

PREPUBLICATION DRAFT

**EQUITABLE PRICING OF NEWER ESSENTIAL
MEDICINES FOR DEVELOPING COUNTRIES:**

**EVIDENCE FOR THE POTENTIAL OF DIFFERENT
MECHANISMS**

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Any views expressed are the views of the author and do not necessarily reflect the views of the World Health Organization.

Abbreviations and acronyms

AAI	Accelerating Access Initiative
AIDS	Acquired Immune Deficiency Syndrome
DALY	Disability Adjusted Life Years
DFID	Department for International Development, UK
DOTS	Directly Observed Treatment Short-Course
DP	Differential Pricing
EC	European Commission
ECDS	Eastern Caribbean Drug Service
EDM	Department of Essential Drugs and Medicines Policy
EU	European Union
GAVI	Global Alliance for Vaccines and Immunization
GDF	Global Drug Facility
GLC	Green Light Committee
GNP	Gross National Product
GSK	GlaxoSmithKline
HAART	Highly Active Anti-retroviral Therapy
HIV	Human Immunodeficiency Virus
HLWG	High-Level Working Group
IAPSO	Inter-Agency Procurement Services Office
IDA	International Dispensary Association Foundation
IP	Intellectual Property
LDC	Least Developed Country
MDR-TB	Multi-Drug Resistant Tuberculosis
MNC	Multinational corporations
MSH	Management Sciences for Health
NGO	Nongovernmental Organization
OAPI	Organisation Africaine de la Propriété Intellectuelle (African Intellectual Property Organization)
OECS	Organisation of Eastern Caribbean States

R&D	Research and Development
TB	Tuberculosis
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UK	United Kingdom
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNDP	United Nations Development Programme
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
US	United States
USA	United States of America
USD	United States Dollars
WHO	World Health Organization
WTO	World Trade Organization

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Executive summary

This report on medicine pricing was commissioned by the World Health Organization (WHO) and the United Kingdom's (UK) Department for International Development (DFID) and aims to analyse the existing and potential impact of a variety of equitable pricing mechanisms. The study was carried out in support of the wider process of developing feasible policy options to increase access to essential medicines.

The terms 'differential pricing', or 'equitable pricing' can be defined as pricing based on ability to pay. As it relates to the policy goal of maximizing health impact through affordability of medicines, a more accurate term might be 'equity pricing', where countries apply a price structure or pricing policy according to some principle of fairness or equity. In practice this may mean proportionality with income per capita, human development index or similar indicators.

The report focuses on the voluntary mechanisms - bulk purchasing and competitive tendering; voluntary tiered pricing agreements; and voluntary licensing - and on how to more effectively capture advantages from these mechanisms. Evidence for the potential impact of other mechanisms, including compulsory licensing; delay in patent protection, as allowed by the Doha Declaration; systematic, government-imposed patent waivers; and price controls has also been analysed..

Equitable pricing is economically feasible due to the fact that variable costs comprise only approximately 15% of the total costs of producing a pharmaceutical product. It is also potentially feasible due to the fact that poor countries contribute so little to overall sales of the pharmaceutical industry; therefore, equitable pricing need not financially damage pharmaceutical companies. On the contrary, equitable pricing should theoretically be desirable to global companies since they would maximize their profits on products that are sold in both low and high-income markets.¹

However, market segmentation is a crucial pre-condition to the willingness of firms to engage in voluntary equitable pricing. Price and product leakage must be tackled jointly, by addressing the primary determinants of leakage: the incentives to leak product and engage in reference pricing and the feasibility of this leakage. Effective segmentation requires the co-operation of all stakeholders, including developed and developing country governments and the pharmaceutical industry.

Two trends account for the need for equitable pricing mechanisms to reach further in order to meet public health needs. On the one hand, the burden of disease in poor countries is large and growing. On the other hand, finance to meet this demand is limited. This gap between need and resources is occurring in the context of a changing intellectual property environment and the switch from chemistry-based to biology-based research and development (R&D). These changes are likely to decrease the levels of competition for new, patented products, and thus inhibit the

¹ The theoretical case for this is more complex than indicated, being dependent the degree to which markets are segmented and on relative demand elasticities. See Scherer and Watal (2001), pp.45-49 for a more detailed discussion.

degree of price reductions seen in recent years, attributable to generic copies of patented drugs.

This report does not present new empirical data or new economic concepts and tools, although it does use existing data and economic tools in new ways. It does not make policy recommendations concerning preferred mechanisms, realising that different readers and institutions will have differing objectives, perspectives and time-frames over which to influence policy, and will be operating in different contexts. However, the study attempts to take a systematic approach to examining objective evidence on the impact and potential of each mechanism. The reader is left to apply the analysis to his/her own situation.

Bulk purchasing and competitive tendering are effective in reducing prices in many different environments, and in combination with many other equitable pricing mechanisms. This study concludes that their potential to achieve more affordable prices has not yet been fully realized. Many governments need to improve their procurement practices at country level and regional level, and demand pooling could take on larger proportions, especially with the advent of new major funding mechanisms such as the Global Fund for AIDS, Tuberculosis and Malaria.

Voluntary tiered pricing agreements have thus far been limited in terms of disease scope and impact on access. Improvements, in terms of increasing the bargaining power of the purchasers, could be made to the structure of these agreements. However, there are numerous other concerns with these agreements, such as lack of transparency, anti-competitive tendency, and high transaction costs relative to benefits gained.

There are multiple interventions that can be taken to facilitate the effectiveness of bulk purchasing and voluntary tiered pricing agreements in terms of protecting the interests of all parties and creating a sustainable, adaptable situation. International organizations have a strong role to play in helping make these relationships more effective.

Although companies sometimes license their patents voluntarily for strategic reasons, the more common model in producing countries is for companies to work through their local affiliates. There are now a few examples of voluntary licenses that have been issued for equitable pricing purposes and these should be monitored for impact. Demand for licenses might increase, as producing countries implement trade-related aspects of intellectual property rights (TRIPS). Theoretically, willingness of firms to supply the licenses should increase as well, if Paragraph 7 of the Doha Declaration, requiring governments to construct incentives for technology transfer, is implemented.

Compulsory licensing is potentially an important instrument, allowable by TRIPS, to ensure that medicines are available to meet public health needs. No developing country has yet invoked a compulsory license; however, they have proven to be an effective bargaining tool for several developing countries in negotiating reduced prices with patent holders. Compulsory licensing has therefore been used to increase the leverage of other equitable pricing mechanisms. Although, as part of

negotiations on Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, there have been attempts to resolve the legal barriers to the use of compulsory licensing in non-producing countries, resolution of the practical, economic and technological barriers must also be sought.

The Doha Declaration on the TRIPS Agreement and Public Health, adopted by the World Trade Organization (WTO) Ministerial Conference in November 2001, resulted in an agreement that the least developed countries would not be required to implement patent protection on pharmaceuticals until 2016. If it were possible for the least developed countries (LDCs) to take full advantage of this delay in patent protection, this would be a very effective mechanism, in the short term, to achieve equitable pricing. However, since most developing countries already observe patents, and since a reliable supply of low-priced copies of newly patented medicines is unlikely to continue post-2006, this extension has little meaning to LDCs.

Another mechanism proposed for equitable pricing is the use of patent waivers. Although pharmaceutical companies might choose to waive their patent rights in certain LDCs in an unsystematic manner², the type of patent waiver that is reviewed in this report is a systematic, internationally agreed, and government-led system. This system would require the patent holder to sign a declaration, when filing for patents in developed countries, that a lawsuit for patent infringement would not be brought against the least developed countries when a generic firm markets a copy of a patented product for a disease prevalent in both developing and developed countries, i.e. 'global' diseases. Patent waivers would not apply to drugs to treat diseases only present in developing countries, thus patent protection would continue to strengthen, according to TRIPS, for drugs that treat these 'local' diseases. This mechanism would provide a transparent, predictable, global framework for pharmaceutical patents that is economically logical, in that it finds the optimal balance between prices and R&D incentives for countries at different stages of economic development. Unfortunately, this mechanism is unlikely to be feasible politically, thus negating all its theoretical advantages.

Price controls levied by governments have been effective in reducing prices. If applied to private sector retail pharmacies, price controls, more than any other mechanism, have the potential to have an impact not just on manufacturer's price, but on the final price the consumer pays. However, the use of price controls may result in withdrawal of the products from the market, thereby reducing access. Access problems caused by market withdrawal could theoretically be minimized by restricting the use of price controls to public sector purchasing, and/or using compulsory licensing as a back-up to this mechanism. The impact of price controls on R&D could be negative, but it would depend on the size of the market in question and on the products to which the price control mechanism is applied.

² In practice, unsystematic, company-led patent waivers would be much less effective than the systematic type reviewed here. See the arguments presented under 'delaying/reversing patent protection' and 'compulsory licensing' regarding the market certainty/volume needed for generic producing firms to be able to enter a market.

In the final section of the report, each mechanism is analysed according to a range of factors, such as impact on price reduction, possible effect on R&D, product and disease scope, impact on the poor, predictability, transparency, and sustainability. The mechanisms are examined individually as well as in relation to each other.

Purpose of the study

This study was commissioned by WHO and DFID to explore the potential impact of equitable pricing, in order to inform discussion and recommendations at the third meeting of the UK Government's High-Level Working Group on Access to Medicines, as well as to support the wider process of developing feasible policy options to increase access to essential medicines.

Methods

The methods used included:

- A review of literature from a range of sources including the WHO/WTO Workshop on Differential Pricing and Financing of Essential Drugs held in 2001 in Høsbjør, Norway, the UK High-Level Working Group, WHO, the Commission on Macroeconomics and Health, the pharmaceutical industry, nongovernmental organizations (NGOs) and others (see Appendix A).
- Interviews conducted by the author with people from industry, WHO, United Nations Joint Programme on HIV/AIDS (UNAIDS), NGOs, bulk purchasing organizations, authors of papers from the Commission on Macroeconomics and Health, the Brookings Institute, London School of Hygiene and Tropical Medicine, as well as academics at other institutions (see Appendix B).
- Analysis of the results of the literature review and interviews, building upon existing empirical data and examining experience against relevant economic frameworks.
- Presentation of the findings to the group that had commissioned the work, to a larger peer group within WHO and to members of the UK High-Level Working Group.

Equitable pricing definition

The term 'equitable pricing' can be defined as pricing based on ability to pay. As it relates to the policy goal of maximizing health impact through affordability of medicines, it might be more accurately termed 'equity pricing', where countries apply a price structure or pricing policy according to some principle of fairness or equity. In practice this may mean proportionality with income per capita, human development index or similar indicators.

When the term 'differential pricing' is used to describe a strategy employed by private companies to price based on what the market will bear,³ and with the goal to

³ As a function of, for example, the value that customers place on the product, the degree of competition it faces, and the purchasers negotiating power

maximize profits, it could more accurately be called 'discriminatory pricing'. Other terms frequently used to refer to various differential and equitable pricing practices include 'tiered', 'preferential', and 'market segmented' pricing.

Some of the mechanisms (such as bulk purchasing) analysed in this paper are policy and management tools that rely on market mechanisms to achieve reduced prices in a given country.⁴ Others (e.g. patent waivers, voluntary tiered pricing, compulsory licensing, delayed patent protection) are directly aimed at achieving equitable pricing.⁵ In practice, many of the mechanisms are unlikely to lead to equitable pricing, as defined above. In fact, developed countries are more likely than developing countries to be successful with many of the equitable pricing mechanisms since they have greater bargaining power, negotiating ability or capacity to produce domestically with issuance of a compulsory license. Therefore, discussion would be very limited if it was restricted to those mechanisms which are likely to achieve equitable prices, or prices that, after covering for the marginal cost of production, have some direct relationship to the level of income or development in each country. Consequently, this report covers a range of mechanisms which policy makers can employ with the objective to achieve equitable pricing. It also includes discussion of the variations, including forms of international mediation or operational approaches, which can be employed to make these mechanisms more likely to achieve equitable pricing objectives.

Scope of the report

The problem of access to medicines in developing countries is multifaceted; the availability of financial resources, health systems and infrastructure, rational selection and use of medicines, as well as affordability, are all important determinants. This report focuses on mechanisms to alter the pricing of medicines, recognizing that pricing is only one of many factors limiting access. On the assumption that international consensus supports the principle of equitable pricing, the report focuses less on the economic and social arguments.

Even within the scope of pricing of pharmaceuticals, the suppliers' price is only one aspect of the final price the consumer pays; additional costs such as taxes, agents' fees, distribution and retail mark-ups can raise the final price significantly above the manufacturers' price. Only some of the equitable pricing mechanisms evaluated in this report would have an impact on these other aspects comprising the final price.

This report focuses on the voluntary mechanisms:

- Bulk purchasing and competitive tendering
- Voluntary tiered pricing agreements
- Voluntary licensing

⁴ Bulk purchasing

⁵ Patent waivers, voluntary tiered pricing, compulsory licensing, delaying patent protection

and on how to more effectively capture advantages from these mechanisms.

Evidence for the potential impact of other mechanisms is also analysed, including:

- Compulsory licensing
- Delay in patent protection, as allowed by the Doha Declaration
- Systematic, government-imposed patent waivers
- Price controls.

The report does not present new empirical data or new economic concepts and tools, although it does use existing data and economic tools in new ways. For example, existing empirical data are further analysed to determine the potential impact of more extensive equitable pricing in a case study of Uganda. Similarly, existing economic frameworks are used to demonstrate how governance structures and contractual arrangements used with some mechanisms can help to make them more effective.

Since different readers and institutions will have differing objectives, perspectives and time-frames over which to influence policy, and will be operating in different contexts, the report does not make policy recommendations concerning preferred mechanisms, but attempts to examine systematically objective evidence on the impact and potential of each mechanism. The reader is left to apply the analysis to his/her own situation.

Recognizing that the factors giving rise to successful application of one approach may affect the likely success of other approaches, the mechanisms are also examined in relation to each other.

Key contextual issues

Motivation for and feasibility of equitable pricing

Equitable pricing is economically feasible because the variable costs comprise only about 15% of the total costs of producing a pharmaceutical product. Non-variable costs, such as fixed production costs, research and development (R&D) expenditure, or marketing and administration costs, can be allocated arbitrarily. This gives pharmaceutical companies pricing flexibility in terms of where (i.e. in which markets) they choose to recover the fixed costs.

Equitable pricing is also made possible due to the fact that less developed countries contribute so little to the overall profits of pharmaceutical firms. Africa, the Indian subcontinent and the developing countries of Asia account for only 1.2%, 1.3% and 2.6% respectively of the global pharmaceutical market (and the percentages are even smaller for the sales of patented medicines).⁶

In theory, equitable pricing should be not only feasible, but also desirable for pharmaceutical companies. It is an economically rational way for global companies to maximize their profits on products that are sold in both low and high income markets.⁷ Since equitable pricing should also be a way to ensure that poorer people have access to less expensive products, the interests of health planners and pharmaceutical suppliers should theoretically be aligned.

Equitable pricing in practice

Although equitable pricing is economically feasible and theoretically desirable both for pharmaceutical suppliers and health planners/purchasers, actual prices appear to vary more or less randomly between countries, with some developing countries paying more than US prices and some less. At best there is a very weak relationship between wholesale drug prices and per capita income.⁸ The actual price to the patient is further complicated by import duties, local tariffs, taxes and wholesaler profits⁹.

These observations are confirmed by studies of multinational company pricing policies, mainly for antiretrovirals (ARVs), which indicate that until recently there was remarkably little correlation¹⁰ between the price of a drug and a country's per capita income. In the last two years this situation may have changed slightly as some

⁶ Friedman, den Besten, Attaran 2003

⁷ The theoretical case for this is more complex than indicated, being dependent the degree to which markets are segmented and on relative demand elasticities. See Scherer and Watal (2001), pp.45-49 for a more detailed discussion.

⁸ Scherer, F. M. & Watal, J. (2001) *"Post-TRIPS Options for Access to Patented Medicines in Developing Countries"*, Commission on Macroeconomics and Health Background Paper, p.45.

⁹ Scherer, F. M. & Watal, J. (2001), p.45.

¹⁰ This correlation is expected on theoretical grounds because companies should be able to make more profits by charging low prices in low income markets and high prices in high income markets (discriminatory pricing), than by charging a uniform global price

companies have lowered prices in response to international pressure, principally from NGOs, and potential competition from generic manufacturers, particularly from India. For instance, between July 2000 and April 2002 the annual cost of a branded triple ARV combination fell from over US\$ 10 000 to just over US\$ 700 per patient for selected groups of consumers. Over the same time period, the lowest price for the generic combination had fallen to US\$ 209 annually.¹¹

Market segmentation and equitable pricing

One of the main reasons why equitable pricing is not practised more is due to lack of separation between poor and wealthy markets. In other words, patent holders fear that lower priced products will be diverted into wealthy markets. This is a real fear, since most companies rely heavily on sales from a limited number of successful drugs to finance continuing R&D. Consequently, companies' concerns are about patent protection and possible price erosion primarily as these affect the "blockbuster" drugs and wealthy markets.

Thus, market separation is a crucial precondition¹² to the mechanisms discussed in this report. Market segmentation relates to the prevention of physical product leakage from poorer to wealthier markets as well as to price leakage, that is, when developed countries use equitable prices in their reference pricing systems. The more successfully wealthy and poor markets can be separated, the more willing firms will be to engage in equitable pricing. Importantly, this is a point on which the interests of industry and of health planners are aligned.

The two primary factors that affect market segmentation are the feasibility of price or product leakage from poor to wealthy markets and the incentives for various agents to engage in arbitrage by moving equitably priced products from poor to wealthy markets, where a higher price can be charged.

The feasibility of price of product leakage from a poor to a wealthy market is a function of:

- The similarity between the marketing mix (product attributes, packaging, distribution channel, promotion messages) of equitably-priced and non-equitably-priced products
- The strength of the regulatory systems to prevent parallel import of equitably-priced products into wealthy countries
- The geographic proximity between the poor and the wealthy markets¹³

11 Médecins sans Frontières (2002) "Untangling the Web of Price Reductions: A Pricing Guide for the Purchase of ARVs for Developing Countries", MSF, Geneva.

12 For detailed explanation of why this is a precondition for equitable pricing, see Commission on Macroeconomics and Health working paper no 1, working group 4, Scherer and Watal.

13 There is a growing phenomenon of US citizens using the Internet to purchase their prescribed drugs in Canada where drug prices are significantly lower. Thus, one might expect that the Internet, over time, would alleviate the need for geographic proximity. However, since Internet penetration is higher and distribution systems more

- The security of the distribution chain through which equitably-priced products flow.

The incentive for agents to move equitably priced products from poor to wealthier markets is a function of the attractiveness of the product to wealthy markets and this depends on:

- The volume of demand for the product in the wealthier market
- The size of the price differential between the markets (which must be at least large enough to cover the transaction costs).

Armed with this information on the variables that affect the incentive to engage in arbitrage and the feasibility of market separation, governments and companies can start to construct interventions to minimize the risk.

advanced in developed countries, it is likely to remain a developed country phenomenon, rather than a trend affecting developing countries, for the foreseeable future.

The increased need for equitable pricing

Burden of disease

One out of every ten deaths in the world is due to only three diseases: AIDS, tuberculosis (TB) and malaria. This burden falls almost entirely on the developing world. For example, the loss of Disability Adjusted Life Years (DALYs) per capita due to HIV/AIDS, TB and malaria is almost 170 times higher in Africa than in high-income countries.¹⁶ The high disease burden in developing countries is slowing economic growth worsening poverty levels. The overall impact of this on the Millennium Development Goals and on poverty reduction is very substantial.

Limited financing

This high disease burden exists in the context of limited financing. For 2002-2005, the total estimated disease-specific financing need for HIV/AIDS, TB and malaria alone is around US\$ 36 billion.¹⁷ Potential national resources are estimated to be approximately one third of that amount, leaving a need for c. US\$ 23 billion from international sources. Currently available international resources for the three diseases are estimated to be around US\$ 1.5 billion per year, indicating a large gap.¹⁸

Furthermore, the need for additional resources will continue to grow in the long term. The annual incremental need, over and above current levels of expenditure, is estimated to be US \$17 billion in 2007 and US \$27 billion by 2015. A substantial part of this financing would go towards the purchase of medicines. Clearly, significant reductions in the prices of these medicines would help close the gap between limited finance and unmet need.

Competitive environment

The gap between health need and resource availability is occurring in the context of:

- A changing intellectual property (IP) environment
- A changing technological environment - the switch from chemistry-based to biology-based R&D.

¹⁵ There is a growing phenomenon of US citizens using the Internet to purchase their prescribed drugs in Canada where drug prices are significantly lower. Thus, one might expect that the Internet, over time, would alleviate the need for geographic proximity. However, since Internet penetration is higher and distribution systems more advanced in developed countries, it is likely to remain a developed country phenomenon, rather than a trend affecting developing countries, for the foreseeable future.

¹⁶ Global Fund Business Plan submitted for the second meeting, April 2002.

¹⁷ Real need is likely to be higher than indicated here. First, estimates reflect the initially limited absorptive capacity in many countries, thereby not always showing real underlying need. Second, costs for R&D and basic health infrastructure are generally not included. Third, low unit cost estimates are often used.

¹⁸ Global Fund business plan submitted to second Board meeting, April 2002

The changing IP environment is likely to decrease the levels of competition for new, patented products, and thus, inhibit the levels of price reductions seen in recent years due to competition from generic copies of patented drugs. As described more fully in subsequent sections, this will impact directly on the effectiveness of some mechanisms for equitable pricing (e.g. compulsory licensing) and on others indirectly (e.g. those that are strengthened by the use of compulsory licensing as a negotiating tool). Thus, consideration of the IP environment is necessary.

The changing technological environment is another key factor likely to result in a decline in competition. On the one hand, as medical treatments become more tailored to the patient's genetic make-up, the number of available treatments will multiply, as could the number of manufacturers. On the other hand, entry into these markets will require considerable financial and technological resources, which few possess. In particular, the complexity involved in the development of pharmacogenomic products, and the diagnostic process of determining for which patients the treatment would be appropriate, may preclude a great deal of generic competition. There are also questions as to whether drugs created via these technologies could be reproducible so that they are 'bio-equivalent' to their branded counterparts.¹⁹ Companies with greater critical mass could therefore dominate, controlling products resulting from genomics-based technologies.

Voluntary licensing is the only mechanism discussed in this report that might be beneficially affected by the changing IP and technological environment.

Uganda case study

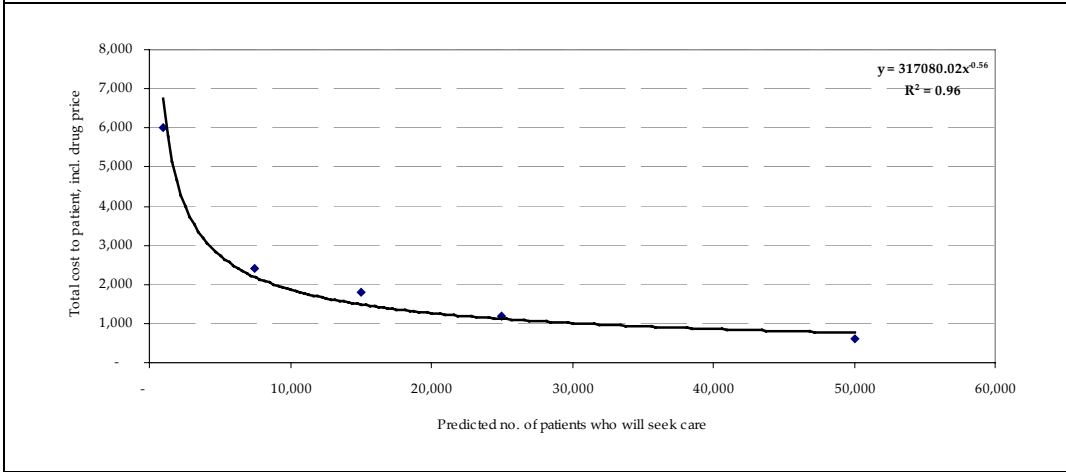
To illustrate the need for equitable pricing to go further and deeper, one particular country – Uganda, is taken as an example. In year 2000, five pharmaceutical companies participating in the UN-sponsored Accelerating Access Initiative (AAI) contracted McKinsey & Company to study the existing capacity for administering ARV therapy in Uganda and to recommend how to scale-up access over time. (N.B. This study was conducted at a time when the diagnostic and monitoring requirements for use of ARVs were much more stringent than current WHO guidelines).

In Uganda, patients pay the full cost of ARV therapy i.e. the drug price as well as the complementary care and monitoring costs. Consequently, McKinsey needed to project forward the theoretical price elasticity curve for ARV triple therapy, i.e. how many patients would demand treatment, given different price points. They constructed the curve by plotting the number of people who pay different amounts per month for rent and school fees. From these data, they plotted a best-fit curve (Figure 1) and used this to project the likely demand for highly active anti-retroviral therapy (HAART) at a given price to the patient (Figure 2) and the consequent infrastructure investment required.²⁰

¹⁹ Moses, Z. May 2002.

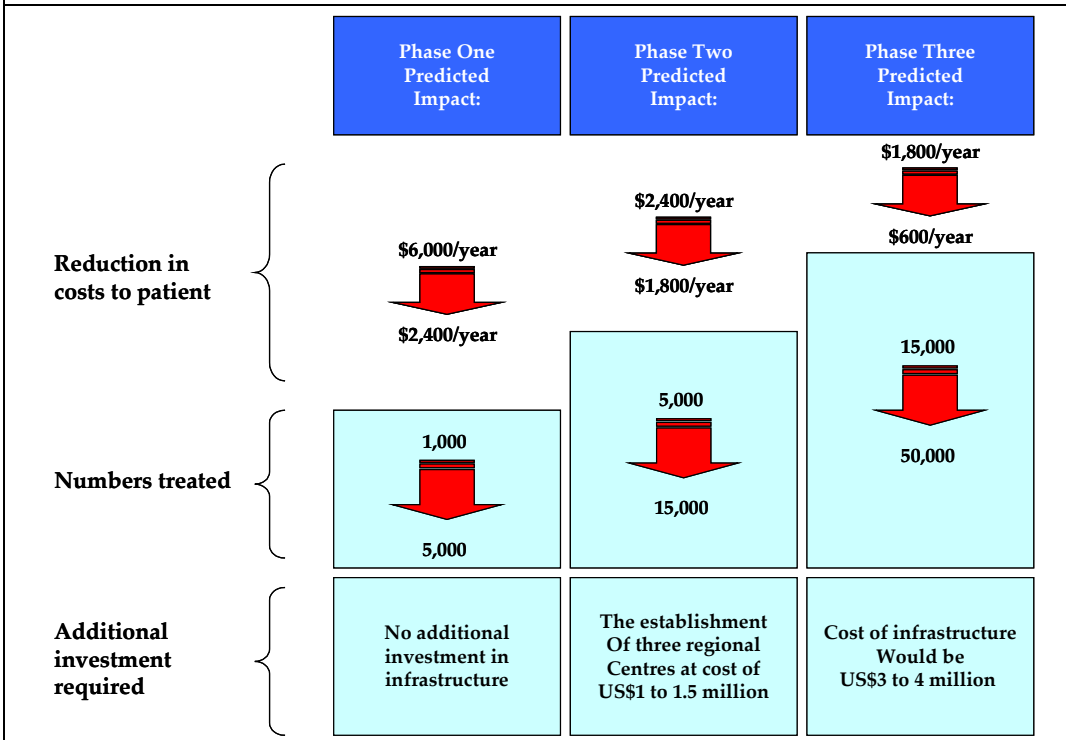
²⁰ Fine, D., Hazelwood, J., Hughes, D. Sulcas, A., 2001.

Figure 1: Price elasticity for ARV drugs in Uganda



The results of McKinsey's analysis are shown in the diagram below:

Figure 2: McKinsey & Company projections



Extrapolation from the McKinsey & Company study

For the purposes of this report, the McKinsey data have been manipulated to address two additional questions:

1. Given the price elasticity curve in Uganda, what percentage of patients currently needing ARV treatment would receive it if a similar public investment were required and a similar price elasticity curve held for various other developing countries?

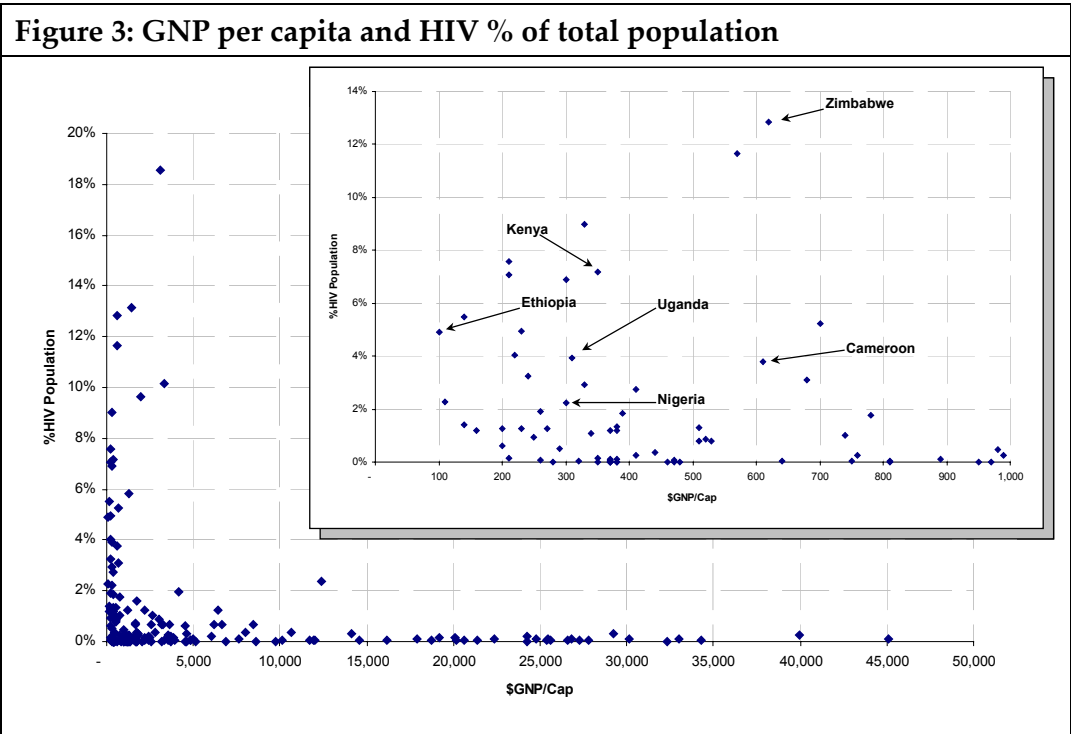
For this analysis the following assumptions have been made:

- Within country income distribution is approximately the same between Uganda and other countries
- Within country HIV/AIDS distribution is approximately the same between Uganda and other countries
- Health infrastructure/constraints are the same between Uganda and other countries
- Financing systems (being a mix of public and private user fees) are similar in all developing countries, therefore financing is a constraint.

Table 1 shows the results for a few selected countries. The results differ primarily according to two variables; the gross national product (GNP) per capita and the HIV rate as a percentage of the total population. In this model, Cameroon reaches a higher percentage of those in need of ARV treatment because its HIV rate as percentage of population (as shown in Figure 3) is relatively low and its GNP per capita relatively high.

Table 1: Predicted impact

	Phase One	Phase Two	Phase Three
Nigeria	1%	3%	9%
Kenya	2%	4%	13%
Cameroon	13%	27%	91%
Zimbabwe	5%	10%	33%
S. Africa	10%	19%	64%
Uganda	5%	9%	30%



2. To what price would ARV triple therapy need to fall in order to treat 100% of those in need in Uganda?

Figure 4 shows that in order for 100% of those needing treatment to be able to afford it, the monthly total cost of treatment should not exceed US\$ 30.61, or US\$ 376 annualized. Furthermore, assuming that the ARV drug cost is 65% of the total treatment cost²¹, the drug cost should not exceed US\$ 238 per year.

When the same question was asked for Ethiopia, which has a relatively higher HIV incidence as percentage of population and a lower GNP per capita, the results (Figure 5) show that the monthly cost of treatment should not exceed US\$ 8.43, or US\$ 101 annualized. Again, assuming that the ARV drug cost is 65% of the total treatment cost, it should not exceed US\$ 65 per year.

Conclusion

The analysis above is intended to be illustrative; limitations in the use of the data prevent it from being definitive. For example, the McKinsey data from which this analysis was constructed assumes that those who have HIV/AIDS are those at higher income levels. Thus, the US\$ 238 and US\$ 65 drug price requirements to treat 100% of sufferers in Uganda and Ethiopia respectively, are over-optimistic. Despite the limitations of the analysis, it illustrates that prices still need to fall significantly if increased access is to be achieved.

Currently, the lowest prices for ARV triple therapy from generic manufacturers are US\$ 200 - 300 per year. This is less than half the price of offers made by research-based companies participating in the UN Accelerating Access Initiative (AAI). Presumably, the generic drug manufacturers' prices could be reduced still further if the scale of production was higher.

Increased donor financing would also help Uganda meet its public health need. But even with the country's successful recent bid for US\$ 97 million over 3 years from the Global Fund for AIDS, Tuberculosis and Malaria (GFATM), approximately half of which is allocated towards HIV/AIDS, it is only possible to offer ARV treatment to two patients per province. Even with substantially increased donor financing, the need is so great in developing countries that further price reduction is needed to achieve substantial access.

²¹ This percentage was taken from 'Cost Estimates of HIV/AIDS commodity requirements 2000-2005', Options Consulting, Barraclough A, et al. (A study commissioned by UNAIDS)

Figure 4: Price/demand function for ARV treatment in Uganda

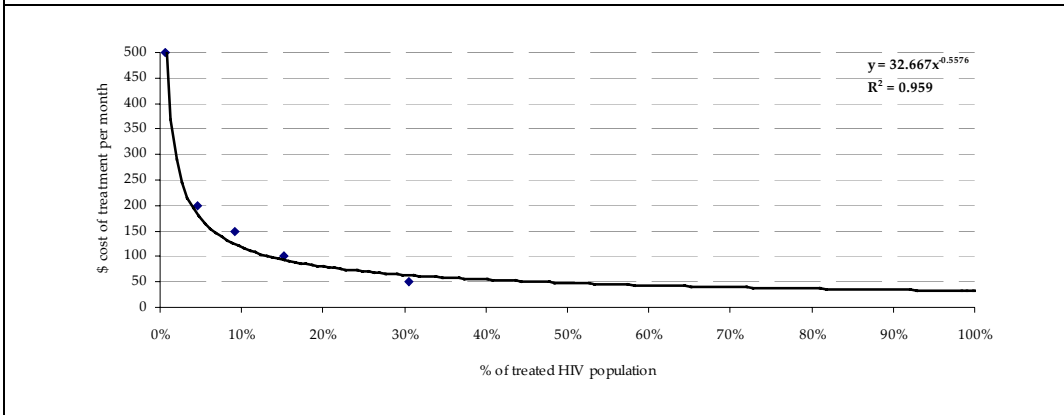
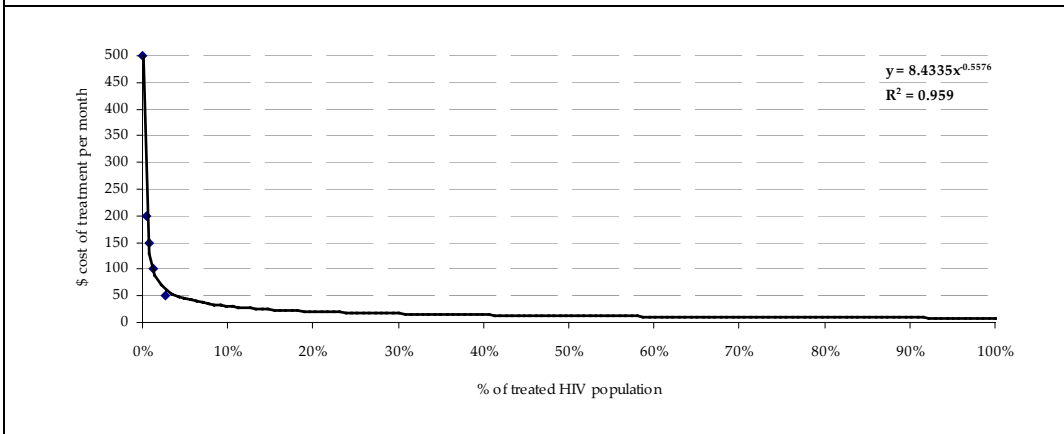


Figure 5: Price/demand function for ARV treatment in Ethiopia



²² This percentage was taken from 'Cost Estimates of HIV/AIDS commodity requirements 2000-2005', Options Consulting, Barraclough A, et al. (A study commissioned by UNAIDS)

Details on Each Mechanism

In the following sections of this report, a range of mechanisms is reviewed with the aim to highlight their successes and failures, and their potential and limitations in achieving equitable pricing.

Bulk purchasing and competitive tendering

Definitions

Bulk purchasing and competitive tendering can be thought of simply as purchasing in large volumes. However, the supply and demand situations in which this mechanism is employed vary, so a wider definition is required to allow for the idea of well-informed purchasing organizations which may pool demand, regularize treatment guidelines, negotiate with suppliers (e.g. for longer-term supply agreements or further discounts), and in some cases, make efforts to expand the supplier base.

National procurement programmes in many developing countries, lacking credible financing, sufficiently large demand, or professional procurement approaches may fall into the narrow definition. The price reductions they achieve are generally limited compared with international prices. Organizations such as the United Nations Population Fund (UNFPA; contraceptives), the Global Drug Facility (GDF; first-line TB drugs), the Green Light Committee (GLC; drugs for multi-drug resistant tuberculosis (MDR-TB), and the Global Alliance for Vaccines and Immunization (GAVI) fall into the wider definition of bulk purchasing, as do organizations such as the International Dispensary Association Foundation (IDA), Echo International Health Services Ltd and UNDP/Inter-Agency Procurement Services Office (IAPSO), which pool demand on behalf of smaller purchasers. Such organizations achieve reductions of up to 50% on generic drugs and up to 95% on single source and patented drugs compared with international prices.

Experiences with bulk purchasing and competitive tendering

Country or regional level procurement

There are a number of examples of regional bulk purchasing schemes. One is the Eastern Caribbean Drug Service, established to manage the procurement process on behalf of member countries of the Organisation of Eastern Caribbean States. This service achieved an average of 44% reduction in price during the first tender cycle. Member countries are charged 15% on each order to cover administrative costs of the service.

The reductions were achieved by incorporating a number of key features:

- A selective list
- Pooled quantities

- Competitive bidding
- Supplier monitoring and quality assurance
- Variable purchase quantities by group members
- Sole-source commitment
- A reliable payment mechanism.²³

The techniques used by regional procurement groups also affect price reductions achieved at country level. In a comparative study of Southern African countries²⁴, Botswana and Mozambique were found to achieve better prices than South Africa for TB drugs, despite having a fraction of South Africa's buying volume. The study also showed that a significant effect on prices is possible through a professional approach to the entire procurement function.

GDF

Established in 2001, the GDF pools the demands of countries and procures seven first-line tuberculosis drugs, all of which are off-patent. The purchasing function was awarded to IAPSO after competitive tender. IAPSO manages to achieve prices on average 30% lower than Management Sciences for Health (MSH)²⁵ prices and 50% lower than WHO prices. A course of first-line therapy for tuberculosis which had cost US\$ 20, now costs US\$ 10. This compares favourably with Brazilian prices (US\$ 60), where government protection of local industry results in higher prices from local producers. In terms of current impact, approximately 8% of people with TB globally receive their drugs via the GDF, although the goal is to reach 80% by 2005. In order to receive drugs through the GDF, countries must qualify by having an appropriate TB Directly Observed Treatment Short-Course (DOTS) programme.

GLC

The GLC was formed to address the needs of patients with multi-drug resistant TB (MDR TB) through DOTS-Plus projects supported by WHO. The added value of GLC is two-fold:

- It pools demand, structures partnerships and negotiates on behalf of countries in a situation where demand is small and extremely fragmented; by 2002, GLC managed to achieve 85 - 99% reductions on US prices of the 14 products procured for GLC-endorsed projects. Drugs for an entire 2-year course of therapy now cost US\$ 500 - 1500.

²³ Management Sciences for Health, *Managing Drug Supply*, second edition, page 172

²⁴ 'TB Bulk Purchasing Study' conducted by Johan van de Gronden, formerly with the International Procurement Agency (IPA), 1999.

²⁵ Management Sciences for Health: a D.C. based organisation that collects price information and makes this public via its Internet site. MSH prices are widely regarded as being the closest one gets to an international benchmark price.

- It provides technical assistance so that the quality of the MDR-TB treatment is improved; consequently demand for drugs has been stimulated and the delivery system for treatment improved.

GLC undertakes negotiations tailored to meet the market situation. Where a drug is single-source or patented, GLC takes a two-pronged approach, attempting to encourage more suppliers to enter the market²⁶ and to align the interests of the existing supplier with those of the programme. When working with monopoly suppliers, GLC communicates the financial commitment of the programme and demonstrates the current market size and market potential. It works with the supplier to help forecast demand and sometimes commits to large purchase volumes over longer time periods. Working with suppliers in this manner helps reduce their risk, should they need to invest in new capital equipment for manufacture.

In terms of impact, only 10 of 17 DOTS-Plus project applications have been approved to date. The approved projects are supported by governments, NGOs and, in one project, a private health centre. Approximately 2% of MDR TB patients (based on a conservative estimate from WHO) have received treatment through GLC. The major constraints are the lack of quality of the DOTS-Plus projects, as well as the drug costs, which are still prohibitive for LDC health budgets.

UNFPA

UNFPA provides an example of the wider definition of bulk purchasing described above - a well-informed purchaser who conducts negotiations and may also encourage other suppliers to enter the market. UNFPA takes a competitive approach when dealing with generic, multi-source drugs, but finds that a partnership approach works best with single-source or patented drugs. When dealing with the latter, UNFPA views the tender as the last stage in a long process. It realizes that pricing a product is risky for suppliers and therefore the more the purchaser can reduce the supplier's risk upfront, the more the potential for price reductions. Also, the more the risk is reduced in the longer term, the more suppliers will be willing to invest in larger batch sizes and changes in packaging.

A good example of the price reductions that can be achieved with a partnership-orientated bulk purchasing arrangement for single-source drugs can be found with oral contraceptives. Although UNFPA pays US\$ 0.17 for a generic oral contraceptives compared to a US market price of US\$ 0.30, it also pays a reduced price for single source oral contraceptives; US\$ 0.36 versus the US\$ 34 US market price.

GAVI

²⁶ This was done successfully, with capreomycin and cycloserine, both formerly exclusively produced by Eli Lilly. GLC induced competition and now there are three new manufacturers for each, with price reductions of 95% and 98% respectively. GLC was able to induce one new manufacturer for a third drug, called PAS, with a price reduction of 70%.

GAVI shares some common features with GLC and UNFPA in that, through its partner organizations, it works closely with the suppliers, attempting to align their interests with those of GAVI. This approach is necessary due to the limited number of vaccine suppliers. GAVI enhances the overall attractiveness of the vaccine market by:

- Stimulating demand in developing markets
- Strengthening vaccine delivery infrastructure
- Guaranteeing future purchasing of the product, at least in the short term.

A recent study commissioned by GAVI recommended that a project management team be set up, overseen by the GAVI Board, and made up of parties from UNICEF, WHO, and The Vaccine Fund. This team will look at all aspects of vaccine provision and will engage in:

- Demand forecasting on a country-by-country basis
- Timing of the introduction of new vaccines
- Reviewing the availability of finance
- A study of global supply as well as supply to UNICEF.

GAVI's approach aims to accomplish two things: through the project management team, to help reduce the manufacturer's risk of investing in research and production capacity that might otherwise end up idle, and to increase the bilateral dependence between GAVI and suppliers, thereby increasing GAVI's bargaining power with the suppliers.

Potential of bulk purchasing to achieve more equitable pricing: suppliers' costs and purchasers' bargaining power

From the supplier's perspective, engaging in bulk purchasing and competitive tendering can lower costs and reduce risks through:

- Reduced risk of capital equipment investment
- Economies of scale
- Reduced marketing and distribution costs
- Better production planning and inventory costs that come with improved demand forecasting.

However, it should not be assumed that these costs would automatically be passed on to the purchaser. The degree to which the cost savings are translated into reduced prices depends on the purchaser's bargaining power. This is a function of the competitiveness of the market and the purchaser's financial credibility, market knowledge, and purchasing size, for example. International organizations have a large role to play in helping developing country purchasers develop their bargaining

power, in the interest of achieving more equitable prices. However, competition for new, patented drugs, currently a significant driver of price reductions, will be reduced after 2006. This is likely to reduce significantly purchasers' bargaining power when they negotiate for these drugs.

With the advent of major financing initiatives like the GFATM, bulk purchasing could take on a larger dimension than currently practised. At present, GFATM does not facilitate bulk procurement on behalf of countries. However it is currently considering mechanisms to facilitate the pooling of demand of countries with successful bids.

Voluntary tiered pricing agreements

Definition

Voluntary tiered pricing agreements can be defined as agreements where prices are based on the supplier's charity, desire for favourable public relations or other criteria not immediately related to market forces. Thus they can be distinguished from bulk purchasing agreements where prices are negotiated between supplier and purchaser based on market criteria.

Two examples of voluntary tiered pricing agreements are described in this section:

- Agreements between companies and countries for supply of ARVs; some of these agreements are through AAI and some are negotiated directly between pharmaceutical companies and developing country governments.
- The agreement between Novartis and developing countries for the equitably-priced antimalarial, Coartem, within the partnership established with WHO.

Experience with this mechanism

AAI

In 1998, the Drug Access Initiative was launched by the United Nations Joint Programme on HIV/AIDS (UNAIDS) in partnership with five research-based pharmaceutical companies (Boehringer Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline, Merck & Co and Hoffmann-La Roche²⁷). At the end of 2001, responsibility for this initiative, renamed AAI, was transferred to WHO. The intention of AAI is to provide developing countries with access to ARV medicines at the lowest possible prices and to technical support for the implementation of national access programmes for ARV treatment.

The launch of the UNAIDS initiative resulted in participating companies reducing their prices for triple ARV therapy from US\$ 12 000 to US\$ 7000 per year per patient. Around the time when AAI moved to WHO, negotiations resulted in further reductions to US\$ 1200. At this point, the Indian generics industry entered the scene and offered the same combination for US\$ 600. When Côte d'Ivoire announced that it was ready to accept the offer from the Indian manufacturer Cipla, Bristol-Myers Squibb and Merck made a further price reduction to US\$ 800.

Currently, four Indian generic companies²⁸ offer triple combination therapy at less than half of the lowest price offered by companies participating in AAI. As of April 2002, the lowest generic price for triple combination therapy was US\$ 209.²⁹

²⁷ Abbott has now joined, so there are now 6 participating companies

²⁸ Cipla, Hetero, Aurobindo, Ranbaxy

Since May 2000, 80 countries have expressed interest in AAI. In 39 of these, national plans to improve access to care have been, or are being, developed. These plans have been used as a framework for dialogue with the pharmaceutical companies, and consequently, 19 countries³⁰ have concluded agreements for the supply of ARV drugs with individual companies participating in the AAI.³¹

Despite this interest at country level, the actual number of patients receiving ARVs through AAI remains disappointingly low - less than 1% of the HIV-positive population currently needing ARV treatment³². As of December 2001, about 27 000 people have gained access to ARV therapy in the 19 participating countries. The only numbers available as of March 2002 are for Africa and are for drugs supplied by the participating pharmaceutical companies both within and outside the AAI framework. These show that about 35 000 people have access. UNAIDS data also reveal that the proportion of patients on triple combination therapy increased from one third to nearly two thirds of patients receiving any ARV therapy through AAI.

The following factors have constrained the impact of AAI:

- High price of ARVs: Despite major reductions in prices, the ARVs offered through the six²⁴ AAI participating companies are still more than double the prices offered by generic companies; the cost of ARV treatment still exceeds the annual GDP per capita of many LDCs. Some have argued that middle-income countries have benefited most from the AAI price reductions achieved to date because of their lower incidence of HIV infection, higher per capita incomes, and therefore ability to take advantage of the price cuts.³³
- High price of diagnostic test kits and reagents, many of which are branded, needed for biological follow-up.
- Weak health systems and infrastructure: The condition placed on the LDCs by patent holder/suppliers that they must have capacity to use ARVs rationally and control their distribution would theoretically limit the numbers accessing treatment. However, in reality many of the countries have under-utilized health system capacity that could be used to expand treatment today.

²⁹ Médecins sans Frontières (2002) "Untangling the Web of Price Reductions: A Pricing Guide for the Purchase of ARVs for Developing Countries", MSF, Geneva.

³⁰ Barbados, Benin, Burkina Faso, Burundi, Cameroon, Chile, Republic of Congo, Cote d'Ivoire, Gabon, Honduras, Jamaica, Mali, Morocco, Romania, Rwanda, Senegal, Trinidad and Tobago, Uganda, and Ukraine.

³¹ UNAIDS, Accelerating Access Initiative, Widening access to care and support for people living with HIV/AIDS. Progress report. June 2002.

³² Estimated to be approximately 15- 20% of those infected with HIV. WHO conservatively estimates that in 2002, around 6 million people in developing countries are in need of ARV therapy. (UNAIDS, Accelerating Access Initiative, Widening access to care and support for people living with HIV/AIDS. Progress report, June 2002.)

³³ For example, with an HIV infection rate of 1.5%, universal access in Chile would cost 0.5% of GDP, compared with 17% in some sub-Saharan African countries).

While investments in health and social service infrastructure are certainly needed, health systems constraints are likely to be more of a limiting factor later if there are attempts to increase ARV access on a much larger scale³⁴.

- Lack of standardization in the dialogue between countries and pharmaceutical companies after plan of action development (especially lack of standard prices and conditions). Negotiations and informal discussions have slowed the process of implementation.
- Technical support needs exceeding supply of available personnel to offer technical support³⁵.
- Limited demand for AAI in some countries possibly because generic drugs are increasingly available as an alternative: Côte d'Ivoire, Jamaica, Nigeria and Uganda are some examples of countries taking advantage of generic supply. Uganda's largest ARV care facility offers both generic and branded drugs.
- Approximately half of one patent holder's 80+ agreements to supply ARVs at equitable prices are outside the AAI framework. This indicates that some groups prefer to approach the patent holder directly. Approximately 30 - 40% of this same patent holder's sales are to customers outside the public sector such as employers and NGOs; it is believed that these groups are less likely to approach industry through a UN framework.

Coartem

Coartem is an antimalarial licensed by Novartis from China, which was conceived as an equitably-priced product from early stages of its development. It has been registered under two different brand names with different prices and different packaging: Coartem in poorer, malaria-endemic countries and Riamet in wealthier, non-endemic markets. In wealthy markets, a course of Riamet costs US\$ 40, whereas as Coartem, it is available in the private sector of malaria-endemic developing countries for US\$ 12 and in a paediatric package at around US\$ 8. A third category of product is available only through WHO and is for use only in the public sector (including approved not-for-profit private sector facilities) of malaria-endemic developing countries. This product costs US\$ 0.9 - 1.90 for paediatric usage, depending on the size of the child. The adult dose costs US\$ 2.4.

Novartis always recognized that this product would have limited commercial potential and this made it ideal for the company's first experiment in working with China, where it has since become one of largest multinationals in operation. The

³⁴ UNAIDS, Accelerating Access Initiative, Widening access to care and support for people living with HIV/AIDS. Progress report. June 2002.

³⁵ Harmonisation of care delivery would facilitate ability to offer integrated technical support and would allow resources stretch further.

capacity and relationships built through the development of Coartem are now being used for other products Novartis manufactures and markets in China.

Coartem has only been introduced on a pilot basis to date. In South Africa, where 24 000 patients used the drug in 2001, there was an 80% reduction in the number of malaria cases reported over the year and hospital admissions for malaria fell from 40 000 to 10 000 between 2000 and 2001. However, some of these dramatic results are believed to be due to the introduction of bed nets impregnated with pyrethroids and insecticide spraying, in addition to Coartem.³⁶

Likely constraints to the voluntary tiered pricing agreement for Coartem having greater impact in future are:

- The fact that the substantially reduced price is only available through the public sector, whereas it has been well documented that patients access their malaria medications primarily through the private sector in developing countries.
- Given that the incentive and feasibility for leakage from poor to wealthy markets *within* developing countries is high for this product, there is a risk that product will be diverted from public sector facilities (where it is free or highly subsidised) to private pharmacies (where it will likely be marked up in price).

However, from Novartis's perspective, there are more benefits than costs to this deal and these are summarised in Box 1. In the case of Coartem, WHO has worked very closely with Novartis and has a good understanding of the benefits and costs of the partnership from the company's perspective. The contributions WHO has made to the partnership have been very transparent and WHO has increased its bargaining power as a result.

³⁶ Dr. P Olliaro, World Health Organization, personal communication.

Box 1: Summary of costs and benefits to Novartis in the Coartem voluntary tiered pricing agreement

Costs	Benefits
Transaction costs (costs of managing the business relationship) of working with WHO and with each country.	Spill-over benefits in terms of capacity-building and relationships that facilitated market entry for other products manufactured and/or sold in China
Opportunity costs (foregone benefit of other business opportunities) of tying up scientific and management time with a product having limited commercial potential.	Public relations: this product features in the corporate social responsibility section of Novartis’s company literature.
Potentially extra costs in developing differentiated packaging. (In fact, WHO specifically asked Novartis to find a way to achieve different packaging without any additional cost, and Novartis was successful in this.)	Branding (indirectly) because the equitably-priced product given through the public sector can help build demand for the more expensive product that is sold in the private sector in malaria-endemic countries.
Potential risk of committing capital to production capacity, but Novartis has minimized this risk by investing in a modular fashion.	<p>Support from WHO with:</p> <ul style="list-style-type: none"> • Expert reviews (decreases scientific risk); • Partial funding of Phase IV trials to determine appropriate dosages; • Skill transfer with packaging; • Global forecasting; • A credit fund to help developing countries pay for Coartem; • In-country infrastructure requirements to collect pharmacovigilance and post-marketing - surveillance data; • Monitoring leakage (on a sample basis, through a survey of pharmacies); • Application to the WHO Model List of Essential Drugs. (Such a listing helps attract public funds.)

Voluntary tiered pricing negotiations: conclusions

In order to be able to fully understand the incentives operating in each of these partnerships, it would be necessary to deconstruct each on a company-by-company, drug-by-drug and country-by-country basis. Manufacturing capacities and benefits and costs to each party differ and thus few general conclusions can be drawn. However, when the examples of voluntary tiered pricing agreements described above are reviewed, some concerns become apparent, as summarized below.

Transparency

In these agreements, pharmaceutical companies negotiate directly with governments or other approved health service providers on a country-by-country basis, each in an independent way, without any supervision by UN agencies. Governments are usually required to keep these agreements confidential and all media communications are handled by the company. This means that the AAI label is attached to, and serves as a guarantee for, negotiations over which WHO and UNAIDS have little information and power.

There have been allegations that companies are using these agreements to leverage other goals. For example, the contract with Bristol-Myers Squibb is structured to appear like a drug donation³⁷; however the company says that it is not applying for tax credit³⁸. Some agreements have also been restricted to very specific drugs, quantities, countries, distribution sectors and medical settings; they have also been tied, allegedly, to commitments by developing country governments to adhere to IP requirements in excess of those stipulated in the TRIPS agreement.

Distortions

These agreements do not follow the WTO trend to remove restrictive practices and many organizations allege that they distort the competitive environment, buying a monopoly for the participating companies at the expense of generic manufacturers. Similarly, there is an issue of distorting national procurement networks. For years, WHO has been promoting the creation of national central purchasing offices, which work on the basis of transparent public tender. AAI however, supports the signing of contracts between Ministries of Health and pharmaceutical companies, resulting in a parallel procurement system, a lack of competitive bidding and transparency as regards prices.

Transaction costs

The costs of managing AAI agreements are high for recipient countries (developing an action plan; going through qualification), for the international organizations

³⁷ The recipient gets the drug free but pays a \$20 'administration fee' per bottle.

³⁸ Bob Lefebvre, personal communication.

managing the AAI programme (providing technical assistance; evaluating and approving countries for participation), and for the private suppliers (negotiating these agreements on a country-by-country basis). The prices through AAI (still higher than generic prices), and access (AAI currently reaches less than 1% of the HIV/AIDS population needing treatment) would need to be improved in order to justify these transaction costs.

Price reductions and impact on access

The price reductions, access impact, disease and product scope for voluntary tiered pricing agreements, AAI in particular, have been limited. The fact is that substantial price differences still exist between branded and generic products (indicating that branded products might not be priced at marginal cost) and these medicines are still unaffordable. In terms of disease and product scope, tiered pricing offers have been rare for medicines other than those for malaria and HIV/AIDS. In terms of access impact, the sheer number of patients receiving medicines through AAI has been extremely low - less than 1% of the patients needing treatment.

Incentives

An overall concern underlying many of the above points relates to incentives inherent in the AAI structure and the consequent potential for impact enabled by these incentives. Unlike GAVI and the GLC, the AAI does not work with any organizations to pool demand or negotiate on behalf of member countries. GAVI and GLC³⁹ rely more on market mechanisms – researching the benefits and costs of their suppliers and how they can create deals that are beneficial to each party. The same can be said of the partnership between WHO and Novartis; there is a fair degree of bilateral dependence, thus both sides had power and Novartis consequently had the incentive to make many investments specific to the agreement, such as differential packaging. But as AAI is currently structured, the purchaser (LDC government) does not gain any bargaining power over the suppliers. There is no pooling of demand. Pricing is left to the discretion of the innovator pharmaceutical companies. The only possible leverage that LDCs have is generic competition, but the use of this as a bargaining tool, after 2006, will be limited to older, off-patent drugs. It is suggested that international organizations have an important role to play in structuring voluntary tiered pricing agreements in ways that increase the bargaining power of LDCs.

Sustainability

Concerns about the sustainability of AAI efforts compound concerns about AAI's incentive structure. Many allege that the factors that have led to agreements such as AAI include threats of compulsory licenses, extraordinary and unsustainable NGO and UN pressures, and the existence of a competitive market for ARVs (also

³⁹ In terms of price and access impact, it can also be said that the cocktail of drugs needed to treat MDR TB remains unaffordable to many LDC governments, and that the percentage of patients treated very small. However, the difference between MDR TB and HIV/AIDS is that the market for MDR TB in developing countries is much smaller and more fragmented than that of the HIV/AIDS market, so one would expect a greater challenge in achieving price reductions and access impact.

unsustainable, at least for new, patented ARVs, after 2006). The fact that Roche, one of the AAI participants, has so far refused to grant price discounts on its HIV products for which there are no generic competitors, supports this latter point, as do findings from large scale studies.⁴⁰ If competitive market pressure and public/media interest eventually decrease, and in the absence of more sustainable, market-based incentive structures, AAI type agreements may fail to live up to their potential.

Benefits of AAI

Despite concerns about transparency, sustainability, distortions, and transaction costs relative to price reductions and impact, the AAI programme has provided a few benefits. The quality of ARV therapy among the beneficiaries seems to have improved (i.e. more patients are now taking triple combination therapy). Also, many health workers have gained experience with use of ARVs for the first time through AAI, offering potential for greater impact if only the medicines became more affordable.⁴¹ The technical support provided by UN agencies to developing country governments is a further benefit provided by the AAI programme. These are potentially very important benefits in the context of the weakest health systems in the poorest countries, where the dangers of a large volume of ARVs irresponsibly used could be grave.

⁴⁰ In a study of drug prices for ten essential AIDS drugs in eight countries, Perez-Casas of Medicines Sans Frontieres (MSF) found that the price of AIDS drugs was 82% less than the US price in the developing countries with access to generic copies of on-patent drugs. According to Perez-Casas, 'The presence or absence of generic competition in the market is a key determinant of pricing levels.' Also, a recent study in the US found that prices fall when generic competition enters the market but at least five generic competitors are necessary to push prices down to a minimum. (Reiffen, D. & Ward, M. (2002) "*Generic Drug Industry Dynamics*".)

⁴¹ UNAIDS, Accelerating Access Initiative, Widening access to care and support for people living with HIV/AIDS. Progress report, June 2002.

Improving bulk purchasing and voluntary tiered pricing agreements

What economic theory⁴² tells us about structuring business relationships

Contracts and economic institutions should be structured in a way that minimize ordinary production costs (such as land, labour capital) as well as the costs of administering an ongoing business relationship. The latter are real economic costs, referred to as transaction costs, and include the costs of negotiating and writing contracts, monitoring contract performance, costs of enforcing contractual promises, and costs associated with breaches of contractual promises.

Some characteristics of transactions tend to raise transaction costs; these include the extent to which the transaction is characterized by uncertainty, complexity, information asymmetries and the extent to which the transaction requires one or both parties to make transaction-specific (idiosyncratic) sunk investments. Where the transaction has any of these characteristics, governance structures such as vertical integration or other partnership structures that align incentives and increase bilateral dependency should be sought.

Application to the examples in this report

When a purchaser is working with a supplier in a situation where there is sufficient therapeutic competition for a drug, information asymmetries are low (there are competitors who will offer alternative prices and therapeutic options), and the purchaser and supplier have relatively equal bargaining power. The degree of competition and information parity makes a 'market' exchange type of relationship with the supplier efficient.

In contrast, when the purchaser is contracting with a supplier of single-source or patented drugs, information asymmetries are higher (the purchaser is less able to determine what is the marginal cost of producing the product since he/she cannot get any comparative price information). The supplier consequently has more bargaining power, based on his/her monopoly position. The purchaser should therefore seek to adapt his way of working with the supplier in line with the characteristics of the relationship and in order to increase his bargaining power.

Specific tactics that help a purchaser gain bargaining power within single-source/patented contexts include:

- Work to increase the supplier base (as in the GLC example from the previous section)

⁴² See Williamson; Joskow; Hart and Moore; Klein, Crawford and Alchian

- Investigate the situation of the supplier, with the goal to reduce information asymmetries. This investigation would ideally reveal the supplier's marginal production cost, the benefits and costs of the relationship from the supplier firm's perspective as well as the benefits and costs of his alternative strategies. Ideally, this would involve a very detailed study of the industry structure as well as the value chain within the specific firm.⁴³ The purchaser should look for ways that he can create value for the supplier, and with the goal to appropriate some of that value creation in the form of price reductions.
- Attempt to create a situation of bilateral dependence, rather than the unilateral dependence that currently exists. One way of doing this with monopoly suppliers, as discussed previously, is via increasing the supplier's dependency on the purchaser, or creating 'sticky' transactions. Bilateral dependency should be the goal when a purchaser is working with a single or few suppliers and is therefore already unilaterally dependent. Bilateral dependence (stickiness) is increased when, for example, suppliers agree to invest in product development and packaging specific to the contractual relationship (as in the Coartem example) or when suppliers, having confidence in the demand forecasts and availability of finance, invest in capital equipment to scale-up manufacturing (GLC example). Bilateral dependence can also be achieved when the purchaser and supplier commit to large volume purchases, or increase the frequency or duration of their contract. The earlier examples of how UNFPA, GAVI and the GLC work with suppliers show that these methods are indeed effective approaches in monopoly/oligopoly supply situations.
- Providing assistance which is valuable to the supplier in the form of public funding or technical expertise to aid in product development (Coartem example).

The way AAI is structured shows a lack of adherence to economic theory. AAI countries sign Memorandums of Understanding with the suppliers of patented or single-source drugs in situations where they have no bargaining power. The bargaining power of these countries would be higher if either they tried to establish a more competitive approach, through fostering legitimate⁴⁴ generic supply, and/or if they could improve their bargaining power through creating a greater degree of bilateral dependence with monopoly suppliers. The latter could be achieved if the demands of the LDCs were pooled, and if companies competed for the pooled demand and for long-term contracts to supply product.

⁴³ See Michael Porter's 'Competitive Advantage', 1985, chapters 1&2 for more detail on the firm value chain concept and structural analysis of industries.

⁴⁴ Generic supply is legitimate where the patent has expired or in situations where the generic product is produced in a country not yet required to implement patent law under TRIPS and the product is imported by a country not yet required to implement patent law under TRIPS.

Operational tactics for managing suppliers

The previous section discussed how adapting the type of contracting structure (or way of working with suppliers) to the transaction characteristics (particularly, the degree of uncertainty and supply/demand context) increases the chance that the following objectives can be met:

- Motivating each side to make efficient investments in resources and effort
- Promoting efficient decision-making, which enables achievement of public health objectives
- Minimizing the potential for either party to behave opportunistically
- Allowing the opportunity for adaptation should circumstances change.

At the operational level, there are certain tactics that can be employed to improve the bargaining power of purchasers, regardless of whether a competitively-or a monopoly-supplied product is being sourced. For example, it is commonly believed that the volume of products procured is the most significant driver of price discounts achieved in bulk purchasing. In fact, volume gets more attention than it should.⁴⁵ One comparative study of procurement practices and prices achieved in country level procurement programmes of 10 Southern African countries proved this point.⁴⁶ The study found a lack of positive correlation between buying volume and low price levels of anti-tuberculosis drugs; rather, low price levels seemed to be a result of proper, open international bidding procedures. High prices were a result of poor specifications, supplier selection method and restrictive competitive practices, bad planning, donor dependence and temporary funding shortages (the latter two often related). The report concluded, 'If we really want to achieve substantial improvements, a broader look on the whole procurement function is inevitable, including the underlying policies, the way we assess our needs and the manner in which we specify.' Thus, specific tactics that may enable a purchaser to improve bargaining power within both competitive and monopoly supply environments include:

- Providing credible financing, or good payment terms in general
- Pooling demand (this lowers marketing, distribution, and transaction costs for suppliers while simultaneously increasing the bargaining leverage of the purchaser)
- Improving quality assurance capacity (or participating in a demand pool that has upgraded capacity)

⁴⁵ The opinion of both Johan A. van de Gronden, Director, UNDP/IAPSO as well as Henk den Besten, Director, IDA, personal communication

⁴⁶ 'TB Bulk Purchasing Study' conducted by Johan van de Gronden, formerly with the International Procurement Agency (IPA), 1999.

- Improving market knowledge (e.g. when WHO or others compile price or quality assurance information, this reduces information asymmetries)
- Engaging in professional procurement practice: good knowledge of the market, good choice of products, good generic specification, good pre-qualification criteria.

Summary

A variety of contractual strategies can be used by purchasers in an attempt to create efficient transactions.⁴⁸ The most efficient situation from a neo-classical⁴⁹ as well as a transaction cost⁵⁰ viewpoint is that of competition. In a competitive environment, the information available to purchasers on competitors' prices increases the purchasers' bargaining power, facilitating pricing that is closer to the marginal cost of production.

Where competition is not possible, the purchaser must research and understand the incentives of the suppliers, thereby raising transaction costs, but with the goal to prevent subsequent problems in the relationship. Understanding the costs and benefits of the partner is essential in order to know how to align the incentives of both parties and to prevent subsequent opportunism on the part of the supplier, who has greater bargaining power. Strategies that seek to create 'sticky' relationships, or relationships where each party is dependent on the other, may help to align incentives and equalize bargaining power in this environment.

At the operational level, there are also certain tactics that can be employed to improve the bargaining power of purchasers, regardless of whether a competitively- or a monopoly-supplied product is being sourced.

⁴⁷ See Michael Porter's 'Competitive Advantage', 1985, chapters 1&2 for more detail on the firm value chain concept and structural analysis of industries.

⁴⁸ We can define efficient transactions here as transactions that achieve pricing as close to the marginal cost of production as possible, while minimising transaction costs and maintaining incentives for each party to continue with the relationship over the long term.

⁴⁹ That is, achieving prices near to production costs in order to maximise health impact

⁵⁰ That is, the costs involved in constructing and managing the business relationship

Voluntary licensing

Description of the mechanism

Voluntary licensing, in the context of equitable pricing, refers to the situation whereby an innovator pharmaceutical company licenses a patent, for purposes of local production, to a third party company in a lesser developed country, with any of the following goals:

- To reduce costs
- To pass the savings on to the consumer in the form of an equitably-priced product
- To aid in market segmentation through a differential product registration and marketing mix⁵¹ compared to that used in a wealthier market
- To facilitate technology transfer and upgrading of local manufacturing capacity
- To promote the initiative as an example of the company's corporate social responsibility.

According to Article 66.2 of the TRIPS⁵² Agreement, developed countries have an obligation to provide incentives that promote and encourage technology transfer to enterprises and institutions in LDCs. Theoretically, this obligation means that developed country governments would provide incentives for patent holders to engage in local production and perhaps, voluntary licensing. However, LDCs have repeatedly raised concerns at the Council for TRIPS about the lack of effective action by developed countries to comply with this article. Paragraph 7 of the Doha Declaration in TRIPS and Public Health reaffirmed the commitment of developed-country members to Article 66.2. Paragraph 11.2 of the Implementation Decision adopted on November 14th 2001 sets out a mechanism for monitoring whether these incentives are put into place.⁵³ However, it remains to be seen to what degree this mechanism will be effective in holding developed countries accountable for achieving their obligation.

Feasibility of voluntary licensing

In fact, innovator companies engage in local manufacturing in developing countries all the time, but with goals which may differ from those outlined above, i.e. to:

⁵¹ The marketing mix refers to the price, product characteristics (product attributes, packaging), and distribution channel and promotion/marketing strategy.

⁵² The Agreement on Trade-Related Aspects of Intellectual Property

⁵³ Correa, C. Implications of the Doha Declaration on the TRIPS agreement and public health, June 2002, WHO publication.

- Obtain cost savings from the use of local labour, local materials, or adherence to less stringent regulatory regimes, but with the goal to appropriate the gains from those savings for shareholders, rather than customers
- Take advantage of 'perks', such as grants or tax relief, offered for local production by developing country governments
- Facilitate easier/wider product reimbursements, or easier local product registration
- Have the potential for shorter cycle times, faster response to marketing requirements, less inventory and lower overhead and logistics
- Have the potential for tax management via healthy margins on the internal transfer price at which primary materials are 'sold' to countries with relatively higher tax environments
- Establish a market presence and brand reputation in a market that is perceived to have rapidly expanding demand and good future potential.

When an innovator company works with a domestic pharmaceutical company, this may involve licensing patents to a third party. However, in countries where local production capacity is sufficient to produce higher technology drugs, and where local demand is rapidly growing, the more common model is for the innovator to approach the market through locally-owned affiliates.

However, it is not always the case that producing locally is less expensive. This depends on such factors as: which part of the production occurs locally (primary or active ingredient manufacture⁵⁴; secondary; or tertiary); the relative capital to labour ratio (production requiring higher fixed costs may be less expensive if centralized to capture economies of scale); and the level of investment needed to raise the quality/technology level of the local manufacturer. Furthermore, for voluntary licensing to contribute to equitable pricing, cost savings achieved in producing locally should be passed on to consumers, rather than appropriated for investors. This is problematic since it relies on charity. The idea that patent owners have an incentive to upgrade the manufacturing and technology capacity of third party companies in developing countries for purposes of passing savings to consumers also assumes a charitable tendency. In fact, the opposite is likely to be true; companies making product or process advances have every incentive to keep these proprietary. Finally, the idea that innovator companies have the incentive to create lower-priced competition for the higher-priced, branded products with which they usually 'skim' the market in these countries also belies the way they usually approach lower income markets.

⁵⁴ The primary, active ingredient stage is the most scale intensive stage, and is the one most likely to be centralised. The minimum efficient scale for secondary (e.g. pill pressing) and tertiary (packaging) production varies by product, but is usually substantially less than that of active ingredient production.

Variations on the voluntary licensing theme

A variation on the voluntary licensing theme put forward by the Commission for Macroeconomics and Health, proposes that these licenses should be awarded on a competitive basis. This is not the way innovator companies conduct business at present and there are obvious reasons why patent holders would oppose such an idea. Even if they did agree, in order for the mechanism to work, there must be sufficient demand in developing countries to generate sufficient competition for the licenses. This may not be the case. First, companies that are capable of high technology work in countries that are not required to implement patent protection until 2006 are not required to have a license to produce copies of patented products until then. This limits demand for licenses at present. Second, there are only a few developing countries with several companies capable of high technology work, so the required level of competitiveness after 2006, will only be possible in a few countries.

In another variation to the voluntary licensing idea⁵⁵ licenses would be awarded on a competitive basis not just for local manufacture, but internationally. Thus a firm in Canada, for example, might be licensed by the patent holder to manufacture medicines for export to developing countries. This option gets around many of the practical and economic hurdles of licensing to a developing country producer. However, the question remains as to whether there are sufficient incentives for innovator firms to engage in such licensing for important products on a wide-scale basis. For important products, patent holders may prefer not to license generic manufacturers based in developed countries, preferring to keep proprietary products or processes secret.

Experience with this mechanism

Despite concerns about the feasibility of voluntary licensing outlined above, some examples can be found. In early 2001, the Indian generic manufacturer, Cipla, approached the five companies involved in AAI, seeking voluntary licenses to manufacture patented products. All the patent owners refused⁶¹ and Cipla went on

⁵⁵ Friedman, M., den Besten, H. Attaran, A.2003.

⁵⁶ These objectives being cost savings, if applicable, differential product registration and differential marketing mix, as well as raising domestic production capacity.

⁵⁷ Lanjouw, J., Intellectual Property and the Availability of Pharmaceuticals in Poor Countries. Forthcoming in: Innovation Policy and the Economy. Vol 3, 2002. April 9, 2002 draft version.

⁵⁸ The Agreement on Trade-Related Aspects of Intellectual Property

⁵⁹ Correa, C. Implications of the Doha Declaration on the TRIPS agreement and public health, June 2002, WHO publication.

⁶⁰ Friedman, M., den Besten, H. Attaran, A.2003.

⁶¹ Charlish, P., The Provision of Drugs to Developing Countries: Implications of Global Property Rights. Scrip Report. 21 November 2001.

to produce generic ARVs (as described previously). However, there are some positive examples of voluntary licensing.

The first example of an arrangement that worked like a voluntary license occurred when Hetero, an Indian manufacturer, struck a deal with Aspen Pharmacare in South Africa, to supply active ingredients and the technology for the manufacture of finished products of Bristol-Myers Squibb's ARVs stavudine and didanosine. Aspen Pharmacare subsequently received an undertaking from Bristol-Myers Squibb that it would not sue the South African company if it produced copies of its ARVs for distribution in South Africa and 47 other countries in sub-Saharan Africa. This was tantamount to granting Aspen a voluntary license to produce these drugs⁶².

There are three subsequent examples of the use of voluntary licensing as a mechanism to achieve equitable pricing. Boehringer Ingelheim licensed Aspen Pharmacare to produce nevirapine and GlaxoSmithKline agreed to license three ARVs to Aspen Pharmacare. Aspen will be allowed to import active ingredient from the producer of its choice, engage in secondary and tertiary manufacturing in country under GlaxoSmithKline's license, and sell only to approved NGOs and government. Aspen must pay 30%⁶³ royalties to a local NGO, rather than to GlaxoSmithKline.

When asked why GlaxoSmithKline did not engage in this kind of arrangement more routinely, the answers were (pers comm.) that there have not been many requests to GlaxoSmithKline for licenses and that local producers must be able to produce the drug for less than GlaxoSmithKline. These conditions are not often met, according to one of the company's representatives⁶⁴.

Another example of voluntary licensing was announced recently and is the first example of a non-exclusive license being offered with the aim to provide product to several developing countries. Pharmacia, in partnership with IDA, will grant non-exclusive licenses for an ARV, delavirdine, to generic manufacturers who agree to produce and supply the medicine to countries with a per capita Gross National Income of less than US\$ 1200 or an HIV infection rate of more than 1 percent.⁶⁵ The non-exclusivity and multiple country targets of this offer provide more potential than previous voluntary licensing examples; however, delavirdine's importance in HIV treatment is relatively less than other medicines on which Pharmacia and its parent company, Pfizer, own the patents.

⁶² The Provision of Drugs to Developing Countries, Scrip reports, Strategic Management Series, by Peter Charlish, 21 November 2001.

⁶³ This is a relatively high royalty rate, when compared with what has historically been used as a royalty rate on pharmaceuticals for compulsory licensing. Canada applied 4% across the board, for example, when compulsory licensing was used routinely in that country.

⁶⁴ An example was given of a request recently turned down due to the fact that production by the third party firm, in Zimbabwe, would have been more expensive than GSK could achieve via centralised production. (Chris Strutt, GSK, personal communication)

⁶⁵ Pharmacia Press Release, January 24, 2003

To conclude, all of the examples of voluntary licensing to date offer fairly limited scope in increasing access to medicines, i.e. the drug's importance in disease treatment, the target population, and/or the opportunity for multiple licensees to participate have been limited.

Future prospects

Despite the problems, voluntary licensing does have some prospects. First, after 2006, when current producer countries have implemented patent protection, there may be more demand for licenses due to new regulatory constraints as well as the need to gain experience with genomics-based technologies. Second, expanding the more narrow 'voluntary licensing' idea to a more wide-ranging 'local production' idea could theoretically accomplish many of the same objectives as licensing to a third party.⁶⁶ It has the advantage of being more in line with the way that patent holders usually conduct their business in developing countries, i.e. through locally-owned affiliates with sufficient technology capacity allowing for local production.

As an example, the anti-ulcer drug, Zantac, was sold by the patent holder, GlaxoSmithKline, at about US\$ 2.80 for 300mg in the USA at the time of patent expiry in early 1996. At the same time, GlaxoSmithKline's local affiliate in India sold the same product, under the brand name Zintec, for less than US\$ 0.6 in this very competitive market.⁶⁷ It is not known to what degree the product was manufactured locally, nor to what degree technology was transferred, but this example shows at least that the market segmentation objective can just as easily be accomplished through locally-owned affiliates as through third party 'licensees.'

Levers for governments and international organizations

This mechanism sits strangely with the others discussed in this report because it is part health policy and part industrial policy.⁶⁸ If voluntary licensing is conceived as truly voluntary, then governments and international organizations have no direct ability to implement the mechanism; they can only offer incentives. If governments want to provide incentives to innovator companies to engage in voluntary licensing (or local production, which may be able to accomplish the same objectives), the most feasible levers they can employ are those that encourage foreign direct investment. Less feasible ways would be either through mechanisms to ensure that developed countries meet their TRIPS obligations to transfer technology or through using

⁶⁶ These objectives being cost savings, if applicable, differential product registration and differential marketing mix, as well as raising domestic production capacity.

⁶⁷ Lanjouw, J., Intellectual Property and the Availability of Pharmaceuticals in Poor Countries. Forthcoming in: Innovation Policy and the Economy. Vol 3, 2002. April 9, 2002 draft version.

⁶⁸ Some might argue that it is bad industrial policy if it encourages countries to deviate from their comparative advantage; others look upon comparative advantage as a dynamic process and would see the encouragement of technology transfer as the first step on the 'value-added' ladder.

compulsory licensing (see below) as a bargaining tool to encourage voluntary licensing as a preferable alternative.

Compulsory licensing

Definition

Compulsory licensing is defined as ‘authorization permitting a third party to make, use or sell a patented invention without the patent owner’s consent’.

Feasibility

Compulsory licensing is potentially an important instrument that is allowable, according to TRIPS, under certain conditions.⁶⁹ On a very practical level, no LDC has yet invoked a compulsory license, so there remains doubt as to whether it is a workable safeguard of TRIPS. In order to be used effectively, several practical, legal, economic and technological constraints need to be addressed.

Legal constraints

The prospect of a legal battle may deter LDCs from using this mechanism. If compulsory licensing is implemented in an overly legalistic manner, it will be expensive to administer and may be easily manipulated. In addition, there do not seem to be reliable rules on royalty compensation; such rules would make compulsory licenses easier to administer and speedier to implement.

A further legal hurdle involves the interpretation of TRIPS as to whether patent-respecting countries with manufacturing capacity would be able to export to countries without production capacity when the latter issue a compulsory license. Paragraph 6 of the Doha Declaration (Box 2) instructs the Council for TRIPS to report to the General Council before the end of 2002 with an expeditious solution to the problem of how Member States with insufficient manufacturing capacity can make effective use of compulsory licensing. Some Paragraph 6 options were presented at the session of the Council for TRIPS held in March 2002.⁷⁰ However, all options require diplomatic negotiations, rely on a number of conditions for successful implementation, and carry a number of negative considerations. No agreement had been reached as at February 2003.

It is the author’s view that a legal solution may not prove sufficient to make compulsory licensing workable; resolution of the practical, economic and technological hurdles must be sought as well.

Box 2

Doha Declaration on TRIPS and Public Health: Paragraph 6

⁶⁹ Article 31 of the TRIPS agreement sets forth a number of conditions for the granting of compulsory licences (case-by-case determination; prior negotiation, in certain cases, with the patent holder; remuneration, etc.) although it does not limit the grounds on which such licenses can be granted, leaving Members full freedom to stipulate the grounds for themselves.

⁷⁰ A moratorium on WTO complaints/disputes against countries that export some medicines to countries in need, under certain conditions

We recognize that WTO members with insufficient or no manufacturing capacities in the pharmaceutical sector could face difficulties in making effective use of compulsory licensing under the TRIPS Agreement. We instruct the Council for TRIPS to find an expeditious solution to this problem and to report to the General Council before the end of 2002.

Box 3

To illustrate the legal hurdle to the use of compulsory licensing, imagine that an LDC, e.g. Malawi, decides to issue a compulsory license for a new ARV in 2006. Since Malawi would not have the capacity for manufacturing such an advanced product, it would need to look to another country – such as India - for a low-cost version of the patented product. Since the ARV is a new, patented product, the only company engaged in the manufacture of this product after 2006 would be the innovator company itself. Malawi would be within its rights to grant a compulsory license for the importation of goods that are under patent in its own territory, as long as the imported goods have been produced in a country where they are not patented, or where the term of protection has expired. Since India is required to implement patent protection in 2005, it would be disqualified to supply under the current interpretation of TRIPS. Since the patent would exist in India, the patent holder may block exports from India to the importing country – Malawi in this example.

Further, since Article 31 (f) of TRIPS requires that a compulsory licensee supplies the domestic market predominately, the provision would prevent the granting of a compulsory license mainly to export to a country in need of medicines.

These are the legal challenges that would prevent a country like India from being able to produce medicines for export, under a compulsory licensing request, to a country like Malawi, after 2006.

Economic hurdles

Even if a Paragraph 6 agreement is reached regarding the definitions of 'predominately' and 'the domestic market' which resolves the scenario outlined in Box 3, economic and technological hurdles remain which would hinder the ability of LDCs to implement compulsory licensing for new products after 2006.⁷¹

Returning to the example in Box 3, questions remain such as:

⁷¹ Since the patent holders will recognise these economic and technological hurdles, the lack of resolution of these hurdles would hinder the ability of LDCs to use compulsory licensing as a negotiating tool as well.

- Does the compulsory license Malawi issued to serve its local market form a sufficient incentive for a company, e.g. in India, to invest in the development of a copy of the patented product?
- Is the market large enough to warrant the production of the active ingredient(s)?

The manufacture of active ingredients and the start-up costs of developing a patent copy are the two most scale-dependent parts of the pharmaceutical production process. It is unlikely that the scale of the Malawi market alone would provide an incentive for a patent copier company to develop and manufacture a product even if, through resolution of Paragraph 6 of Doha, this scenario is legally acceptable.

One solution to the economic problem would be for countries like Malawi to team up with other LDCs and issue joint, systematic and predictable compulsory licenses as a group. This might give sufficient scale and predictability to warrant market entry by a patent copier firm. A second possibility is if producing countries, like India, issue compulsory licenses for their own domestic market. A larger, wealthier market like India would be more attractive and thus would be more likely to provide the incentive for a domestic patent copier to enter and serve the market created by the compulsory license. Once the product has been developed, and the start-up costs recovered from large domestic sales, then the patent copier could supply other countries that issue compulsory licenses, such as Malawi.

Technological hurdles

Another barrier is technological. The increased use of biology-based R&D and the complexity involved in the development of pharmacogenomic products means that meeting regulatory bio-equivalence requirements will likely be problematic. Such tailored products would require increased diagnostics ability and extensive monitoring, requiring a strong customer service component. These sorts of investments would be problematic for generic companies⁷² and may result in decreased generic competition over time. One solution would be to enforce the technology transfer conditions Article 66.2⁷⁰ of the TRIPS⁷⁴ Agreement. This would theoretically create manufacturing capacity in the country in need; however, this would be a longer-term solution and not an 'expeditious' one as envisaged under Paragraph 6.

⁷² Moses, Z. May 2002.

⁷³ Moses, Z. May 2002.

⁷⁴ Article 66.2 of the Agreement on Trade-Related Aspects of Intellectual Property obliges developed countries to provide incentives that promote and encourage technology transfer to enterprises in least-developed countries.

⁷⁵ i) To amend Article 31 (f) in order to allow for the granting of a compulsory license which is not 'predominately' for the domestic market, and ii) to provide for a specific exception for exports under Article 30 of the TRIPS Agreement, possibly by means of an authoritative interpretation

⁷⁶ A moratorium on WTO complaints/disputes against countries that export some medicines to countries in need, under certain conditions

Experience with compulsory licensing

The credible use of compulsory licensing as a negotiating tool is what makes it effective in the current environment, as evidenced in Brazil in its negotiations with Merck over ARVs, and the US government with Bayer over ciprofloxacin. In fact, ciprofloxacin was subject to a fast-track form of compulsory licensing, called 'government use' provision, similar to the UK 'Crown Use'. Thus, public health in the USA and UK is safeguarded by 'government use' and 'Crown Use' powers respectively, and these powers have been invoked when necessary⁷⁷.

The UNDP Human Development Report 2001 states,

“Strong government use provisions: The TRIPS agreement gives governments broad powers to authorize the use of patents for public non-commercial use, and this authorization can be fast-tracked, without the usual negotiations. No developing country should have public use provisions weaker than German, Irish, U.K. or U.S. law on such practice⁷⁸”.

R&D effect

Innovator pharmaceutical companies allege that compulsory licensing has a strong negative effect on their incentives to invest in R&D for medicines that have been the target of compulsory licenses. The International Federation of Pharmaceutical Manufacturers Associations quotes two industry leaders as saying that 'if enthusiasm for compulsory licenses becomes great, there will soon be no more patents on AIDS drugs to compulsorily license – because new product development in this critical field will decline dramatically'⁷⁹. However, it is difficult to imagine how compulsory licenses for AIDS drugs in developing countries would so substantially affect incentives for R&D, given the fact that Africa represents only 1.2% of the global pharmaceutical market and AIDS is a global disease, for which R&D expenditure is recovered in wealthy markets.⁸⁰ The real issue may be lack of market segmentation and consequent fears that compulsory licences will erode pricing power in developed markets.

Conclusion

Although a resolution for Paragraph 6 of DOHA has yet to be agreed, concern remains that the legal system may not be able to provide a solution that would address the practical, economic and technological hurdles. Unless these are

⁷⁷ For example, in 1965, the UK government exercised the Crown Use provisions to import a generic version of tetracycline from Italy to supply the NHS after its patent holder, Pfizer, had demanded too high a price. Pfizer v. MoH 1965 RPC 261 (HL).

⁷⁸ <http://www.undp.org/hdr2001/chapterfive.pdf>, page 107.

⁷⁹ <http://www.ifpma.org>.

⁸⁰ Attaran, 2001

comprehensively addressed, the effective use of compulsory licensing for new products post-2006 is likely to be hindered.

Delaying or reversing patent protection

The Doha Declaration on the TRIPS Agreement and Public Health, adopted by the WTO Ministerial Conference in November 2001, affirmed that the TRIPS Agreement should be interpreted and implemented so as to protect public health and promote access to medicines for all. One of the agreements reached as part of Doha was that LDCs would not be required to implement patent protection on pharmaceuticals until 2016 (see box 5).

Box 5

Doha Declaration on TRIPS and Public Health: Paragraph 7

We reaffirm the commitment of developed-country members to provide incentives to their enterprises and institutions to promote and encourage technology transfer to least-developed country members pursuant to Article 66.2. We also agree that the least-developed country members will not be obliged, with respect to pharmaceutical products, to implement or apply Sections 5 and 7 of Part II of the TRIPS Agreement or to enforce rights provided for under these Sections until 1 January 2016, without prejudice to the right of least-developed country members to seek other extensions of the transition periods as provided for in Article 66.1 of the TRIPS Agreement. We instruct the Council for TRIPS to take the necessary action to give effect to this pursuant to Article 66.1 of the TRIPS Agreement.

If LDCs could take full advantage of this extension, this would be a very effective mechanism in the short term to achieve equitable pricing. However, the following paragraphs describe why the extension will have very little meaning in practice.

Of the 30 LDCs in sub-Saharan Africa, only Angola and Eritrea do not currently observe patent protection on pharmaceuticals.⁸¹ Some countries observe patent protection through regional groupings, e.g. the Bangui Agreement of the Organisation Africaine de la Propriété Intellectuelle (OAPI). This agreement was initially developed in 1977, revised in 1999, and is binding on all 16 West African Member States. It resulted in an IP protection regime which is much stronger than the minimum level required by TRIPS. For example, Bangui 1999 allows parallel importing only among Member States, despite the fact that medicines can be found at lower prices outside the OAPI region. For example, one tablet of GlaxoSmithKline's Combivir, a one-pill combination of the two ARVs Zidovudine and Lamivudine, costs US\$ 1.96 in Togo and US\$ 0.94 in Senegal (lowest price within

⁸¹ Presented by Carlos Correa at the March 28 conference, 'Implementation of the Doha Declaration on the TRIPS Agreement and Public Health: Technical Assistance – How to Get It Right'

⁸² In French, the acronym is OAPI

the OAPI region), but only US\$ 0.65 in India. According to TRIPS requirements, Togo would be allowed to import from India,⁸³ however, Bangui 1999 restricts Togo to importing from Senegal – at a price that is 45% higher than that in India⁸⁴. In addition, Bangui 1999 does not allow compulsory licensing for imports and has extended patent protection on pharmaceuticals from 10 to 20 years.

Thus the Bangui Agreement has resulted in a situation where the 12 LDC Member States⁸⁵ are complying with TRIPS now rather than delaying to 2016. It would be nearly impossible to rescind the Agreement as all the sixteen members would have to agree.

Other countries have instituted patent protection in response to bilateral pressures, before being required by TRIPS. For example, Chile, Indonesia, Korea, Mexico, Thailand, and the Andean Group of countries amended their patent laws from 1984 onwards in response to a revision of the US Trade and Tariff Act. This Act authorized the US government to take retaliatory action against countries failing to give adequate protection to IP.⁸⁶ Although politically unlikely, if these developing countries were able to reverse their current levels of patent protection, this mechanism would be very successful in bringing down prices before 2006.

After 2006, however, such a reversal carries similar economic challenges to the compulsory licensing mechanism. That is, although the LDCs not required to respect patents could legally import the generic copies of patented drugs, there would be less capacity on the market to produce copies of new, patented drugs, since most of the producing countries will be observing patents as of 2006. Thus, the lack of patents in small developing countries is irrelevant if these countries cannot import a low-cost generic version due to patent protection in the producing countries.

In summary, the 2016 delay would be more valuable pre-2006 if most of these countries had not already implemented patent protection, and post-2006, if a reliable supply of low-priced copies of newly patented medicines continued. Since neither of these conditions applies, delay or reversal of patent protection has little meaning to developing countries.

⁸³ TRIPS does not govern countries use of parallel importation, as was clarified in paragraph 5(d) of the Doha Declaration.

⁸⁴ Example presented by Catherine Gavin, legal advisor to Medicines Sans Frontieres, at the March 28 conference, 'Implementation of the Doha Declaration on the TRIPS Agreement and Public Health: Technical Assistance – How to Get It Right'

⁸⁵ Of the 16 countries in OAPI, 4 are considered to be developing countries and 12 are LDCs, the latter having until 2016 to implement TRIPS in full.

⁸⁶ Drahos, P. 2002.

Systematic, government-led patent waivers⁸⁷

Description of the mechanism

Government-led patent waivers are semi-voluntary mechanisms to achieve equitable pricing. They are to be distinguished from company-led patent waivers, whereby the patent holder decides where and when it is (or is not) of commercial interest to register patents. Due to their unpredictable nature, company-led patent waivers would not provide sufficient certainty to generic manufacturers to enable entry into production of new medicines. Company-led patent waivers would therefore have little potential for equitable pricing, and are not discussed here. The mechanism described in this chapter is a more systematic, semi-voluntary variation on this theme, whereby when registering its patent in major developed markets, a company would sign a declaration that it will not sue for patent infringement in LDCs for products to treat 'global diseases'. That is, for diseases which affect both poor and wealthy countries and where R&D recovery is expected to come from major developed markets.

Premise

The premise underlying the idea of patent waivers is that new pharmaceutical patents, coming into force with TRIPS implementation, promise benefits and costs that differ with the characteristics of diseases. Some diseases ('local diseases') primarily affect developing countries, and for treatment of these, patents will not be sufficient to attract substantial private investment because purchasing power is low. However, globally-available and well-defined patent rights could increase the benefits derived from greater public financing⁸⁸ of research on pharmaceutical products for the developing world. In contrast, the justification for extending patents in developing countries is less clear for major 'global diseases' – those which affect both poor and wealthy markets. Thus, patent waivers differentiate the protection given to products in accordance with their widely differing global markets, as illustrated in Figure 6.

The mechanism of government-led patent waivers, if politically feasible, would provide an economically logical, global framework for pharmaceutical patents and an optimal balance between static efficiency (access to existing medicines at

⁸⁷ Jean Lanjouw, Commission on Macroeconomics and Health, working paper number 11, group 2. 'A Proposal to Use Patent Law to Lower Drug Prices in Developing Countries'.

⁸⁸ The presence of a patent system in a developing country would be useful to publicly financed 'pull' programmes, that is, programmes that promise to pay for a specific product with defined characteristics only once it has been developed. Since no innovation is made by one person perfectly at one time, but rather cumulatively in bits and pieces by many firms, the presence of a patent system i) provides incentives to individual firms for all these tiny innovations, and ii) allows the firms to decide amongst themselves how to cross license appropriately. Absent a patent system, the 'pull' purchase fund would have to figure out a way to grapple with defining which inventors have contributed the most novelty to the innovation, and therefore, what compensation each should receive. These decisions would be very difficult for the purchase fund to make, and this might undermine the required certainty that the fund must convey convincingly to potential donors.

affordable prices by those who need those medicines) and dynamic efficiency (the ability to meet health need in the longer term) for countries at different stages of development.

Figure 6: Conflict between price/access to existing medicines and incentives to develop new ones

Wealthy markets	R&D recovered here therefore favour R&D Incentives (via patents) over price reductions	R&D recovered here, in niche markets therefore favour R&D Incentives (via patents) over price reductions
	R&D not recovered here therefore favour Price reductions/access to existing medicines over R&D incentives (via patents)	R&D recovered here therefore favour R&D Incentives (via patents) over price reductions Will be necessary to utilise other mechanisms to address insufficient R&D incentives, despite patents (e.g. 'push' and 'pull' mechanisms) as well as inability of poor countries to pay prices which recover R&D (e.g. increased financing)
Poor markets	'Global' diseases	'Local' diseases

How it would work

The patent waiver declaration form would look something like Box 6.

Box 6: Example of a patent waiver declaration

I, the undersigned, request a license to make foreign patent filings covering the invention described in US patent application no. X, with the understanding that this permission will not be used to restrict the sale or manufacture of this drug for countries with income and/or human development index of less than X.

Once the patent owner has signed the patent waiver declaration form, then if a patent copier enters the market, e.g. in India with an ARV, the innovator company has two choices:

- Sue the patent copier for patent infringement, and by doing so, lose the patent in the developed markets⁸⁹

⁸⁹ He would lose his patent in the developed country where he signed such a declaration by virtue of the fact that he has not abided by the agreement, and therefore he would invalidate the declaration, and with it, his patent.

- Ignore the patent infringement and by doing so, retain the patent in the developed markets.

The patent holder will obviously choose the second of these. Thus, by signing such a declaration, the innovator company will be essentially waiving patent rights for the specified medicine in qualifying LDC countries. .

With this mechanism, protection could be allowed to continue increasing worldwide in situations where stronger incentives to invest in research could be important (for local diseases), but not in those where the marginal increase in profits derived from LDC markets would be unlikely to generate innovation (for global diseases).

The real challenge with this mechanism comes in how one determines which drugs and which LDC countries should be included in the waiver. . The most logical and fair approach would be to specify a range of diseases, from global to local, and a range of countries, from wealthy to poor. This could be done in three steps:

Step 1: Identify broad groups of developing countries e.g. by GDP tiers, called country groups A, B, C, etc.

Step 2: Identify appropriate diseases for each country group and calculate, using data on pharmaceutical sales by disease class, total world sales and sales in each of the country groups A, B, C, etc.

Step 3: Include in disease class list 1 all country groups where the sales are less than 2% of world sales, and similarly for disease lists 2 and 3.

Where sale of medicines in a disease class contribute less than 2% of world sales in a country group, patent waivers would apply and where a disease class contributes to more than 2% of sales, patent waivers would not apply.

For the poorest of poor, probably all disease classes would qualify and effectively no patent protection would be afforded to pharmaceuticals in those countries. The declaration could evolve each year to reflect changes in pharmaceutical markets and the economic development of countries.

R&D effect

Since Africa represents 1.2% of the global pharmaceutical market,⁹⁰ it is difficult to imagine how lack of patent protection there for global diseases would affect companies' profits and hence ability to invest in further research. Even where diseases like HIV/AIDS are prevalent in less wealthy countries, inability to pay makes effective demand low, and hence profit potential low. However, lack of market segmentation is likely to be the larger issue for the patent holder.

Political feasibility

Only a handful of drugs recoup their development costs and most companies rely heavily on a limited number of successful drugs to finance continuing R&D. The fact

⁹⁰ Attaran, 2001

that 90% of prescription drugs generate less than US\$ 100 million annually supports this statement⁹¹. Consequently, companies have an incentive to care about patent protection and possible price erosion primarily as it affects sales of “blockbuster” drugs in wealthy markets.

Patent waivers would apply in LDC markets to products that are marginal profit-makers for the patent holders as well as to blockbuster drugs. Because they apply to the latter, patent waivers may therefore be seen as very threatening to the research-based pharmaceutical industry in an environment where market segmentation cannot be guaranteed. If it could be assured that leakage of products and of prices could be prevented, companies might accept patent waivers when they apply to global diseases in LDCs. However, as long as there is doubt that market segmentation can be achieved, research-based companies will presumably do all that is within their power to protect the pricing and patents of their large money-earners.

Pros and cons of government-led patent waivers

Pros:

- High initial but low ongoing transaction costs: implemented once, updated yearly. Uses existing patent registration systems;
- No amendments to TRIPS required;
- Current instability and negative press received by research-based multinational pharmaceutical companies could be resolved with a global, systematic and fair framework;
- Transparency and predictability good for planning purposes both for generic producers and research-based multinationals;
- Prices of medicines to treat local diseases would likely remain the same, or increase; prices of medicines to treat global diseases would decline (current competitive environment continues to grow);
- The market for drugs to treat such global diseases as HIV/AIDS, cancer, heart disease and diabetes would retain its current level of competitiveness in lower income countries. These diseases already account for 16 % of all DALYs lost in low- and middle-income countries. This is four times the DALYs lost to malaria.⁹² Governments could save money on HIV/AIDS, cancer and heart disease drugs that could be redeployed towards purchasing drugs to treat ‘local’ diseases, such as antimalarials;
- Since the market for drugs to treat ‘global’ diseases would retain its current level of competitiveness, incentives for R&D for global drugs would remain as they are currently.

⁹¹ Datamonitor research quoted in ‘The Pharmaceutical Industry Paradox: A Strategic analysis of the countertrends of consolidation and fragmentation, Reuters Business Insight, Zelik Moses. May 2002.

⁹² World Health Organization (1999) *The World Health Report*. Statistical Appendices. Geneva

Cons:

- Mechanism relies on political will of major developed countries (e.g. the European Union, Japan, USA) for implementation;
- Would require an international treaty, therefore time-consuming and politically difficult;
- Unless market segmentation can be assured, research-based pharmaceutical companies are unlikely to support any mechanism that threatens their large markets;
- R&D incentives for drugs for local diseases increase only if implemented in parallel with 'push' and 'pull' mechanisms⁹³;
-

⁹³ 'Push' or 'Pull' mechanisms refer to different methods of subsidizing research with public funds. Push mechanisms subsidize research inputs up front, while pull mechanisms promise to pay for a specific product with defined characteristics only once it has been developed. See Kremer 2001 for details.

Government-led price controls

The idea of price controls is not a new one. The mechanism summarized here is not a global price control system, but rather, the idea of price controls levied at national level, with each government choosing how to administer the system and to which drugs the controls apply. Price controls could be implemented in the context of a public purchasing programme, or could be levied at the pharmacy retail level, or both.

Pros and cons

Pros:

- Price controls do not require any modification to TRIPS. The strengthening of worldwide IP protection could continue for all pharmaceutical products as required by treaty;
- Price control regulation is already a feature of the pharmaceutical markets in both rich and poor countries. Hence, although firms may not like the idea, the principle of regulating prices is not likely to be challenged in the international arena;
- Price controls levied at national level could not logically be used as a rationale for developed country reference pricing systems. This mechanism would therefore partially solve the market segmentation problem;
- The innovator company who chooses to serve the price-controlled market would retain control over distribution, and therefore control the colour, shape and size of products manufactured and distributed in poor countries; this lessens the opportunities for the production of counterfeit goods or the possibility that these products can be easily exported to developed countries (again, good for market segmentation). Control over distribution also means that the innovator can perform the necessary pharmacovigilance.

Cons:

- Developed countries which use price controls successfully (known as evidence-based purchasing or reference pricing) do so in conjunction with large public financing programmes. Thus, the purchaser has a certain degree of leverage that makes the price control more or less acceptable to the supplier. LDCs, with smaller scale, might not have the same leverage.
- Assuming that costs can be correctly ascertained and prices fixed on a cost-plus basis, regulating through price controls demands continuous monitoring to ensure that price ceilings are not evaded by manufacturers or retailers. This is difficult for countries with limited regulatory capacity. The experience

of Colombia and India in monitoring costs and enforcing prices has been poor.⁹⁴

- Price control decisions would be made within a domestic context, therefore subject to political pressures; decisions may be made based on political logic rather than on economic/health logic.
- The transaction costs are likely to be very high with this approach; price disputes will surely go on between governments and companies. Governments will want to see the company's costs and might threaten to issue compulsory licenses should communication break down. Patent holders would retain control over sales in the developing world market and could, if controlled prices were viewed as too low, simply keep patented products off the market altogether.⁹⁵

Summary

Government-led price controls would be effective in reducing prices but may result in withdrawal of the products from the market, thereby reducing access. This could theoretically be minimized by:

- Restricting the use of price controls to public sector purchasing where the government has relatively more leverage because of the large bulk being purchased
- Using compulsory licensing as back-up to this mechanism.

The impact of price controls on R&D could be negative, but this would depend on the size of the market and on the products to which the mechanism is applied. Application in the poorest countries and towards products to treat global diseases should have a less negative impact on R&D investment decisions, if market separation can be achieved. Simulation studies which applied Indian price controls to 1994 price data, showed that such price controls, where effective, leave consumers better off while leaving patent owners only negligibly worse off. In particular, price decreases for widely used patented pharmaceuticals that have few substitutes would increase consumers' surplus significantly.⁹⁶

⁹⁴ Scherer, F. M. & Watal, J. (2001), pgs.49-53.

⁹⁵ This already happens. Recently the head of Pfizer announced that the company would threaten to withhold new treatments for France unless the government would allow higher prices. Similar threats were put into practice in Pakistan during 2000, when government price controls (levied at retail pharmacy level) had not kept up with inflation and new import taxes, and therefore were seen as too restrictive by MNCs, and many products were consequently withdrawn from the market. Under current rules, a refusal to supply might be sufficient to trigger the national emergency provision allowing compulsory licensing. However, as discussed, compulsory licensing may not be economically feasible for some countries, unless certain conditions exist.

⁹⁶ Watal, 2000.

Framework for comparative analysis of equitable pricing mechanisms

Criteria for assessing impact of the mechanisms

The equitable pricing mechanisms discussed in this report have been evaluated against a variety of parameters (Figure 7), starting with the mechanism's effectiveness in bringing prices to the lowest possible level and the effect on incentives to invest in R&D for new drugs. The former can be thought of as static efficiency -- access to existing medicines at affordable prices by those who need those medicines, and the latter as dynamic efficiency -- the ability to meet health need in the longer term.

Any policy discussion around the mechanisms should start from the recognition that static and dynamic efficiency are in conflict in this instance. The conflict is not, as is sometimes thought, between corporate profits and public health, but rather, between two equally important public health goals - widespread access to existing drugs and the maintenance of incentives to create new ones. Incentives to create new drugs are sustained by patents and these in turn sustain higher prices; thus, dynamic efficiency is improved but static efficiency suffers. Conversely, widespread access to existing drugs – static efficiency – is enabled when more consumers can afford to purchase goods incorporating new innovations.

The public policy dilemma is how to balance static and dynamic efficiency – that is, making new medicines affordable to all those who need them, whilst retaining strong incentives for investing in development of new and better treatments. Ideally, the balance between static and dynamic efficiency should differ according to:

- The wealth of the country
- Whether the access problem relates primarily to diseases present in both wealthy and poor countries, or those primarily found in poor countries.

In small LDC markets,⁹⁷ where demand for products to treat global diseases adds only marginally to the profits of multinational pharmaceutical companies and hence has, at most, a small impact on their R&D decisions, the balance would favour static efficiency. Thus, mechanism(s) that keep patented medicine prices at the lowest level consistent with international obligations would be employed.

In practice, different institutions and policy makers will have different political constraints and operational realities, and thus an optimal economic framework may not be feasible. For this reason, a variety of equitable pricing mechanisms are needed.

The mechanisms described in this report have been assessed according to a range of factors (see below). It is not appropriate to attempt to assign numerical values to the analysis; rather, the analysis is meant to be illustrative and should be read critically

⁹⁷ The volume of demand for health products may be very large in many LDCs, but the lack of purchasing power makes the effective demand, in revenue terms, very small.

with the accompanying notes (see section 'Detail behind the analysis') which explain why the ranking has been assigned. An attempt has been made to be exhaustive to allow the options to be compared in a more systematic way. Inevitably, however, the criteria will have different importance to different readers. For example, patent waivers are evaluated positively on most parameters, but since it seems unlikely that such a mechanism would be acceptable to the US government or the European Commission, those positive benefits have no way of materializing. Thus, for readers who are most concerned with the practically optimal model rather than the economically optimal model, the low ranking for 'political feasibility' for patent waivers would counteract all of its high rankings on the other measures.

Figure 7: Summary of impact of different mechanisms according to selected criteria

	Bulk purchasing	Voluntary tiered pricing agreements	Voluntary licensing	Compulsory licensing	Delay patent protection	Patent waivers	Price controls
Price reduction	high	low	medium	high	high	high	high
Negative for R&D	low	low	low	medium	medium	low	medium
Product scope	wide	narrow	narrow	narrow	narrow	narrow	wide
Disease scope	wide	wide	medium	medium	medium	medium	wide
Buyer scope	wide	narrow	medium	narrow	wide	wide	wide
Domestic manufacturing	no	no	yes	yes	no	no	no
Population/income	yes	yes	yes	no	no	no	no
Scale	high	low	medium	low	low	medium	medium
Impact poor	medium	low	low	medium	high	medium	high
Predictability	medium	low	medium	low	high	high	medium
Sustainability	high	low	low	low	low	high	medium
Transparency	high	low	medium	high	high	high	medium
Political feasibility	high	high	medium	medium	low	low	medium
Legal feasibility	high	medium	high	medium	high	high	high
Transaction costs	low	high	medium	high	high	medium	high
Negative competitive effects	low	high	low	low	low	low	low
Retail price impact	low	low	low	low	low	low	high

Detail behind the analysis

Price reduction

What has been, or is likely to be (where the mechanism has not yet been applied) the effect on static efficiency, or price reductions?

Chapter 8 of this report provides details of price reductions that have been achieved with different mechanisms that are already in use. It is not possible to draw a general conclusion that says 'Mechanism X will deliver a price reduction of Y.' It is only possible to show specific examples in their context. Mechanisms that restrict patent protection (e.g. compulsory licensing, patent waivers) will have a significant impact on reducing prices where a competitive market for the medicines exists. The price reductions achieved with bulk purchasing, voluntary tiered pricing agreements, and voluntary licensing are more context specific and will depend on such factors as the relative bargaining power of the purchasers/suppliers as well as the way in which the mechanism is implemented. Experience with voluntary tiered pricing agreements has not shown to be very effective in achieving equitable prices; drugs offered through these agreements are not affordable to the recipient populations and do not appear to be priced at marginal cost.

Two mechanisms, bulk purchasing and patent waivers, best meet the criteria of having a high impact on reducing prices, while having a low negative impact on R&D investment decisions. Although compulsory licensing and delaying patent protection have been graded 'high' on price reductions, this is a theoretical grading. In reality, due to the lack of feasible implementation (pre 2006 due to political infeasibility and post 2006 due to economic infeasibility) their impact would be minimal. The impact of price controls on price reduction depends on such factors as the drugs and markets to which they are applied, and the capacity of government to implement and monitor the price controls. Potentially, price controls could be very effective means of achieving price reductions.

Impact on R&D

What has been, or is likely to be (where the mechanism has not yet been applied) the likely effect on dynamic efficiency, or incentives to invest in further R&D?

In order to determine the degree of negative impact on R&D investment decisions, it is necessary to know in which countries, and to which products, the equitable pricing mechanism would be applied as well as the extent of price reduction. If the mechanism is applied in LDCs and towards medicines to treat global diseases, the negative effects would be limited. If applied in relatively higher income developing countries to treat diseases for which R&D costs cannot be recovered in wealthy markets (local diseases) then the R&D impact would be much more negative. It is assumed that voluntary mechanisms have a minimal negative impact on R&D incentives because they are voluntary. In addition there is evidence indicating that

research-based companies are not pricing at marginal cost with these voluntary mechanisms, and therefore would not seem to be losing money by offering equitable prices.

Product scope

Is this a mechanism that would affect the price and R&D incentives of patented products only (narrow), or both patented and generic drugs (wide)?

The equitable pricing mechanisms reviewed in this report would generally have more effect in reducing prices for patented drugs than for generics, although bulk purchasing and price controls are effective for reducing prices on both. Patent waivers, compulsory licensing and delayed patent protection would affect patented drugs only. Although voluntary licensing and voluntary tiered pricing agreements have the potential to be applied to drugs other than just those that are patent protected, their actual use thus far has been narrow; they have been limited to supply of patented drugs only.

Disease scope

Would the mechanism preferentially affect drugs to treat local (narrow), or global (medium diseases or is it non-preferential, affecting all categories (wide)?

Bulk purchasing and voluntary tiered pricing agreements have been applied to treatments for both global and local diseases. Demand for voluntary licenses is likely to be higher for global diseases. Compulsory licensing can be applied to medicines for both global and local diseases, although it is more economically feasible to find suppliers if the request is for a global disease (the same goes for delays in patent protection). Patent waivers would affect prices for patented global drugs and therefore generic entry and prices for these preferentially. The IP environment for local diseases would remain strong with patent waivers, restricting generic entry and consequently price reductions. Price controls could be applied to products for global and local diseases alike.

Purchaser scope

Could this mechanism be used only by institutional purchasers, such as governments or large NGOs, to bring down prices (narrow scope), or it is a mechanism that could be used by the private sector or by individuals, thereby affecting prices on the market as a whole (thus, wider in scope)?

Voluntary tiered pricing agreements and compulsory licensing are, by their nature, restricted to institutional purchasers, restricting the scope of buyers that can make use of the mechanism. Bulk purchasing is a mechanism that can be used in both private and public sector. Delayed patent protection, price controls, patent waivers,

but to a lesser degree, voluntary licensing, are mechanisms which could affect prices throughout the market – including those paid by private, for-profit entities.

Domestic manufacturing

Would the existence of domestic manufacturing capacity facilitate the use of this mechanism (yes/no)?

Domestic manufacturing capacity is not needed to take advantage of bulk purchasing, voluntary tiered pricing agreements, price controls, delayed patent protection or patent waivers. It is necessary in order to take advantage of voluntary licensing as a mechanism. Depending on how the Doha Declaration is interpreted regarding exports to LDCs without manufacturing capacity, domestic manufacturing capacity may also be necessary to take advantage of compulsory licensing.

Population/income

Does this mechanism work better where populations are larger and/or incomes are higher (yes/no)?

In theory, bulk purchasing works better where populations are larger, although some countries achieve better price reductions than larger countries⁹⁸ due to more professional, less restrictive, procurement practices. Voluntary tiered pricing agreements have so far been more beneficial to higher income countries, because price reductions have not been sufficient for LDCs to take full advantage of the opportunity. In principle, however, there is no reason why voluntary tiered pricing agreements could not go further in aligning prices with ability to pay – whereby countries with lower incomes and smaller populations could be offered lower prices. Voluntary licensing is also more feasible where incomes and populations are higher, since domestic manufacturing capacity tends to be more prevalent in this environment.

The use of compulsory licensing as a negotiating tool has so far been effective in countries with production capacity (e.g. Brazil) and relatively larger populations and higher incomes, although smaller LDCs could theoretically use compulsory licensing as a negotiating tool at present. After 2006, the feasibility of a LDC invoking a compulsory license for new, patented products will decline substantially because of the diminishing base from which to import generic copies of new patented products. However, if economically possible, it is more likely to be politically acceptable (less apt to attract legal retaliation from patent holders) in poorer countries, and it is more likely to be economically feasible where populations are larger (therefore offering sufficient scale to a generic patent copier).

⁹⁸ See the example, a comparative study of Southern African countries, offered in the Bulk Purchasing chapter of this report.

Delayed patent protection and patent waivers would be preferentially applied to poorer countries with smaller populations. With patent waivers, the patent protection the country must observe changes over time as the national economy develops. Price controls can be implemented regardless of the population/income level.

Scale of access

Is the number of patients who would have access to lower prices via this mechanism, low, medium or high?

As indicated in previous chapters, the improvement in access has been low with voluntary tiered pricing agreements for HIV/AIDS, TB and malaria and high with bulk purchasing.

The scale of access is a direct function of the degree of price reduction relative to income as well as the degree of restrictions placed on recipients and the levels of investment needed in complementary infrastructure. These points are discussed in the case study of access to ARVs in Uganda. It is fairly obvious that if less public funds go towards high drug prices, then there will be more funds available for investment in infrastructure. As for other diseases that are treated through existing healthcare infrastructure (e.g. malaria and childhood illnesses), the increase in access when drugs are publicly funded should be nearly proportional to decreases in price.

Assuming that there is sufficient demand for voluntary licenses, and a willingness of patent holders to supply such licenses for equitable pricing purposes, then voluntary licensing might bring down prices in countries with sufficient domestic manufacturing capacity, increasing access in those countries. The scale of impact on access achieved through compulsory licensing is theoretically high, but likely to be low in practice, given its political and legal limitations pre-2006 and its lack of economic feasibility post-2006. Delaying or reversing patent protection applies only to the very least developed countries and only until 2016. Besides it lacks political feasibility pre-2006 and economical feasibility post-2006, so the access scale is low. Patent waivers should have a high access scale impact since they provide a global mechanism. However, they have been graded medium since they are targeted preferentially at improving access to treatments for global diseases and would have a neutral effect on access to medicines for local diseases (although patent protection for these drugs would be a useful complement to 'push' and 'pull' mechanisms designed to increase access to these medicines). The access scale achievable with price controls could be high if applied in both public and private sectors, but it has been ranked as medium due to the possibility that products would be withdrawn from the market.

Impact on the poor

To what degree does this mechanism have the ability to directly influence prices in the poorest countries or the prices paid by the poor within countries? Is the mechanism's impact on the poor likely to be low, medium or high?

Bulk purchasing is commonly used in the public sector and non-profit health sectors, so since the poor utilise these sectors, they would benefit.. However the impact would be higher if the mechanism affected private sector prices as well, since studies have shown that a large percentage of the poorest people (up to 80% in some countries) access their drugs through the private sector. Since price controls can be levied at retail pharmacy level, they have therefore been given a score of 'high'. Given the high prices of drugs relative to per capita income available through most voluntary tiered pricing agreements, it is unlikely that the poor benefit.

Voluntary licensing, if used, would be destined for countries with manufacturing capacity; this presently applies to higher income developing countries (except Bangladesh). Prior to 2006, compulsory licensing theoretically could be used in rich or poor countries, although experience with using it as a negotiating tool has so far been limited to those manufacturing countries with higher incomes and populations. After 2006, the economic feasibility of compulsory licensing substantially declines, but, if economically possible, it would more likely to be politically acceptable (less apt to attract legal retaliation from patent holders) in poorer countries. Patent waivers would affect prices of medicines for global diseases like HIV/AIDS but not directly the prices of drugs to treat local diseases. The poor suffer from both global and local diseases.

Predictability

Is the mechanism predictable? Are the rules of the mechanism easy to predict so that a company (for purposes of planning and risk reduction) can determine the size of a potential market and its likely competitors? Do the mechanisms clarify what innovator and generic companies can expect during their five and ten year business plans? (Note that predictability and ability to plan become more important after 2006.) (high, medium, low)

The most highly predictable system would be the patent waiver mechanism, since it would be a globally-recognized, well-defined international treaty. Delayed patent protection, if effectively implemented, would also rank highly, for similar reasons. Since it would not be clear to generics manufacturers in which circumstances the patent holder would wish to supply a price-controlled market, price controls may be somewhat more problematic in terms of ensuring that generics companies have the information they need to plan and enter markets to supply certain products.

Bulk purchasing has been rated as medium, since predictability varies with the degree to which the tendering process is professionally managed and open. Voluntary licensing would be relatively predictable, since these agreements would be made over several years duration. Voluntary tiered pricing agreements and compulsory licensing are the least predictable. The former are negotiated on a country-by-country basis; making predictability low. Compulsory licensing is also

implemented on a country-by-country, case-by-case basis. This means that, after 2006, a generic patent copier who needs to determine whether it is economic to supply a copy of a patented product to one or a number of LDCs, upon a compulsory license request, would have difficulty in making this calculation.

Sustainability

Is the mechanism sustainable, or is it dependent on public and NGO pressures, the policy/support of a certain board of directors or senior managers in a firm, or unsustainable threats (high, medium or low)?

Sustainability would be the highest with patent waivers, followed by bulk purchasing. Sustainability is low with voluntary tiered pricing agreements like AAI, with compulsory licensing, and with delayed patent protection; the last two are temporary arrangements by definition. Voluntary licensing has been given a sustainability ranking of low until such time as there are more examples to prove otherwise.

Transparency

Is the mechanism transparent, or is it open to manipulation to achieve other, hidden, aims (high, medium or low)?

Transparency is lowest with bilateral negotiations, since these are agreements between a company and a recipient country which have not, in practice, been made public. Voluntary licensing ranks slightly better only because some parameters of the examples cited have been made public. Transparency with bulk purchasing is high unless corruption enters the picture. Similarly, transparency with compulsory licensing, if feasible, would be relatively high, because of all the royalty negotiations, supplier qualification and public attention it would receive. Patent waivers fare the best on the transparency scale, since the mechanism would be a globally-accepted, well-publicized declaration signed by patent holders.. Delayed patent protection would also be transparent for similar reasons. Price controls levied at domestic level could be open to political manipulation.

Political feasibility

How politically feasible is the mechanism (high, medium, low)?

Although not the area of the author's expertise, it is suggested that political feasibility might be high with bulk purchasing, voluntary tiered pricing agreements, medium with voluntary licensing and price controls, and low with delayed patent protection and patent waivers. Assurance that leakage of goods and of prices can be prevented would be a necessary pre-condition for companies to even consider patent waivers. Political negotiations regarding aspects of compulsory licensing have

continued beyond 2002, the deadline at which they were scheduled to end. Thus, compulsory licensing has been ranked medium to account for the delay in resolution.

Legal feasibility

Is the mechanism legally feasible according to TRIPS (high), or is there some uncertainty in the interpretation of TRIPS as applied to this mechanism (medium)?

Most of the mechanisms are legally feasible. There are some unresolved questions around the situations in which compulsory licenses can be implemented as well as whether product can be manufactured for export to countries which have issued compulsory licenses but do not have manufacturing capacity. There are also unresolved questions about the anti-competitive nature of voluntary tiered pricing agreements which raise entry barriers for generic firms.

Transaction costs

Are the transaction costs (i.e. the costs of setting up, negotiating, maintaining, revising, managing conflicts) high, medium or low relative to the benefit achieved ?

Transaction costs with voluntary tiered pricing agreements are high, especially when considered in light of the limited benefits (price and access) that have been achieved. Transaction costs with compulsory licenses would also be very high (although perhaps not high relative to price/access achieved) due to the potential for dispute over legalities and royalty rates, the need to find a supplier, etc. The cost of setting up the patent waiver system would be high, but once set up, the ongoing transaction costs would be very low. Voluntary licensing would involve medium transaction costs between the patent holder and the licensee. The transaction costs, relative to benefit achieved, for bulk purchasing would vary according to the size and professionalism of the organization conducting the purchase, but are likely to be relatively low when compared to the other mechanisms. Since the delayed patent protection mechanism would actually require reversing patent protection in most LDCs, and would involve renegotiating bilateral and regional agreements, this mechanism has been rated high in transaction costs. National price controls would be expensive to set up and administer.

Negative competition effects

To what degree might the mechanism have a negative competitive effect, particularly on local manufacturing in lesser-developed countries? (low = positive or neutral effect on competitive environment, high = mechanism is possibly anti-competitive)

Negative competitive effect would be low with patent waivers and compulsory licensing. Bulk purchasing, if not professionally managed, has the potential to have a negative competitive effect. However, in some countries, bulk purchasing has actually had an encouraging effect for domestic producers, helping them enter the

market when they win tenders for institutional supply, and gain sufficient scale to invest in equipment and eventually participate in international tenders.

Voluntary licensing also benefits some companies at the expense of others; this is not necessarily anti-competitive but can be supportive of a competitive environment. The only mechanism that has an obviously restrictive effect on competing companies ability to enter markets would be voluntary tiered pricing agreements. These agreements, which use a parallel procurement system, are also contrary to the aim that each country should have a central purchasing system which works on the basis of a transparent public tender.

Retail price impact

To what degree could the mechanism have an effect not just on the ex-manufacturer price, but on prices right through to the retail/consumer level?

None of the mechanisms discussed in this report has the ability to control prices to the consumer except for price controls levied at the retail pharmacy level. Theoretically, medicines offered through controlled channels, such as public sector facilities, would be able to control the price to patients. However, many studies have shown that this is not reality. A study recently commissioned by WHO and conducted in Uganda for purposes of this report, showed an inconsistency between ARV prices offered to Uganda through AAI and the prices paid by patients, indicating that drugs were being marked-up on their journey to the patient.⁹⁹

Interdependence of the mechanisms

The preceding sections examined the mechanisms based on their independent merits. It is also worth examining how the mechanisms relate to each other, recognizing that some mechanisms either facilitate or preclude others. Some mechanisms have been widely employed and for these there are practical examples of their interaction with other mechanisms. In contrast, others have only had limited use, and for these we can only imagine their theoretical interaction with other mechanisms.

For example, some voluntary mechanisms may inhibit the development of other voluntary mechanisms. If the voluntary license route is employed, the patent holder may be unwilling, or even unable, to also offer product manufactured by the patent holders' factories in tiered pricing agreements. The opposite may also be true; companies already offering products through voluntary tiered pricing agreements might see little reason to also offer voluntary licenses. Experience with both of these voluntary mechanisms is limited, therefore it can only be supposed that these mechanisms might preclude one another.

⁹⁹ Ochola, D. MD, Access to Antiretroviral Drugs in Uganda: A Country Case Study. April 2002. Unpublished. Commissioned by the Essential Drugs and Medicines Policy Unit, World Health Organization.

Another situation where one mechanism would likely impede the use of another is in delaying/reversing patent protection and compulsory licensing: if a country does not observe patents, then it would not be able to invoke a compulsory license on patented products.

Empirical evidence exists on the interaction between some of the more widely-used mechanisms. For example, it would appear that mechanisms that rely on market forces and competition serve to enhance or strengthen all of the other mechanisms. e.g. the opportunity to bulk purchase generic ARVs has provided the incentive for patent holders to participate in AAI and to lower prices of ARVs. Similarly, the opportunity that TRIPS affords developing countries to gain access to therapeutic equivalents through compulsory licensing, has also provided incentives to patent holders to engage in voluntary mechanisms as an alternative to compulsory licensing. In this sense, we see how use of the more 'compulsory' mechanisms, which allow for greater competition, has provided a framework within which patent holders are persuaded to use their monopoly powers more reasonably in the interests of public health in developing countries.

APPENDIX A: REFERENCES

Background papers for World Health Organization and World Trade Organization differential pricing conference in Høsbjør, Norway, in April 2001:

Texts or PowerPoint slides presented at the workshop can be downloaded from the following site:

http://www.who.int/medicines/library/edm_general/who-wto-hosbjor/hos_sessions.html

Seth Berkley, International AIDS Vaccines Initiative: [IAVI: Accelerating the global effort to create an AIDS vaccine: IP issues for future global public goods products](#) (MS PowerPoint, 39 pages, 1.96MB)

Chuck Hardwick, Pfizer: [Access to Medicines in the Developing World Through Partnerships](#) (MS Word, 8 pages, 31KB)

Ellen 't Hoen, Médecins Sans Frontières: [Affordable Medicines for Developing Countries](#): Concepts and Issues (MS PowerPoint, 17 pages, 961KB)

Albert Itschner, Novartis: [Market segmentation and price differentiation: a novel approach](#) (MS Word, 4 pages, 31.5KB)

Patrick Kadama, Government of Uganda: [Role of government in healthcare](#) (MS Word, 4 pages, 37.5KB)

Cecile Miles, Ranbaxy, India: [Experience with Generic Drugs](#) (MS PowerPoint, 13 pages, 69KB)

Dorothy Ochola, Uganda HIV/AIDS Drugs Access Initiative: [Current experience with differential pricing of HIV/AIDS related drugs in Uganda](#) (MS PowerPoint, 18 pages, 120KB)

Jonathan D. Quick, World Health Organisation: [Ensuring access to essential drugs – framework for action](#) (MS PowerPoint, 20 pages, 848KB)

F.M. Scherer, Harvard University: [The economics of parallel trade in pharmaceutical products](#) (MS Word, 4 pages, 34KB)

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APPENDIX B: LIST OF THOSE INTERVIEWED OR CONSULTED

UN organizations

Name	Subject
Andrew Creese	Various -Input throughout the report development
Jonathan Quick	Various -Input throughout the report development
Hans Hogerzeil	Various -Input throughout the report development
Paula Munderi, WHO	HIV/AIDS, Uganda case study
Robin Gray, WHO	Childhood diseases, dosage regimen for selected high priced drugs for costings
Rajesh Gupta, WHO	Green Light Committee, Multi-drug resistant TB
Marthe Everard	Drug prices, selection of shortlist of drugs for costings
Jos Perriens, WHO	HIV/AIDS, Accelerating Access Initiative
Badara Samb, WHO	HIV/AIDS, Accelerating Access Initiative
Souly Phanouvong, WHO	Global Drug Facility (GDF), TB
Dermott Maher, WHO	TB, cost of providing complementary health care services
Giorgio Roscigno, WHO	GDF, voluntary licensing
Gini Arnold, WHO	GDF, TB
Clive Ondari, WHO	malaria
Dorothy Ochola, consultant to WHO	Uganda case study
Rob Ridley, WHO	Public private partnerships
Peter Evans, consultant to WHO	GDF/TB
Mamadou Mariko, WHO	Price elasticity to health care costs, including drugs
Andrea Bosman, WHO	malaria, Coartem
Janis Lazdins, WHO	malaria, Coartem
Ernesto Jaramillo, WHO	Green Light Committee, Multi-drug resistant TB
Salah Ottmani, WHO	TB costings
Mukund Uplekar, WHO	TB costings

Kathryn Floyd, WHO	TB costings
Piero Olliaro, WHO	malaria, Coartem
Dr SA Qazi, WHO	Childhood diseases: selection of high priced drugs
Thiru Balasubramaniam, WHO/WTO	Impact of TRIPS on public health
Jaysheree Watal, WTO	Impact of TRIPS on public health, compulsory licensing, voluntary licensing, Doha extension until 2016.
Neth Walker, UNAIDS	Costings for scaling up HIV/AIDS

Industry

Name	Subject
Phil Rush, Novartis	Coartem
Martin Bates, GSK	Lapdap and malarone
John Horton, GSK	Lapdap and malarone
Kathleen Laya, GSK	Accelerating Access Initiative
Simon Sergeant, GSK and Association of British Pharmaceutical Industry	Accelerating Access Initiative and general policy of ABPI regarding differential pricing
Chris Strutt, GSK	Voluntary licensing, esp. Aspen in S. Africa
Robert Lefebvre, Bristol-Myers Squibb	General policy on differential pricing, Accelerating Access Initiative
Sangeeta Sharma, Cipla pharmaceuticals	antiretrovirals available in India
Patricia Garlevaro, Eli Lilly	voluntary licensing

Academic

Name	Subject
Carlos Correa, University of Buenos Aires	Doha extension until 2016, Compulsory licensing
William Jack, Georgetown University	Price controls and economics of Lanjouw patent waivers
Jenny Lanjouw, Brookings	Economics of Lanjouw patent waivers

Micheal Kremer, Brookings	Costing work done for Performance and Innovation Unit, price elasticity to drugs
Al Engelberg, Columbia University	Economics feasibility of pharmaceutical production post 2006. Price controls.
Virginia Wiseman, London School of Hygiene and Tropical Medicine	Price elasticity to malaria medications
Christoph Kurowski, London School of Hygiene and Tropical Medicine	Price elasticity to drugs

Other

Name	Subject
William Haddad, pharmaceutical consultant to Cipla	Voluntary licensing and economics of pharmaceutical manufacturing
Sean Gallaher, Department of Health	Needs of working group re: my work and patent waivers
Ramil Burden, Department of Trade and Industry	Market segmentation and division of labour on this subject
Alison Kilburn, Cabinet Office	Costing work done for Performance and Innovation Unit
Maria Flaviano	Bilateral agreements in relation to implementation of patent protection
Ellen 't Hoen, Medicines Sans Frontieres	Examples of effect of competition of price reductions
Andy Barraclough, consultant to UNAIDS (Options consulting)	Costing work done for UNAIDS
Mohga Smith, Oxfam UK	Potential health impact from differential prices
Michael Bailey, Oxfam UK	Potential health impact from differential prices
Hans Binswanger, The World Bank	Costing work done on HIV/AIDS
Judith Hazelwood, McKinsey & Company	HIV/AIDS scale up costing work done for the Accelerating Access Initiative
Christian Saunders, UNFPA	Relationship between price and volume via different types of competitive tendering (and other factors affecting price reductions achieved)
Wilbert Bannenberg, Public Health Consultant	Relationship between price and volume via different types of competitive tendering (and other

Consultant	factors affecting price reductions achieved)
Hilbrand Haak, Consultants for Health and Development	Relationship between price and volume via different types of competitive tendering (and other factors affecting price reductions achieved)
Henk den Besten, IDA	Relationship between price and volume via different types of competitive tendering (and other factors affecting price reductions achieved)
Johan van de Gronden, IAPSO	Relationship between price and volume via different types of competitive tendering (and other factors affecting price reductions achieved)