulsory licenses for supply of the domestic market of the member state issuing the license, the Doha Declaration raised concern that many countries hardest hit by HIV/AIDS had no domestic manufacturing capacity. To address this, the WTO General Council subsequently created an amendment to TRIPS known as the August 2003 "Paragraph Six" solution,[6] which permits WTO members without domestic manufacturing capacity to issue a compulsory license to import medicines with minimal royalties.

The process for employing the Paragraph Six "system" is straightforward. A member state must make the TRIPS Council aware of its intention to proceed, and register details of each compulsory licence. Specifically, the importing country must register the conditions attached to the compulsory license it is issuing, including the name and address of the licensee, the products and size of production batch being licensed, and the country (or countries) to which the products are to be supplied and the duration of the licence.

The member state exporting the drugs must also register details of each order that it aims to fulfil.[7] To ensure delivery is made and not deviated elsewhere, the contents of the order must be clearly labelled as such. Under Article 31 (h), royalties that are commensurate with the economic value of the compulsory licence in the importing country, not the exporting country, are to be paid by the exporting manufacturer to the original rights-holder.

In sum, the flexibilities added to TRIPS at Doha allow for a broad interpretation, and the legal mechanisms and regulatory requirements to issue a compulsory license, for domestic consumption or for export, are not especially burdensome. For instance, the grounds to determine what constitutes a "health emergency" are open for domestic interpretation.

Given that AIDS activists have long claimed that intellectual property rights are a significant barrier to AIDS treatment, the Doha Declaration should have resulted in a mass uptake of compulsory licenses in poor countries. The reality has proven different given how few governments have excercised the right to produce or import generic copies of patented ARVs:

- South Africa's 2001 announcement that compulsory licenses would be issued on ARVs used to treat HIV/AIDS owned by GlaxoSmithKline (GSK) and Boehringer Ingelheim (BI).[8]
- In May 2002, Zimbabwe declared a period of emergency (subsequently extended to 2008) which allowed the abrogation of existing ARV patents. Zimbabwe has begun local production of ARVs though the generic company Varichem Pharmaceuticals (Private) Limited. The company's facility was inspected by the WHO for Good Manufacturing Practice in May 2010 and its first product was officially pre-qualified by the WHO in September 2010.[9, 10]
- In 2003, Malaysia issued a government-use compulsory license for import of generic combavir, didanosine and zidovudine from an Indian generic manufacturer. The order was taken up by Cipla.
- In 2004, Indonesia issued a government-use compulsory license on lamivudine and nevirapine until the end of the patent term in 2011 and 2012

respectively. Production of the medicines has been undertaken by PT Kimia Farma.

- On April 5, 2004, Mozambique issued a compulsory license for lamivudine, stavudine and nevirapine. The license was granted to Pharco Moçambique Lda. According to Tenu Avafia of the United Nations development Programme, the price of active pharmaceutical ingredients (APIs) meant that local production was not economically viable.[11]
- On September 21, 2004 Zambia issued a compulsory license for lamivudine, stavudine and nevirapine. The license was granted to Pharco Ltd, a local producer. As of September 2010, the drug was not WHO Prequalified or approved by the US FDA.
- In June 2005, Eritrea invoked the Doha declaration in issuing a compulsory license for the import of ARVs.[12]
- In 2005, Brazil's Ministry of Health threatened a compulsory license on Kaletra, an ARV owned by Abbott, but did not follow through as the rights-holder agreed to reduce the price.
- In October 2005, Ghana issued government use compulsory licenses for importation into Ghana of Indian generic ARVs.
- In 2007, Rwanda announced its intention to invoke Paragraph Six for the import of a generic fixed dose combination of zidovudine, lamivudine and nevirapine. The Canadian generic manufacturer Apotex fulfilled one order in 2009, under the auspices of the Canadian Access to Medicines Regime but declined to produce subsequent batches (see box).
- In 2007, Brazil issued a compulsory licence on Merck's efavirenz.[13]
- In 2007, Thailand's issued compulsory licenses on efavirenz, lopinavir+ritonavir combination and clopidogrel (for coronary disease), which was subsequently manufactured by the government-owned GPO.
- In late 2009, Ecuador's President Correa invoked the Doha declaration in signing a decree allowing compulsory licences. In April 2010, a local distributor of Cipla was granted a license to manufacture Ritonavir, whose patent is owned by Abbott Laboratories.

Canada's access to medicines regime – big promise, minimal delivery

Canada became the first WTO Member to incorporate the September 2003 General Council resolution into domestic law, weeks after the August 2003 TRIPs General Council resolution. Known as the Canadian Access to Medicines Regime (CAMR), this move was widely praised by activists within the health community in Canada and around the world, who launched a "Don't Let Pharma Hijack Jean Chretien's Pledge to Africa" campaign to generate emotive public support for its passage.[16]

Rwanda announced its intention to use the Paragraph Six system in 2007 to find cheap ARVs.[17] But it was only in 2008 that it was able to locate a willing generics supplier. Apotex, a Canadian generics manufacturer, was only able to fulfil the order (for Apo-TriAvir, a fixed-dose combination therapy) in 2009 and then subsequently declined to supply a second order from the Rwandan government.

The response from Apotex and its allies in the advocacy community has been to blast the CAMR as "unworkable" and overly bureaucratic. In lieu of CAMR, they support the passage of two new Bills (C-393 and S-232) which they say would make the system more workable. Among other things, it suggests that Canadian generics produced under the CAMR should be exempt from regulation, which in theory could speed up the approval time for their products, but opens up the possibility of dubious quality control.[18]

However, Canadian legal scholar Amir Attaran points out that Apotex lodged its application with Canada's Commissioner of Patents on 10 September, 2009 and received its approval just one week later.[19]

Attaran points out that the origins of Apotex's difficulty and delay in meeting the Rwandan order have less to do with CAMR and more with the Canadian generics industry's lack of global competitiveness. Indeed, Apotex admitted as much when it priced its medicine as low as it could, at 39 cents a tablet between 2006–2008, which was uncompetitive in comparison to the prices charged by manufacturers in India, Finland, and the United States. It was only when Apotex slashed its prices by 50 per cent, to 19.5 cents, that the order could be completed. But this price was uneconomical for Apotex and therefore a second order could not be carried out.[20]

It is notable that many compulsory licenses were not actually fully implemented. Many such instances are used erroneously as examples of compulsory licenses by advocates of that approach.[14] For example, the Indian government was being urged by NATCO, a domestic

generics manufacturer, to override Pfizer's patent on Tarceva, a cancer medicine, so that it could export cheaper versions to Nepal. However, a compulsory licence was never actually issued as Pfizer stepped in to fill this need.[15]

Philanthropic and governmental efforts to promote access to medicines for HIV/AIDS

Despite the fact that TRIPS flexibilities have only been infrequently used, the number of patients treated for HIV/AIDS increased more than twelve-fold between 2003 and 2010 (Figure 1). In 2003, only 50,000 patients were on ARV treatment. By 2005, this number had increased to 1.57 million patients in January 2005, a number that increased to 5.2 million patients by December 2009.[21]

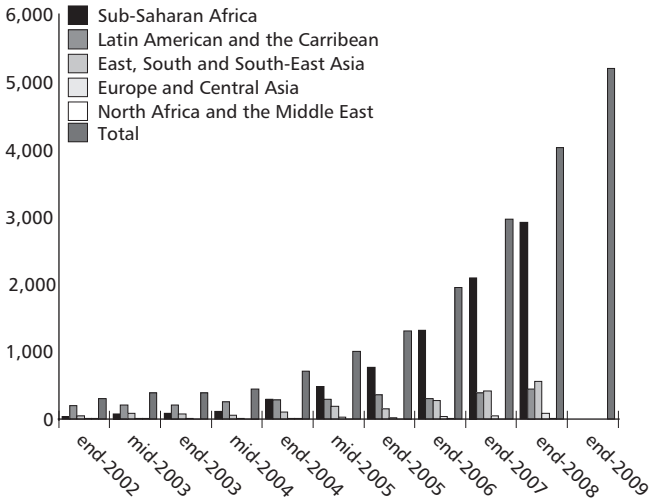
The vast majority of patients gaining access to HIV/AIDS medicines have done so as a result of programmes such as the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund to Fight AIDS, Tuberculosis and Malaria, as well as the private-sector and other public-private partnerships.

By the end of 2009, PEPFAR was responsible for 2,485,300 people on treatment in developing countries. A further 2.8 million people in June 2010 were receiving treatment underwritten by the Global Fund, a rise of 22 per cent on the previous year.[22]

The private and philanthropic sectors have also underwritten a large proportion of these increases in access to ARVs, often in partnership with the public sector. Two groundbreaking examples are the Bill and Melinda Gates Foundation-Merck AIDS program in Botswana and the Bristol Myer-Squibb "Secure the Future" Program in ten Southern African states, which both began in 1999. The Gates-Merck partnership allowed Botswana to become the first sub-Saharan African country to give ARV treatment to every eligible patient. Building on these successes, the UN/Industry Accelerating Access Initiative (AAI) program was launched in 2000, which up until 2006 was the single biggest platform in for delivering ARVs in the world.

In spite of minimal exploitation of TRIPs flexibilities by WTO member states, generic medicines now constitute

Figure 1 **Patients receiving HIV/AIDS treatment, 2002–9**



the majority (65 per cent) of first line ARV medicines used in sub-Saharan Africa.[23] Multilateral agencies such as the Global Fund and philanthropic bodies such as the Clinton Foundation have pursued pro-generic procurement policies without the need to rely on WTO Member States implanting TRIPS flexibilities.

However, insisting on the quality of medicines remains paramount in the effort to scale-up access to medicines. The distribution of low-quality copied ARVs can do more harm than good by accelerating the emergence of drug resistance or increasing the chances of clinical failure. To this end, there are several on-going initiatives which encourage the approval and dissemination of high quality generics that are rigorously tested and are certified as truly equivalent to the original drug. One notable example is the US FDA's fast-track review programme, which since 2004 has reviewed for certified quality generic ARVs manufactured overseas, free of charge. This enables public and private procurement programmes to ensure their drugs are of the highest quality.

113 of the 185 ARV and Opportunistic Infection therapies on the WHO's authorised list have been approved as true generics by the FDA.[24] According to the FDA Commissioner, this approval system enabled an extra $150 million to be spent on medicines for distribution in 2009 alone.[25]

Table 1 **A selection of Public Private Partnerships for AIDS treatment**

Partnership	*Country*	*Summary*
PEPFAR / Societe des Caoutchoucs de Grand Bereby	Cote D'Ivoire	Provides HIV education, prevention of mother-to-child transmission (PMTCT) services, and access to care and treatment services to surrounding communities
PEPFAR / Virgin Unite, Anglo Coal, Ndlovu Medical Trust	South Africa	Create a community health center that offers basic health care services at an affordable price and provides free diagnosis and treatment for HIV/AIDS, tuberculosis, and malaria
PEPFAR / Accenture Development Partners, GSM Association Development Fund, Motorola, MTN, Voxiva	Rwanda and 9 other PEPFAR supported countries	Help fulfill the need for a health care infrastructure that adequately addresses the HIV/AIDS pandemic and make timely, relevant information available to program managers and service providers
USAID / Pfizer	Africa	Several projects, including the mothers2mothers program (m2m) in Cape Town, South Africa, focusing on care for HIV-positive mothers
USAID / Standard Bank (largest bank in Africa), NamDeb (subsidiary of DeBeers), Namibia Business Coalition on AIDS	Namibia	Providing sachets of nutritious yogurt to young children, coupled with HIV/AIDS prevention education. The yogurt offers children at least one healthy meal supplement per day, helping them to be less vulnerable to HIV/AIDS.
Government of Botswana / the Bill & Melinda Gates Foundation, Merck	Botswana	Leveraging private sector perspectives and experiences to resolve social issues in support of Botswana's response to the HIV and AIDS pandemic through a comprehensive approach to prevention, care, treatment and support.
China's Ministry of Health / Merck	China	This partnership with China's Ministry of Health, established in 2005, provides HIV and AIDS prevention, patient care, treatment and support. The project focuses on a range of interventions including: education, counseling, testing, harm reduction and health services, including treatment and care for people living with HIV and AIDS.
Cambodian Ministry of Health/Roche	Cambodia	In 2007 Roche committed to fully fund the operational costs of CTAP's clinic in Phnom Penh for a further year. The Cambodian Ministry of Health is identifying other sources of funding, both national and international, to help the clinic become fully independent of Roche.

This expansion of access has been underwritten by a massive increase in the level of government-funded programmes and philanthropic donations in terms of cash and in-kind giving, totalling over $48 billion between the years 2004 – 2008. The International Monetary Fund (IMF) reports that expenditures for AIDS alone were $8 billion in 2004[26]; WHO reports that they were $8.3 billion in 2005, and UNAIDS says they reached at least $9 billion in 2006. The Global Health Council estimates that spending increased in 2007 to $10 billion and then increased further to $13.7 billion in 2008.[27] Expenditures on TB and malaria, while lower than on AIDS, nonetheless are estimated at $6–7 billion over this same time frame.

The pharmaceutical industry has also made significant non-profit and for-profit investments into research efforts for tropical diseases and to revamp dilapidated health infrastructure within poor countries. Some specific examples include, but are not limited to: the first paediatric AIDS hospital and the first AIDS laboratory in Africa[28], both based in Botswana, constructed by Bristol Myer-Squibb[29]; the first Infectious Disease Institute built by Pfizer in Uganda, which has trained half of Africa's AIDS cadres[30]; the Novartis Institute for Tropical Diseases (NITD) in Singapore[31]; Tanzania's first Pediatric AIDS Hospital was built by Abbott Laboratories[32]; a non-profit vaccine research centre operated by Novartis in Siena, Italy since 2007[33]; and GlaxoSmithKline's Tres Cantos research facility which is geared exclusively for investigation into improved treatments deemed "essential" by the WHO. A selection of public private partnerships for AIDS treatment are shown in Table 3.

Access to generic ARVs is increasing outside of TRIPS

One of the main underpinnings of the flexibilities clarified by the Doha Declaration is the notion that IPRs represent a barrier to the manufacture and export of patented drugs to a foreign country undergoing a health emergency. However, a great deal of such exporting already takes place without resorting to mechanism such as Paragraph Six, particularly for ARVs. Many versions of patented drugs are manufactured (mainly by Indian companies) for export to sub-Saharan African countries

Table 2 **Unlicensed generic versions of on-patent ARVs that have received WHO prequalification or FDA approval**

Company	*Drug*	*Generic manufacturer*
Abbott	Lopinavir/ ritonavir	Aurobindo, India
		Matrix Laboratories, India
	Ritonavir	Aurobindo, India
		Matrix Laboratories, India
Boehringer Ingelheim	Nevirapine	Aurobindo, India
		Cipla, India
		Hetero, India
		Huahai, China
		MacLeods, India
		Ranbaxy, India
		Strides, India
Bristol Myers Squibb	Didanosine	Barr, USA
		Matrix Laboratories, India
	Stavudine	Cipla, India
		Matrix Laboratories, India
		Ranbaxy, India
		Strides, India
Gilead	Tenofovir	Cipla, India
GlaxoSmithKline	Abacavir	Aurobindo, India
		Cipla, India
		Matrix Laboratories, India
	Combivir	Apotex, Canada
		Aurobindo, India
		Cipla, India
		Emcure, India
		Hetero, India
		MacLeods, India
		Ranbaxy, India
	Trizavir	Aurobindo, India
		Cipla, India
		Emcure, India
		Hetero, India
Merck	Efavirenz	Matrix Laboratories, India
		Ranbaxy, India
		Strides, India
	Indinavir	Hetero, India
		Ranbaxy, India

Table 3 **Voluntary Licenses between R&D-based companies and generics manufacturers in developing countries.**

Company	*Drug*	*Licensee*
Boehringer Ingelheim	Nevirapine	Aspen, South Africa
		Cosmos, Kenya
Bristol Myers Squibb	Didanosine	Aurobindo, India
	Stavudine	Aspen, South Africa
		Aurobindo, India
Gilead	Tenofovir	Aspen, South Africa
		Aurobindo, India
		Ranbaxy, India
GSK	Combivir	Aspen, South Africa
	Trizavir	Aurobindo, India
Merck	Efavirenz	Adcock Ingram, South Africa[34]
		Aspen, South Africa
		Aurobindo, India
		Cipla Medpro, South Africa

and elsewhere (see Table 2). As yet, none of these have been subject to legal challenges by the rights-holders, despite the fact that India became TRIPS-compliant in 2005. Moreover, many of these products have been accepted by the WHO's Prequalification Programme or have been approved as safe by the US FDA, in addition to many "Fixed Dose Combinations" the involve several patented ARVs. Additionally, eight Indian companies were making generic copies of GSK's Lamivudine before its patent expired in February 2010, again without challenge from the rights holder.

Boehringer Ingelheim and Bristol Myers Squibb have made "non-assert"/"immunity from suit" statements which replace or complement licensing activities.

There are also several examples of generic companies manufacturing unlicensed products that have not been admitted onto the WHO Prequalification list nor approved by a stringent regulatory authority. These include Cipla and Hetero's versions of Roche's saquinavir, and Varichem of Zimbabwe's version of GSK's combivir.

Table 4 **Voluntary licenses between R&D-based companies and generics manufacturers that have not yet resulted in products**

Company	*Drug*	*Licensee*
Boehringer Ingelheim	Nevirapine	Cipla MedPro, South Africa
		Cosmos, Kenya
		Gemini, USA
		Memphis, Egypt
		Universal, Kenya
Bristol Myers Squibb	ATV	Aspen, South Africa
		Emcure, India
	ddI	Aspen, South Africa
Gilead	TVA	Aspen, South Africa
	TDF	Alkem, India
		Emcure, India
		Hetero, India
		Unique Pharma, India
		Matrix, India
		Medchem, India
		Shasun, India
		Strides, India
GSK	CBV	Cipla, India
		Cosmos, Kenya
		Feza, South Africa
		Sonke, South Africa
	AZT	Cosmos, Kenya
		Feza, South Africa
		Sonke, South Africa
Roche	SQV	Addis, Ethiopia
		Alkem, India
		Aspen, South Africa
		Beximo, Bangladesh
		CAPS, Zimbabwe
		Cosmos, Kenya
		Regal, Kenya
		Universal, Kenya
		Varichem, Zimbabwe

Voluntary licenses

Additionally, many holders of patents for ARVs have entered into voluntary licenses with generics manufacturers in developing countries in order to increase access to those products. Typically, the rights holder agrees to transfer technology to the generic partner in return for a royalty, who then manufactures and markets the drug

locally. In many cases this takes place on a non-profit basis. Most of these agreements are negotiated on the condition that the licensed products should not be diverted to other, wealthier markets. Some examples of licensed ARVs that have been Prequalified by the WHO and/or approved by the FDA are listed in Table 3.

Also of note in table 4 is the fact that many voluntary licenses have not resulted in manufactured products, indicating that voluntary licenses alone are not likely to be a silver bullet solution to improving and increasing access to medicines.

Differential prices

Voluntary licenses or unlicensed generic manufacture are two ways of increasing access to medicines. In the long term, however, these methods do little to support future R&D as they typically only recover a fraction (if any) of the innovator's sunk costs. Another method of increasing access while recouping those costs – and thereby incentivise future R&D – is for companies to sell a product at different prices to different consumers. This enables companies to ensure that their products reach as many consumers as possible while still maximising revenue, given some degree of exclusivity. If a company is able to segment markets precisely according to each individual's willingness to pay, then every consumer willing to pay at least the marginal cost of production for the product should be able to purchase that product. This would both maximise the number of people who benefit from the product and would also maximise revenue to the company, which in principle would enable more to be spent on R&D.

Innovator companies have long pursued this strategy by selling ARVs into African and other markets in poor countries at prices well below those of the developed world. This practice was first brought into the mainstream in 2000 with the Accelerated Access Initiative, a partnership between seven pharmaceutical companies and five UN agencies. This programme involves selling branded ARVs into poorer markets at low prices, in many cases below those of generic competitors. This practice is made sustainable by selling at a relatively higher price into wealthier markets such as the USA.

Although this practice was initially focused on HIV/AIDS, it is now expanding to encompass a wide range of diseases. In 2008, drug manufacturer GSK announced plans for tiered pricing across its entire product range. In 2009, its sales in emerging markets rose by 20%,[35] suggesting greater sales volumes – and, by implication, greater numbers of patients getting access to their products.

Segmenting the market in this manner is dependent on the respect of intellectual property rights, especially patents and trademarks. If the intellectual property rights and contracts are respected, firms can operate freely within the marketplace without running the risk of having separate national or international markets compromised by the resale of the lowest priced medicines into markets where prices are relatively higher (so-called "grey imports").

However, infringements upon intellectual property rights mean that firms cannot control their own pricing schemes, with serious consequences. Not only does this act as a disincentive for firms to sell their products or invest in supply chain delivery systems in poor countries, it may also inhibit future innovation.

Differential or tiered pricing this strategy depends on the ability of manufacturers to retain control of their patents and impose contractual restrictions on re-sale or international agreements with regards patent exhaustion, so they can set prices in different market segments. Indiscriminate use of mechanisms which abrogate property rights prevents this from happening.

In short, price differentiation allows companies to cater for people who otherwise could not afford to purchase their products. It allows countries that are not able to shoulder the costs of R&D themselves to afford expensive medicines. It also means output is higher than the level that would occur if no differentiation were possible. Moreover, the innovator is able to generate more revenue, providing a greater pool of resources for investing in new drug development. Because the product sold bears the trademark of the originator company, there are also strong reputational pressures to guarantee its quality.

The real barriers to access

From the foregoing, it is clear that recent years have seen significant increases in access to HIV/AIDS medicines, largely due to the massive intervention by aid agencies and the new multilateral funding bodies. Beyond HIV/AIDS, however, wider primary healthcare remains in a parlous state in many countries, hobbled by a lack of investment, corruption and staff shortages, amongst other things. These fundamental determinants of good healthcare are unrelated to ongoing debates surrounding TRIPs and intellectual property, yet they have been largely overlooked in the debate until relatively recently.

An estimated 30 per cent of the world population lacks regular access to existing drugs, with this figure rising to over 50 per cent in the poorest parts of Africa and Asia. The vast majority of essential medicines are off-patent, suggesting that the lack of access to medicine is largely down to factors other than intellectual property and patents.[36] Fewer than five per cent of the medicines on the WHO Essential Medicines List, which forms the backbone for public procurement in poor countries, are currently protected by patents.[37] Paradoxically, many of those medicines that are still protected by patents are advanced second- and third-line ARVs, which have become much more widely available over the past decade as a result of the aforementioned effort to come to grips with the HIV/AIDS epidemic in poor countries.

The example of India reinforces this notion. From 1975, the country weakened intellectual property laws in the belief that it would drive down the price of medicines. It certainly did for some drugs, but this did not translate into improved health outcomes. Access to even basic medicines in India remains unacceptably low. Children go without routine vaccinations. Relatively cheap off-patent anti-infectives are out of reach of the majority of the rural poor. Despite pumping out cheap generic AIDS drugs for years, only 123,000 of India's 2.5 million AIDS sufferers were receiving the drugs at the end of 2007.[38]

The price of the vast majority of medicines was not the most relevant barrier for India's rural poor. The more pressing issue for them was and remains the state of their healthcare infrastructure. State healthcare systems are under-funded and patchy, riddled with inefficiency and corruption. The number of public health facilities seriously inadequate.

It is estimated that India requires 74,150 community health centres per million population but has less than half that number. In addition, at least 11 Indian states do not have laboratories for testing drugs, and more than half of existing laboratories are not properly equipped or staffed.[39] Even though the country has relatively high numbers of pharmacies and pharmacists standards of pharmaceutical care are often poor. Patients are often ill-advised and inadequately supported in relation to purchasing and using medicines. The transport network is so porous, hampered in part by intra-state government imposed barriers to trade, that rural people struggle to get to a clinic, even if one exists within a day's travel from their home. Meanwhile, dirty water and cooking fuels exact a terrible toll of disease on the poor.

So, when the Indian government strengthened its IPR laws to become compliant with TRIPs, it was able to do so because there was no domestic political connection between international patent laws and the reality of local healthcare. There are similarities with many other countries. In the Philippines, for instance, 40 percent of people will never see a doctor in their entire lives. Clinics and hospitals are rare. PhilHealth, the government-run social insurance scheme, provides very basic cover for only around half of the population. Private alternatives are becoming increasingly available in these and other poor countries, but current regulation and other policies make the scaling up of these options uneconomical.[40]

In fact, the majority of low-income countries lack the basic infrastructure required to distribute medicines successfully. Road networks are often unreliable or non-existent, making it difficult to ensure a constant supply of medicines to remote areas.[41] Electricity is often unavailable, especially in rural areas; where it is available, it is often supplied irregularly. This increases the cost and difficulty of running refrigeration systems in clinics and hospitals. As a result, vaccines are often not maintained at sufficiently low temperatures to ensure product stability. Many drugs, such as protease inhibitors (used in second-line ARV treatments) need to be refrigerated, yet due to erratic power supplies and

Table 5 **Physicians per 100,000 people, sub-Saharan Africa, 1990–2004**[45]

Equatorial Guinea	30
Namibia	30
Sudan	30
Gabon	29
Madagascar	29
Nigeria	28
Congo	20
Cameroon	19
Djibouti	18
Swaziland	16
Comoros	15
Ghana	15
Kenya	14
Côte d'Ivoire	12
Guinea-Bissau	12
Zambia	12
Congo, Dem Rep	11
Gambia	11
Guinea	11
Mauritania	11
Angola	8
Central African Rep	8
Mali	8
Uganda	8
Senegal	6
Burkina Faso	5
Eritrea	5
Lesotho	5
Rwanda	5
Benin	4
Chad	4
Somalia	4
Togo	4
Burundi	3
Ethiopia	3
Liberia	3
Mozambique	3
Sierra Leone	3
Malawi	2
Niger	2
Tanzania	2
Zimbabwe	1

other issues, it is impossible to ensure constant refrigeration in the world's poorest countries.[42]

An additional problem is that all sub-Saharan African countries suffer from shortages of qualified healthcare personnel, many of whom have emigrated to richer countries (see Table 5). For instance Ghana, with only 0.09 physicians per thousand people, sends doctors to the United Kingdom, which has 18 times as many physicians per capita.[43] The United States, with 5 percent of the world's population, employs 11 percent of the globe's physicians. One study shows that more than 23 per cent of America's 771,491 physicians received their medical training outside the USA, the majority (64 per cent) in low-income or lower middle-income countries. Of this total 5,334 physicians come from sub-Saharan Africa, a number that represents more than 6 per cent of the physicians practicing in sub-Saharan Africa now.[44]

Corruption is another problem that hinders access to medicines. Corruption in healthcare takes many forms, ranging from direct embezzlement at the ministerial level, through to local medical staff selling "free" drugs on the grey market, institutionalised absenteeism, and illegal payments to health care personnel that allow patients to jump queues or obtain treatment.[46] More than 20 per cent of medicines supplied to government-run facilities in LDCs are stolen and resold by staff.[47] This in part explains recurrent stock shortages in public health system dispensaries. And when some aid money does make it to local clinics, it is most often the educated urban classes who benefit, rather than the rural poor for whom the aid is really intended.

Intervention by global public health authorities and the provision of public funds is not a guarantee that existing medicines will be effectively distributed. A major 2009 study by the WHO attempted to gauge the impact of the $196bn spent on global health in the last 20 years. While it listed some successes, such as increased diagnosis of tuberculosis cases and higher vaccination rates, it also found some U.N. programs were counterproductive because they undermined basic services and resulted in big falls in domestic health spending (World Health Organization Maximizing Positive Synergies Collaborative Group, 2009). New examples of failing aid-financed health spring up with depressing regularity. A 2009 examination of a US$27m UNICEF programme to

reduce child mortality in West Africa found that children were more likely to survive in areas outside of the programme. Also in 2009, an independent appraisal of a separate multimillion dollar UNICEF / WHO child health programme in Bangladesh found it had no discernible impact. In 2008, dozens of low-income countries were found to be exaggerating the numbers of vaccinations administered to children in order to claim more money from UN-sponsored programmes.[48]

Because of these myriad failings, the average cost of saving a life through government health care in less developed countries is US$50,000 to $100,000, in contrast to the estimated $10–4000 for cost effective treatments to avert the largest causes of child mortality in developing countries.[49] Meanwhile, children in these countries are not receiving cheap, lifesaving treatments for diarrhoea, Oral Rehydration Therapy and other basic interventions such as vaccinations, which can save lives for a few cents (Black, 2003).

Conclusion

Access to ARVs has increased rapidly over the last decade, with generic medicines constituting the majority of first line ARVs available in Africa. Many of these generic medicines derive from originator drugs that are still on patent. This transformation of the HIV landscape has occurred even though TRIPS flexibilities have rarely been used. This suggests that the intellectual property is, at most, a marginal determinant of access, and it is not clear how reform of the TRIPS system can change this.

The real issue in access to ARVs – and all medicines – is poor health infrastructure. Speaking in 2009, Bill Clinton has summarised the situation thus: "… my experience has been that almost no one in the world will die this year because of the cost or the lack of availability of AIDS medicine. But many people will die of AIDS this year because of the absence of effective health care systems in rural areas of the poorest countries."[50]

Spending political energy discussing peripheral issues such as TRIPS is counterproductive when much of sub-Saharan Africa and other poor countries are suffering an ongoing health infrastructure crisis. This mis-prioritisation allows local political leaders to continue to ignore the crucial issues of investment in healthcare, and instead blame the under-performance of local healthcare systems on international factors outside of their control.

In 2001 African governments signed up to the Abuja declaration, in which they pledged to commit 15 per cent of their budgets to health. A 2010 study published in the Lancet found only four countries had met this figure and in seven countries health spending was below five per cent. Nigeria, for example, spent 3.5 per cent of its 2007 budget on health care, nearly 2 per cent lower than in 1999.[51] Increases of foreign aid for health have generally enabled many of such governments to reduce domestic health spending further.[52]

Without significant improvements in health infrastructure, Africa will continue to lag the world in terms of life expectancy, maternal and child mortality. TRIPS, compulsory licenses and the Paragraph Six solution has consumed a great detail of political and intellectual energy. It would be better if this energy were directed to the issues that will really make a difference.

Notes

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