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June 2008**Intellectual Property and Public Health:
An Overview of the Debate with a Focus on U.S. Policy**
By Carsten Fink**Abstract**

Over the past fifteen years, the United States and other developed countries have employed trade agreements to substantially strengthen the protection of intellectual property rights for pharmaceutical products in the developing world. The associated rules changes have already had an effect on pharmaceutical prices in developing countries, prompting conflicts between developing country governments seeking to promote drug access and Western pharmaceutical companies wishing to protect their exclusive rights. If anything, such conflicts are bound to intensify as more patent protected drugs enter pharmaceutical markets outside rich countries. This paper describes the global shift in intellectual property policies and employs economic analysis to evaluate its consequences for developing countries. It also puts forward several recommendations for policymakers in developing countries and in the United States, seeking to better reconcile innovation incentives and access needs.

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**Intellectual Property and Public Health:
An Overview of the Debate with a Focus on US Policy**

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Foreword

I am delighted to sponsor this working paper by Carsten Fink on intellectual property rights policy and developing countries' access to affordable pharmaceuticals. Fink, an economist with the World Bank who will soon be joining the faculty of the University of St.Gallen in Switzerland, has written widely on the role of innovation, technology transfer, and intellectual property rights in development. He is the author of numerous papers and articles on these issues and the co-editor, with Keith Maskus of the University of Colorado, of the major World Bank study, *Intellectual Property and Development: Lessons from Recent Economic Research*.

In this paper, Fink traces the evolution of intellectual property rights rules in the World Trade Organization and in bilateral U.S. trade agreements and analyzes their effects on developing countries. In addition, he explores the particular problems that traditional pharmaceutical patent regimes pose for developing countries with low incomes and markets that are too small to induce research and development into treatments for diseases that affect mainly poor countries. Fink concludes with a review of policy options, both to stimulate increased innovative activity in areas of interest to developing countries and to ensure that existing pharmaceuticals are available at affordable prices to the poor of those countries.

Kimberly Elliott
Center for Global Development
June 4, 2008

1. Introduction

People in the poorest countries still live 20 fewer years on average than those in rich countries and they continue to suffer and die from diseases that have been largely conquered in rich countries. Of the 5 million people that die each year from AIDS, malaria, and tuberculosis, virtually all of them (97 percent) live in countries with average incomes below \$3,600 per year.¹ In addition, people in developing nations suffer from the chronic illnesses also found in the developed world: cardiovascular diseases, diabetes, cancer, and other diseases.

To some extent, poor health is the direct result of economic underdevelopment. Poor people often live in rural areas with only limited access to medical facilities. Even where such facilities are available, they most often cannot afford the best medical treatment that today's technologies can offer. Insufficient education about medical conditions and available solutions further add to the health challenges directly attributable to economic underdevelopment. That said, health outcomes are not only the result of economic performance. Being poor does not necessarily condemn people to being sick. Indeed, one of the few development success stories of the past decades has been the improvement of health outcomes in countries which have seen little overall economic development. For example, life expectancy in the group of least developed countries increased from 40 years in 1960 to more than 50 years in 2000 and infant mortality fell from 172 to 102 deaths per 1,000 births.² In other words, health interventions can make an important contribution in improving poor people's quality of life.

Vaccines and drugs are an important element of such interventions. For example, the eradication of smallpox in the 1970s involved widespread vaccination of populations in affected countries. The introduction of the drug ivermectin by pharmaceutical company Merck in 1988 has made important strides in reducing morbidity and infection rates from river blindness. Similarly, treatment of patients infected with the AIDS virus using antiretroviral drugs can delay the onset of the disease and reduce the risk of transmitting the virus.

Effective use of pharmaceutical solutions to the world's health problems embeds two distinct objectives: widespread access to existing medicines and the development of new drugs and vaccines against conditions for which no pharmaceutical solutions are currently available. However, there is a tension between these two objectives. The most frequently used mechanism for stimulating research and development (R&D)—temporary market exclusivity conferred by invention patents—leads prices for newly invented pharmaceutical products to exceed their production costs, raising questions of affordability for poor patients.³

¹ Levine (forthcoming); Over (forthcoming).

² These numbers were taken from the World Bank's World Development Indicators database. More generally, Kenny (2005) argues that quality of life variables such as health have been converging for some time, even as incomes have diverged.

³ Laxminarayan, Over, and Smith (2005) point to another tension in promoting widespread access to medicines: cheaper prices may encourage drug misuse, leading to a more rapid development of drug resistance and thus a shortened duration of a drug's usefulness.

Conflicts between innovation and access objectives are on the rise. Prompted by US (and European) demands, the Uruguay Round of international trade negotiations (1986-93) established new norms for the protection of intellectual property, including patents on drugs. Recent US Free Trade Agreements (FTAs) have introduced additional health-related intellectual property obligations for a number of US trading partners. The new global intellectual property regime has begun to impact on prices in developing countries. Concerned about adverse consequences for drug access, a number of developing countries have in recent years decided to override the market exclusivity of patent drugs—to the celebration of health activists and to the dismay of pharmaceutical companies.

What precisely is the nature of the global policy shift on intellectual property? Does it promote social welfare? This paper offers an overview of this debate and puts forward several recommendations for policymakers on how innovation and access objectives can be better reconciled. Even though much of the paper's discussion is of general applicability, I place a special focus on the implications of US policy and, in the end, develop several policy proposals specific to the United States.

The paper is organized as follows. The next section will review the evolving global intellectual property regime for pharmaceuticals. In doing so, it will discuss the key obligations and flexibilities under the intellectual property accord that came out of the Uruguay Round and outline how recent US FTAs have introduced even stronger standards of protection. In Section 3, I turn to the economics of pharmaceutical innovation and pricing. In particular, I will discuss the main advantages and drawbacks of the patent system, highlight concerns specific to developing countries, and briefly outline alternatives to the patent system for promoting drug innovation. The final Section 4 will outline several policy recommendations, divided in those applicable to developing country policymakers and those specific to the US.

2. Evolving rules: TRIPS and US FTAs

Trade agreements have brought about substantial changes in the rules governing intellectual property rights for pharmaceutical products. At their core, these rules determine whether drugs are supplied under market exclusivity or in a competitive market involving generic producers. Precisely understanding which products are subject to market exclusivity in a particular country at a particular point in time and what flexibility that country's government has in introducing generic competition involves arcane legal details. In this section, I summarize the evolving global intellectual property regime for pharmaceutical products, focusing on the situation of developing countries. In doing so, I advance two propositions:

- While key rules changes have already had an effect on the supply of certain pharmaceutical products, most of their impact will only materialize in the next 10 years.
- Even though developing country governments have considerable *legal* flexibility in overriding market exclusivity, it is uncertain how effectively they will be able to exercise this flexibility.

The TRIPS Agreement

The most natural starting point for understanding global intellectual property rules is TRIPS—the World Trade Organization’s Agreement on Trade Related Aspects of Intellectual Property Rights. TRIPS was a product of the Uruguay Round of Trade Negotiations and constituted one of the major demands of the United States and other developed countries for agreeing to the elimination of global textile quotas. Among its most important provisions, TRIPS requires World Trade Organization (WTO) members to provide for 20 years of patent protection without discrimination as to the field of technology. In other words, countries could not any more exclude pharmaceutical products from eligibility for patent protection—as was previously practiced by a number of large developing countries, such as Argentina, Brazil or India.⁴ As I will argue below, it is this provision that has led to the most fundamental shift in the global intellectual property regime for pharmaceuticals.

The TRIPS Agreement did not come without flexibilities. First, reflecting long-standing practice in national patent laws, WTO members retain the right to issue so-called compulsory licenses—government authorizations to use patented subject matter without the consent of the patent holder. However, this right is disciplined in several ways. Such licenses have to be considered on their individual merit; governments cannot override exclusive patent rights on any product that comes onto the market without specific review and authorization. Rights holders have to be compensated through payment of an ‘adequate remuneration’. In addition, a reasonable attempt first has to be made to obtain a voluntary license from the patent holder. This latter requirement can be waived in the case of national emergency or other circumstances of extreme urgency or in cases of public non-commercial use. It is important to emphasize that TRIPS does not restrict compulsory licenses to emergency situations, as is often wrongly asserted in journalistic writings on global intellectual property rules. Emergency situations merely trigger the additional flexibility of not first seeking a voluntary license.

Second, the Agreement did not apply to subject matter that was already in the public domain at the time TRIPS requirements became effective. In other words, pharmaceutical compounds that were open to generic competition before the implementation of TRIPS did not benefit from patent exclusivity. Importantly, this group of compounds includes many products on essential drug lists. In addition, the provisions of TRIPS entered into force on a staggered schedule. For developed countries, the agreement’s obligations became applicable at the beginning of 1996. Least-developed countries (LDCs) are still entitled to a transition period ending in 2016, with the possibility of a further extension. Developing countries other than LDCs were allowed to delay the introduction of pharmaceutical product protection until the beginning of 2005. However, a convoluted negotiated compromise obliged developing countries that opted for this delay to

⁴ Admittedly, many developing countries already introduced pharmaceutical product protection before the conclusion of the Uruguay Round. Some governments faced bilateral pressure from the United States to do so in the context of the ‘Special 301 Annual Review’ of intellectual property rights enforcement by US trading partners; others may have changed their laws in anticipation of the signing of the TRIPS Agreement. In any case, TRIPS still marked an important landmark in these cases, as it cast 20 years of patent protection for pharmaceutical products into stone. Governments deviating from their TRIPS obligations are liable under the WTO’s dispute settlement mechanism with the possibility of other WTO members imposing punitive tariffs in case of non-compliance.

accept applications for pharmaceutical product patents during the transition period (so-called ‘mailbox’ patents) and grant exclusive marketing rights to these products.

To understand the practical implications of the transition period for (non-LDC) developing countries, one needs to appreciate that it usually takes 8-10 years from the grant of a patent before a new medicine is introduced in the market. Since important developing countries reformed their patent laws or adopted the provisional mailbox regime between 1996 and 2005, this means that market exclusivity has only started to kick in recently. For example, several of the second-line antiretroviral drugs introduced in recent years already benefit from patent protection in a number of developing countries. As time goes by, we can expect the share of medicines supplied under exclusive rights to rise, with the full impact of the TRIPS-induced rules changes materializing over the next 10 years.

Third, at the WTO Doha Ministerial Conference in November 2001, WTO members issued a special Declaration in which they agreed that “*the TRIPS Agreement does not and should not prevent members from taking measures to protect public health.*”⁵ The Declaration also reaffirmed the right of WTO members to grant compulsory licenses. While the Declaration does not offer much new in legal terms, it represented an important political milestone.⁶ In light of the spreading HIV/AIDS pandemic, governments and NGOs had expressed concern about higher prices and curtailed access to medicines upon implementation of their TRIPS obligations. Without this declaration, many developing country WTO members might not have agreed to the launching of a new multilateral trading round. Equally, the United States Government’s willingness to compromise on what pharmaceutical interests perceived to be a weakening of the TRIPS Agreement has to be seen in the special context of the Bush administration’s desire to launch this round, directly following the September 11, 2001 terrorist attacks.

Finally, in the run-up to the Doha Ministerial Conference, a special concern emerged that WTO members without pharmaceutical manufacturing capability might not be able to effectively use the compulsory licensing option. It was uncertain under the terms of the TRIPS agreement whether producers in another country would be allowed to export to the WTO member in question, if the product needed was under patent protection in that other country. The Doha Declaration established a mandate to negotiate a solution to this problem. The ensuing negotiations were marked by acrimonious debate. At one point, the United States alone opposed the proposed compromise, seeking to limit the scope of diseases to which the solution would apply.⁷ However, in the run-up to the Ministerial Conference in Cancún in September 2003, the United States dropped its opposition and WTO members agreed on a mechanism enabling

⁵ See Doha Declaration on the TRIPS Agreement and Public Health, available at http://www.wto.org/English/thewto_e/minist_e/min01_e/mindecl_trips_e.htm.

⁶ The Declaration extended the implementation deadline for LDCs until 2016 (as stated in the text; the original deadline in the TRIPS Agreement was 2006). In addition, where LDCs nonetheless provide for pharmaceutical patent rights, they are allowed to not enforce these rights.

⁷ See Abbott (2005) and Fink (2005) for a more detailed treatment of the August 2003 Decision.

countries without manufacturing the capability to import generic drugs—the so-called August 2003 Decision.⁸

In light of these efforts to reaffirm and expand the flexibilities under the TRIPS Agreement, it is natural to ask: have countries used these flexibilities? To some extent, the answer is ‘yes’. A number of developing countries have issued compulsory licenses in recent years, most prominently Brazil and Thailand (see Box 1). In addition, Rwanda on July 19, 2007 became the first country to notify the WTO of its intention to use the August 2003 Decision for the import of an antiretroviral drug from a Canadian generic manufacturer.⁹

Box 1: Examples of compulsory licenses

Compulsory licenses are not a new phenomenon brought about by the coming into force of TRIPS. For example, in the 1970s and 1980s, Canada made extensive use of compulsory licenses in the pharmaceutical and food industries. Between 1969 and 1992, the government granted 613 such licenses for the manufacture or import of medicines. In addition, competition authorities throughout the world regularly grant what amounts to compulsory licenses to remedy anti-competitive behavior in private markets.

Following the Doha Declaration in 2001, several developing countries have granted compulsory licenses on antiretroviral drugs for the treatment of HIV/AIDS. These countries include Zimbabwe (2002), Malaysia (2003), Indonesia, Mozambique and Zambia (2004), Eritrea and Ghana (2005), Thailand (2006/2007), and Brazil (2007). In most cases, the authorizations in question were for government use, enabling the purchase of generic medicines for public treatment programs. Patent holding companies continued to enjoy market exclusivity in private markets (where such private markets existed). As mentioned in the text, governments mostly relied on imports from Indian companies in sourcing the generic drugs.

The recent cases of Thailand and Brazil generated substantial media interest and strong reactions from pharmaceutical patent holders on one side and health activists on the other. Brazil had previously used the threat of compulsory licensing in its price negotiations with pharmaceutical companies—for example, prompting Roche to offer a 40 percent price reduction on its AIDS drug nelfinavir in 2001. However, it had never issued such a license before. Thailand issued three government use licenses within a two-month period. As an important precedent, one of those licenses pertained to the drug clopidogrel produced by Sanofi-Aventis—a drug to fight heart disease. Subsequent to the issuance of the compulsory licenses, Abbott—the patent holder of one of the other two drugs subject to compulsory licensing—announced it would withdraw

⁸ The August 2003 Decision takes the form of a waiver to existing TRIPS rules. In 2005, WTO members decided to amend the TRIPS Agreement in light of the August 2003 Decision. This amendment has not yet taken legal effect, as it has not been ratified by the required two-thirds of members. In the meantime, the August 2003 Decision continues to apply.

⁹ See WTO Document IP/N/9/RWA/1. Three months later, Canada notified the WTO that it has granted a compulsory license so that the generic manufacturer—Apotex—can make the drug for export to Rwanda (see WTO Document IP/N/10/CAN/1).

applications for marketing approval of seven new drugs. It justified its move by arguing that the Thai Government “*decided not to support innovation by breaking the patents.*”¹⁰

Finally, questions of compulsory licensing of life-saving medicines surfaced in the United States in 2001, when several letters containing anthrax spores were mailed to a number of news media offices and to two US Senators. Some parts of the US Government advocated the grant of a compulsory license on the antibiotic drug ciprofloxacin. Bayer, the patent holder, subsequently agreed to supply the drug at a heavily discounted price to the US Department of Health and Human Services (HHS). The US Government later stated that it “*never threatened to break Bayer’s patent.*” However, in a January 2002 filing with the US Securities and Exchange Commission (SEC), Bayer informed investors that “*... in response to the recent bioterror attacks in the United States, the U.S. and Canadian governments contemplated compulsory licensing of our ciprofloxacin antibiotic—in effect, permission to generic manufacturers to market ciprofloxacin before the expiry of our patent rights.*”^a

^a See <http://www.os.dhhs.gov/news/press/2001pres/20011024.html>, http://www.ustr.gov/Document_Library/Press_Releases/2001/November/TRIPs_Health_Emergencies.html, and www.investor.bayer.com/user_upload/469/

Sources: Fink (2005), Oh (2006), Reichman and Hasenzahl (2002), and www.cptech.org/ip/health/cl/.

The experience thus far needs to be put in perspective, however. As already pointed out, much of the impact of TRIPS-induced patent reforms has only started to kick in recently. As new medicines addressing health concerns of developing countries come onto the market, controversies over drug prices are bound to intensify and more countries may resort to compulsory licenses. At the same time, broader patent coverage of new drugs in the developing world will also render the use of this option more difficult. In most recent cases of compulsory licensing, including Brazil and Thailand, governments relied on importation of relevant generic medicines from India, where they were still available generically. As more and more drugs will benefit from patent protection in the developing world, it will become harder for governments to use compulsory licensing because they can no longer draw on already existing generic supplies. Indeed, as one of the largest producers of generic medicines worldwide, the evolving patent landscape in India plays a crucial role in this context. I describe India’s special situation in Box 2.¹¹

How difficult will it be for a government to grant a compulsory license in the absence of existing generic supplies? Depending on the pharmaceutical compound in question, it may easily take a year or more for a generic manufacturer to reverse-engineer the product and deliver quality medicines. Ensuring interim supplies from the patent holding firm and finding generic

¹⁰ See <http://www.medicalnewstoday.com/articles/65274.php>.

¹¹ China also has significant capacity in pharmaceutical production and is becoming more important as a source of generic medicines. However, China introduced pharmaceutical product patent protection in 1993, before joining the WTO. As such, generic versions of medicines patented over the past fifteen years are not generally available from China.

companies willing to take on the business risk involved—especially if the quantities involved are small—may not be straightforward. Use of the August 2003 Decision involves additional procedural requirements and the cooperation of governments, though these hurdles seem manageable in relation to the commercial constraints involved.

Box 2: IPRs developments in India

India hosts one of the world's most dynamic pharmaceutical industries. Having experienced rapid growth at more than 15 percent annually in the 1990s, the industry's overall production value in 2003 stood at \$7 billion. The sector is made up of more than 20,000 companies, though the majority of production is accounted for by 250-300 large companies. Exports have grown rapidly and pharmaceuticals now represent India's second largest export industry. Companies such as Ranbaxy, Cipla, and Dr. Reddy's Laboratories have become household corporate names in international pharmaceutical markets. The US Food and Drug Administration (FDA) has approved more than 100 Indian drug manufacturing facilities—the largest number outside the United States.

Much of the success of the Indian industry can be traced to the Indian Patent Act of 1970, which abolished patent protection for pharmaceutical products (though other factors also played a role). Indian companies excelled at quickly reverse-engineering new pharmaceutical compounds patented abroad and producing quality products at competitive prices, including active pharmaceutical ingredients. It is thus not surprising that the implementation of the TRIPS pharmaceutical obligations proved controversial in India—involving several rounds of legislative reforms, acrimonious debate, and even one WTO dispute.

In a nutshell, India initially opted for the 'mailbox' transition mechanism, allowing pharmaceutical companies to file patent applications for later examination. Full pharmaceutical product patent protection only became available with the 2005 amendments to the Indian Patents Act. Significantly, the March 2005 amendment contained a provision allowing Indian manufacturers to continue generic production of drugs for which 'mailbox' patents are granted, under certain conditions. It is unclear how many pharmaceutical compounds were affected by this provision, though it may have served to reduce the number of medicines supplied under market exclusivity in the short term.

India's new patent law came to a critical test in 2006, when the multinational company Novartis sued the Government, alleging that India's standard of patentability is unconstitutional and not in compliance with TRIPS. Previously, the Indian Patent Office in Chennai had rejected Novartis' patent application for the leukemia drug Gleevec/Glivec on the grounds that the claimed molecule was only a new form of a known substance which did not show any enhancement of efficacy. Novartis' court challenge quickly stirred heavy protest from health activists and politicians all around the world. Among others, the European Parliament and several US Congressmen called on the company to drop the case. In 2007, the Chennai High Court dismissed Novartis' challenge, saying that the law's standard of patentability is constitutional and that it had no jurisdiction on whether Indian patent laws complied with TRIPS rules. Novartis decided not to appeal.

Looking ahead, recent data suggest that India's 2005 patent reforms are already having a noticeable impact. In 2004, Indian companies introduced 2,878 'copy-product' brands for pharmaceutical compounds first launched in prior years. By 2006, that number had fallen to 2,076—a one-third drop. As time goes by and an increasing number of pharmaceutical compounds will benefit from patent protection, there will likely be adjustment pressure in the Indian industry. At the same time, there will still be substantial demand for older drugs where patents have expired and Indian companies are well-placed to expand in international markets for these drugs. Some of the larger companies are also stepping up their own R&D efforts and they may in the long term emerge as players in the research-based industry segment.

Sources: Amin (2007), IMS (2006) and Sampath (2006).

Somewhat ironically, LDCs could emerge as a new source of generic medicines, given that TRIPS does not yet require them to protect or enforce pharmaceutical patents. In selected LDCs, some pharmaceutical production capacity is already available, though it typically does not extend to the technologically more complex production of active pharmaceutical ingredients and companies often do not meet standards of quality and compliance with Good Manufacturing Practices. At the same time, the market opportunity created by the special status of LDCs under TRIPS may well lead technologically more advanced generic producers to invest in LDCs, helping to alleviate these constraints.

In sum, TRIPS—the result of multilateral trade negotiations which ended more than 10 years ago—is beginning to affect the supply of newly marketed pharmaceutical products and controversies about drug prices in developing countries are bound to intensify in the coming years. While developing countries have the legal option to resort to compulsory licensing to have drugs produced competitively, it remains uncertain how effectively they can make use of this option—especially in the absence of generic supplies from India.

US Free Trade Agreements

Since the end of the Uruguay Round, the United States has concluded bilateral and regional free trade agreements (FTAs) with seventeen trading partners, although three agreements still need to be approved by the US Congress. FTA negotiations with additional trading partners have been launched, but these have not led to the conclusion of any agreement (see Table 1).

Table 1. Recent U.S. Free Trade Agreements

FTA signed and approved by US Congress	FTA signed, but not yet approved by US Congress	FTAs negotiations launched, but no agreement concluded
Jordan (2001) Singapore (2003) Chile (2003) Morocco (2004) Australia (2004) DR-CAFTA (Dominican Republic, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, 2005) Bahrain (2006) Oman (2006) Peru (2007)	Colombia Korea Panama	Malaysia Thailand Southern African Customs Union (SACU) United Arab Emirates Free Trade Agreement of the Americas

Source: United States Trade Representative (www.ustr.gov).

A central element of US FTAs is the establishment of intellectual property standards which go beyond those set in the TRIPS Agreement. A number of these so-called TRIPS-plus standards serve to broaden and strengthen the exclusive rights of pharmaceutical companies. While there is some variation, the TRIPS-plus provisions in FTAs have key elements in common:¹²

- Most agreements include a requirement to extend the patent term for delays in obtaining authorizations to market new drugs and to make patents available for new uses of known products. The latter requirement can lead to the *de facto* prolonging of a product’s patent life, as companies often seek patents for minor modifications of existing pharmaceutical compounds.
- Some agreements limit the use of compulsory licenses to emergency situations, anti-trust remedies, and cases of public non-commercial use.
- Most FTAs prevent marketing approval of a generic drug during the patent term without the consent of the patent holder. This provision—sometimes referred to as “regulatory

¹² Abbott (2004) and Fink and Reichenmiller (2005) offer more detailed overview of the different TRIPS-plus provisions found in US FTAs. In addition to intellectual property obligations, the Australia-US and the Korea-US FTAs establish separate rules for pharmaceutical reimbursement decisions under government-operated health care programs. These rules are mostly of a procedural nature. For instance, governments must permit pharmaceutical manufactures to apply for an increased reimbursement amount, based on the submission of evidence on a product’s safety and efficacy. On balance, these rules may strengthen the bargaining position of research-based pharmaceutical companies in reimbursement decisions, though their precise relevance does not yet seem clear.

linkage”—has at least two effects. First, it turns drug regulatory authorities into agencies enforcing patent rights. Since patents are private rights, the responsibility of enforcing them normally rests with the rights holders, relying on a country’s judicial system. Assigning a direct enforcement responsibility to drug regulatory agencies strengthens the position of rights holders, especially when patents are disputed. Second, it may render the use of compulsory licensing ineffective, as generic drug manufacturers benefiting from a compulsory license may not be able to obtain regulatory permission to enter the market.

- Most FTAs mandate the protection of test data submitted to regulatory agencies for marketing approval through exclusive rights lasting at least 5 years.¹³ Such exclusive rights may again pose an obstacle for governments to effectively use compulsory licensing, because generic suppliers may find it prohibitively expensive to generate their own test data for seeking marketing approval. In addition, pharmaceutical companies can benefit from market exclusivity even if they have not obtained any patent in a particular country.¹⁴
- Selected agreements introduce restrictions on the parallel importation of pharmaceutical products. As will be further discussed in the next section, restraints on parallel importation allow pharmaceutical companies to segment markets and charge different prices in different countries.¹⁵

The adoption of these TRIPS-plus standards in US FTAs has received much criticism, as they are seen to undermine developing countries’ flexibility to address public health needs and thereby contradict the spirit of the Doha Declaration.¹⁶ Over time, these standards also became controversial within the United States. The US Congress has over the past few years considered legislation that would have authorized the parallel importation of medicines from Canada and other countries. Concerned that such legislation would violate obligations under FTAs, Congress inserted language in a 2005 appropriations bill which effectively prohibits the Office of the United States Trade Representative (USTR) from negotiating FTA provisions that would block parallel imports of patented pharmaceuticals.¹⁷

More fundamentally, with Democrats winning both houses of Congress in the November 2006 elections, the Administration and Congressional leadership started to negotiate a new bilateral trade policy framework. The resulting May 2007 Bipartisan Agreement contains a number of

¹³ See ICTSD-UNCTAD (2005). TRIPS does not mandate test data exclusivity, but merely the protection of such data against unfair commercial use. For instance, India has adopted a mechanism for the protection of pharmaceutical test data that does not entail any exclusive right.

¹⁴ A number of US FTAs require the grant of test data exclusivity on an extra-territorial basis. Thus, competing generic manufacturers are prevented from using test data submitted to a drug regulatory agency in another territory (e.g., the US).

¹⁵ TRIPS does not have any obligation on the permissibility of parallel importation. It only requires countries not to discriminate in the application of their policies towards parallel importation. See ICTSD-UNCTAD (2005).

¹⁶ See, for example, MSF (2004) and Oxfam (2006).

¹⁷ See Abbott (2006).

flexibilities that roll back some of the TRIPS-plus provisions outlined above. Among other things, the Agreement eliminates the obligation to grant patent term extension for delays in obtain marketing authorization. Similarly, drug regulators would not be required any more to deny marketing approval based on a drug's patent status. Crucially, the Agreement creates an exception to test data exclusivity rules for measures to protect public health. In other words, the Agreement restores the ability of countries to make effective use of compulsory licensing.¹⁸

The immediate impact of the bipartisan trade deal will be limited, as it only applies to the FTAs negotiated with Colombia, Panama, and Peru (with the former two still awaiting ratification by the US Congress). However, the deal marks an important political shift in US trade policy towards greater sensitivity of public health concerns in global IPRs rules and may herald additional policy changes in the future.¹⁹

3. Economics of innovation and drug pricing

At the core of many of the controversies surrounding pharmaceutical policy lie several well-known market failures. It is worth briefly recalling these market failures:

- *Public goods nature of pharmaceutical research and development (R&D).* As first pointed out by Kenneth Arrow more than 40 years ago, knowledge possesses the classical characteristics of a public good—non-rivalry and non-excludability.²⁰ Left alone, private markets would under-provide knowledge in desired quantities. A company incurring the initial cost of generating knowledge is unable to recoup this cost, as competitors can free ride on the creator's efforts once the knowledge is public. This situation applies to pharmaceutical markets: it takes several years and billions of dollars to market a new drug; yet once that drug is on the market it is relatively easy and inexpensive for other companies to produce generic versions of it.
- *Uncertainty of R&D process.* At the time of discovery of a promising molecule, it is uncertain whether that promise will turn into marketable product. Indeed, in the overwhelming number of cases, it will not. Only few discoveries pass preclinical testing to enter the clinical trial stage. That stage is the most resource and time-consuming part of the R&D process. Yet again, many drugs do not survive clinical trials, as their hoped-for therapeutic properties are not confirmed or unacceptable levels of side effects emerge. By one estimate, out of 5,000-10,000 initially promising molecules, only five will enter clinical trials and only one pharmaceutical compound will gain marketing approval.²¹ Due to the large size of R&D outlays and contracting problems, no insurance markets exist that would protect firms against the risk that initially promising products do not reach the stage of commercialization.

¹⁸ See http://www.cpath.org/sitebuildercontent/sitebuilderfiles/2007_new_trade_policy_details5-10-07.pdf.

¹⁹ See Roffe and Vivas-Eugui (2007) for a more detailed review of the May 2007 Bipartisan Agreement.

²⁰ Arrow (1962).

²¹ See <http://www.phrma.org/files/RD%20Brochure%20022307.pdf>.

- *Asymmetric information between buyers and sellers of drugs.* Pharmaceutical products fall into a class of goods economists call experience goods. Simply by observing their physical characteristics, patients cannot tell whether different products can cure their ailments. Information asymmetries apply at two levels. First, patients usually do not possess the medical knowledge to assess which active pharmaceutical ingredient offers the best treatment, often leaving that choice to a doctor. Second, buyers of drugs cannot straightforwardly tell whether a product on the market contains the claimed active pharmaceutical ingredient or is a mere placebo, opening the door to trade in counterfeit medicines.

To respond to these market failures, governments intervene in a number of ways. Of primary interest in this paper is the grant of intellectual property rights—chiefly patents—for pharmaceutical inventions. In what follows, I first briefly review the general advantages and drawbacks of the patent system, then discuss how this system works for developing countries, and finally consider policy responses to the above market failures outside the patent system.

Advantages and drawbacks of the patent system

The idea of the patent system is well-known. By granting producers a period of exclusivity on newly invented drugs, they can recoup their initial R&D outlays and thus have an incentive to invest in R&D in the first place. In theory, benevolent governments can set the exclusivity period such that the resulting distortion of competitive markets and society's needs for inventions are optimally balanced.²² (In practice, such optimization rarely occurs and the current 20-year patent term reflects an outcome of history and politics). The patent system also addresses the second market failure of uncertain R&D outcomes. Through large R&D portfolios, companies can pool the risk of promising molecules failing at one point in the R&D process. Profits from the sale of products that succeed on the market can cover the costs of unsuccessful R&D undertakings.

The main advantage attributed to the patent system compared to R&D being undertaken by the public sector is that decisions on R&D investments are guided by the invisible hand of the private market. To the extent that society's preferences for new drugs are reflected in the willingness of patients to pay for them, profit-driving companies will invest in the development of those medicines that have the greatest societal value.

Unfortunately, the patent system also comes with substantial drawbacks. First, it offers little incentive to invest in R&D for drugs for which there is only a small commercial market—either because the diseases treated by these drugs are rare or patients suffering by from them are poor. At the same time, societies typically value the development of such drugs, out of compassion, or equity or public health concerns. Similarly, during the period of market exclusivity, drug prices typically far exceed marginal manufacturing cost, raising concerns about their affordability to poor patients.

²² This optimization problem was first formalized by Nordhaus (1969). See Langinier and Moschini (2002) for a review of the economic literature on the patent system.

Second, while benefiting from patent exclusivity, pharmaceutical companies generate substantial rents. While these rents have an economic logic—the recovery of fixed R&D outlays—they create incentives for economically inefficient behavior. For one, pharmaceutical companies have a strong incentive to heavily market their products. Compared to a firm selling in a competitive market, the equilibrium marketing investment by a firm with market exclusivity will be larger, because each additional sale generates larger rents out of which marketing investments can be financed.²³ The problem of asymmetric information outlined above makes pharmaceutical markets prone to marketing activities, with patent-holding firms sending out large sales forces to market their latest drugs to doctors and advertising directly to consumers through the media. By one estimate, the US research-based pharmaceutical industry spends a larger share of earnings on marketing (16 percent) than on R&D (13 percent).²⁴

The end result is that the promotional activities of pharmaceutical companies serve to enlarge their pricing hold. That, in turn, creates a distortion in the incentive to invest in pharmaceutical R&D. Companies may not necessarily invest in drugs for which society's true willingness to pay is highest, but those which can be most effectively marketed to large population segments.²⁵

The second form of inefficiency associated with large rents is political lobbying. The market failures outlined above imply heavy regulatory intervention by governments. For example, drug producers' bottom-line depends critically on the scope and length of patent protection, the decisions of drug approval agencies, the permissibility of marketing activities, price regulations, and reimbursement rules under public health programs. To the extent that political lobbying can influence the outcome of public policy, there is a strong incentive to invest in such lobbying. As in the case of marketing activities, the larger share of rents in each sale generated by lobbying activities increases the equilibrium investment in lobbying compared to a firm selling in a competitive market. Predictably, the pharmaceutical and health products industry ranked first in spending on lobbying activities in the US, investing close to \$1.2 billion between 1998 and 2007.²⁶

From this view, it is also not surprising that the research-based pharmaceutical industry has been a key supporter for the inclusion of IPRs obligations in trade agreements—where political lobbying is often seen as a legitimate tool to promote free trade. Similarly, pharmaceutical

²³ See Nelson (1970) for a formal treatment of this argument. Nelson also argues that in contrast to a producer in a competitive market, marketing investments by a firm with exclusivity can be more fully appropriated by that firm, rather than the firm's industry more broadly.

²⁴ As reported by *Frontline* documentary "The other drug war", June 19, 2003. (see <http://www.pbs.org/wgbh/pages/frontline/shows/other/>)

²⁵ Evidence of distortive marketing activities by research-based pharmaceutical companies has emerged from lawsuits challenging such behavior. For example, in a September 2007 settlement with the US Department of Justice, Bristol-Meyers Squibb (BMS) agreed to pay more than \$515 million to resolve allegations of illegal drug marketing and pricing. Among other allegations, the US Government accused BMS of having paid illegal remuneration to physicians and other health care providers to induce them to purchase BMS drugs. See http://www.usdoj.gov/opa/pr/2007/September/07_civ_782.html.

²⁶ See <http://www.opensecrets.org/lobbyists/overview.asp?txtindex=i>.

companies lobby governments to refrain from issuing compulsory licenses and controlling drug prices (more on these issues below).²⁷

Developing country concerns

The first drawback of the patent system raises concerns specific to developing countries: inadequate incentives for R&D into diseases specific to poorer countries and high prices undermining access to drugs by poor patients.

Table 2a presents available data for global pharmaceutical sales by countries' level of per capita income. These data were generously provided by IMS Health, the most comprehensive source of information on international pharmaceutical markets. The figures show a skewed distribution of these sales, with high income countries accounting for 85-90 of the global pharmaceuticals market. The remaining 10-15 percent share is largely accounted for by middle income countries. Low income countries represent less than 1.5 of worldwide sales.

Table 2a: Global sales of prescription medicines

Income group	2001		2004	
	Value, US\$ billion	Percent	Value, US\$ billion	Percent
Low-income (4 countries)	5.9	1.3	7.6	1.3
Middle-income (23 countries)	43.6	9.9	67.8	11.6
High-income (25 countries)	391.6	88.8	508.3	87.1
<i>Of which: United States</i>	<i>184.1</i>	<i>41.8</i>	<i>250.8</i>	<i>43.0</i>
TOTAL	441.0	100.0	583.7	100.0

Source: Based on IMS Health data in a communication with the author, covering retail sales and, where available, sales by hospitals.

To some extent this skewed distribution reflects a bias in the availability sales data: the low income group is made up of just 4 countries and the middle income group consists of only 23 countries. The size of this bias is likely to be small, however. Using the IMS Health data and population figures from the World Bank, I calculated per capita sales for the different income groups and then applied the resulting figures to the total population figures in those groups (including the countries for which no sales data are available). The resulting imputed market

²⁷ The large share of rents in pharmaceutical sales also explains why drug companies vigorously defend their market exclusivity by challenging the entry of generic producers in courts. Even a few days of extended market exclusivity can generate millions of dollars of rents sufficient to finance expensive law suits. When the prospects of winning a court case are small, innovative drug producers have a strong incentive to settle with generic producers and share the patent rents—a practice that has caught the attention of the US Federal Trade Commission. See <http://www.ftc.gov/opa/2007/01/leibowitztestimony.shtm>.

shares are shown in Table 2b. The share of high income countries decreases by no more than 1.3 percentage points.²⁸

Table 2b: Estimated global sales of prescription medicines

Income group	2001		2004	
	Value, US\$ billion	Percent	Value, US\$ billion	Percent
Low-income	9.2	2.0	11.9	2.0
Middle-income	47.8	10.4	74.7	12.3
High-income	402.8	87.6	523.1	85.8
<i>Of which: United States</i>	<i>184.1</i>	<i>40.4</i>	<i>250.8</i>	<i>41.1</i>
TOTAL	459.8	100.0	609.7	100.0

Interestingly, the United States accounts for nearly one-half of sales in high income countries, a significantly larger share than two or three decades ago.²⁹ At their face values, these figures suggest that it is most profitable for pharmaceutical companies to gear their R&D efforts towards the health needs of developed countries, and within the developed countries to focus on the demands of the American market.

In principle, the skewed distribution of pharmaceutical purchasing power would not pose a problem if rich and poor countries faced a similar health burden. Indeed, there are a number of diseases with large numbers of vulnerable populations in both rich and poor countries—called “type 1” diseases by the World Health Organization (WHO). Examples of such diseases include non-communicable illnesses such as measles, hepatitis B, diabetes, cardiovascular diseases, and tobacco-related illnesses. However, there are also diseases which mainly affect poor countries, mostly communicable illness. The WHO considers “type 2” diseases to be those for which poor countries account for a great majority of cases and “type 3” diseases are those that are overwhelmingly or exclusively found in poor countries. Examples of a “type 2” disease are HIV/AIDS and tuberculosis, while “type 3” diseases include African sleeping sickness and African river blindness.³⁰

The patent system does not offer adequate incentives for investing in R&D for treatment of such diseases. Even if patents were available throughout the developing world and remained

²⁸ A second bias may stem from the fact that price discounts extended by pharmaceutical companies are not always captured by IMS audits, inflating sales figures in some countries. Educated guesses suggest that this type of sales inflation may be more pronounced in developed countries, though its precise empirical significance is not clear. Finally, sales data from IMS are incomplete, because hospital sales are not recorded in some countries and sales to the public sector are generally excluded. However, it is not clear whether these omissions would necessarily lead to an upward bias in the global market share of high income countries.

²⁹ Using a different sample of countries, WHO (2004) estimates that the share of the US market in global pharmaceutical sales has increased from 18 percent in 1976 to 53 percent in 2000.

³⁰ See WHO (2006).

undiluted by compulsory licenses, pharmaceutical companies—accountable to private shareholders—will direct their R&D activities mainly towards “type 1” diseases. To put it starkly, commercial incentives are such that pharmaceutical companies are more likely to direct investments towards treatments for erectile dysfunction than treatments for malaria. Reflecting these incentives, patenting related to tropical diseases, for example, has never exceeded more than about half of a percent of overall pharmaceutical patenting.³¹ Below, I will outline alternative funding and incentive mechanisms for R&D into “type 2” and “type 3” diseases.

The second concern related to the patent system is that prices far above marginal cost will not be affordable to most consumers in poor countries. In many developing countries, health insurance coverage is limited and patients often pay for drugs out-of-pocket. While many developing countries have public health programs for HIV/AIDS, tuberculosis, and malaria, the reach of these programs is not universal and depends on the price governments pay for needed medicines. As discussed in the previous section, concerns about high prices for antiretroviral drugs have led several developing countries to grant compulsory licenses in recent years.

One important question in this context is whether drug companies will establish differentiated pricing structures, with lower prices charged to poorer countries. Such an outcome is, in principle, consistent with profit-maximizing behavior. Economists refer to this practice as discriminatory pricing and it occurs when markets are segmented (i.e., no arbitrage between markets is possible) and firms have market power. In theory, under these conditions a firm will set lower prices in countries with higher demand elasticities. If these elasticities vary inversely with countries’ per-capita incomes, a profit-maximizing discriminatory pricing structure would appear to be consistent with equity objectives. It could also increase economic welfare, as explained in Box 3.

Box 3: Does free-market discriminatory pricing coincide with Ramsey pricing?

Some commentators have likened a free-market discriminatory pricing structure to the concept of Ramsey pricing (see, for example, Scherer and Watal, 2002, and Danzon, 2007). This concept has its origins in the design of a pricing structure for regulated public utilities that need to recover a fixed infrastructure cost. Constrained optimization leads to discriminatory pricing whereby consumers with higher demand elasticities pay less. The underlying logic is that recovery of the fixed costs requires prices above marginal cost and it turns out that discriminatory prices minimize the consumption distortion inherent in above-marginal cost pricing.

At first, this situation bears similarity to the problem of recovering a fixed R&D cost in pharmaceutical markets. However, there is a crucial difference. Ramsey prices are prices set by a regulator and not determined by market forces. Indeed, Ramsey prices have the same relative structure as free-market discriminatory prices set by a monopolist, but they are lower in absolute terms. Danzon recognizes this difference, but then goes on to argue that competition between therapeutic substitute drugs drives free-market discriminatory pricing down to a level where they

³¹ See Lanjouw and Cockburn, 2000.

are “similar” to Ramsey prices. This argument seems conceptually problematic, however. The level of Ramsey prices depends on the size of the fixed costs to be recovered. This size—the allowable patent rent—is not exogenously given, but itself a choice of policy.

Traditionally, the economic literature has modeled that policy choice by the length of the patent term, assuming that prices are set by market forces. But it is equally possible to take the length of the patent term as given and adjust—up to the free-market upper bound—the patent rent by regulating prices. In fact, policymaking in the real world appears to approximate the latter situation. While the patent term in most countries is fixed at 20 years across all fields of technology (and a minimum of 20 years is cast in stone in the TRIPS Agreement), most governments have chosen to regulate pharmaceutical prices, at varying levels. (That said, national price regulations are most often rooted in containing expenditure on healthcare rather than in following some global Ramsey pricing rule.)

In any case, free-market discriminatory pricing will only coincide with Ramsey pricing if the corresponding patent rent is exactly at the socially optimal level. That will usually not be the case. If it is too low, free-market discriminatory pricing will be the constrained optimum, though it will provide socially inadequate R&D incentives. If it is too high, Ramsey pricing calls for lower regulated levels of prices. If regulated Ramsey pricing is not feasible, free-market discriminatory pricing may or may not lead to higher welfare than uniform pricing. Consumers in low price countries and companies will be better off under discriminatory pricing, whereas consumers in high price countries usually will be worse off.³² The effect on overall world welfare is ambiguous and will depend on the shape of countries’ demand functions (Malueg and Schwartz, 1994).

Unfortunately, such an outcome is not guaranteed. Discriminatory prices in the countries with the highest demand elasticity may still be far above marginal cost and the poorest segments of society may still not have access to patented medicines. In addition, there is no guarantee that demand elasticities correlate (negatively) with countries’ per capita income. Such a correlation may hold for some demand functions, but not for others.

Is there any empirical evidence for differentiated pricing of patent-protected pharmaceutical products? The picture emerging from studies done so far is as follows. Scherer and Watal (2002) analyze the correlation between national wholesale prices for 15 antiretroviral drugs and countries’ per-capita income between 1995 and 1999.³³ While there are notable price variations across countries, they do not find a correlation between these two variables. This finding does not provide evidence against the hypothesis that countries price discriminate. But it would seem to question the hypothesis that demand elasticities correlate negatively with per-capita incomes

³² In some cases, free-market discriminatory pricing can even be Pareto-superior to uniform pricing—for example, when a small market would not be served if companies were forced to price uniformly (see Hausmann and MacKie-Mason, 1988).

³³ Wholesale prices, unlike retail prices, are likely to reflect discriminatory pricing decisions of pharmaceutical producers, as they are not directly affected by transport and distribution costs, volume discounts, purchasers’ solvency, import duties and other taxes.

or, at least, it suggests that other influences outweigh the influence of cross-country differences in demand elasticities. In any case, Scherer and Watal's result suggests that markets, left alone, do not provide for a pricing structure in harmony with equity considerations.

Evidence consistent with Scherer and Watal's finding is provided by Wong (2003). This study empirically assesses the effect of income inequality on drug prices in seven anatomical therapeutic categories in thirteen high- and middle-income countries for 1994 and 1998. While confirming that per capita income does not have any effect on ex-manufacturers' selling prices, the study finds that income inequality, as measured by the Gini-coefficient, has a positive and significant effect on these prices. This result suggests that pharmaceutical companies respond to local demand conditions, but the resulting pricing structure does not necessarily conform to equity considerations. Instead, Wong's finding is consistent with the notion that pharmaceutical companies target well-off population segments in lower income countries.

A more equity-consistent picture emerges from an analysis of price offers of first-line antiretroviral drugs from patent-holding companies to developing country governments, not-for-profit organization and international aid agencies.³⁴ Starting in 2000, several of these companies dramatically reduced their prices to eligible developing country governments—sometimes to levels representing a fraction of US retail prices. However, these special discounts seem to be at least in part brought about by competition from generic producers, as most first-line antiretroviral drugs were not patent protected in major developing countries in this period (see Section 2). Indeed, pricing discounts for second-line antiretroviral drugs—many of which benefit from patent protection in developing countries—seem far less pronounced.³⁵

The existing empirical evidence can thus be summarized as follows. Prices for patented pharmaceuticals do not appear to correlate with per capita incomes in private markets, though some income-oriented price discounting seems to occur in public markets. To the extent that poor people in poor countries benefit from access to medicines under public health programs and rich people buy their medicines in private markets, this outcome could still be argued to be consistent with economic efficiency and equity considerations. Unfortunately, such a conclusion is not warranted. As already pointed out, even poor patients often purchase their medicines in private markets. In addition, this approach is ad hoc and arbitrary and it is not clear that discounted price offers in the public sector are such that poor country governments can finance poor people's access to medicines on a sustainable basis.

As a final point, the apparent lack of per capita income-oriented discriminatory pricing in private markets may reflect what has been pointed out above: demand conditions being such that the companies' profit-maximizing strategy is to always focus on the richer market segments. However several other explanations are possible:

³⁴ In addition, Scherer and Watal (2002) cite a study undertaken by the John F. Kennedy School of Government, documenting discriminatory pricing according to countries' per capita incomes in the case of vaccines. Unfortunately, this study does not seem to be publicly available.

³⁵ These price reductions are documented in various editions of the publication "Untangling the Web of Price Reductions" by Médecines sans Frontières, available at www.accessmed-msf.org. See also Oxfam (2007).

- *Measurement problems.* The two studies discussed above rely on data supplied by IMS Health—the source offering the most comprehensive information on pharmaceutical markets worldwide. However, there are concerns about the comparability of price data across countries. One particular problem is the treatment of various forms of price discounts, which are often secret and not always reflected in the recorded data. If discriminatory pricing mainly occurs through these channels, it may not be observable in the data available from IMS Health.
- *Government price controls.* Many developed country and developing country governments have policies to contain drug prices, often directly controlling their levels. In other words, observed price differentials between countries may not reflect profit-maximizing behavior by pharmaceutical companies, but differences in government pricing policies.
- *Imperfect market segmentation.* As pointed out above, discriminatory pricing relies on market segmentation. If arbitrageurs can buy drugs in the low-price market and sell them on in the high-price country, it is optimal for a profit-maximizing firm to price uniformly across countries. In pharmaceutical markets, arbitrage occurs through so-called parallel trade. It is legal in some jurisdictions, for example within the European Union. At the same time, all developed countries restrict the parallel import of pharmaceutical products placed onto developing country markets (Fink, 2003).

Having said this, there may be other forms of international price spillovers. Lower drug prices abroad may result in political pressure to lower prices at home. It is difficult to empirically evaluate this hypothesis, except to note that high price jurisdictions like the United States have long faced lower prices abroad with little effect on domestic prices. More relevant may be price control regimes in a number of countries that are based on a basket of reference prices in foreign jurisdictions. Indeed, the current “web” of such price references is extensive.³⁶ Thus, pharmaceutical companies have to take into account the effect of their pricing strategy in one country for price controls in another country. The resulting pricing structure will likely be more uniform and geared towards the markets of richer countries. At the same time, reference-based price regulation schemes in OECD countries suggests that these developed countries confine the set of reference countries to other developed countries and do not include developing and least developed countries (see, for example, Productivity Commission, 2001). Thus, existing reference-based price controls do not seem to be a barrier toward North-South differential pricing.

More empirical research is needed to better understand the exact determinants of pharmaceutical companies’ pricing decisions.

³⁶ See Schonveld (2001).

Policy responses outside the patent system

The most obvious solution to the public goods problem of pharmaceutical R&D is public provision, financed by lump-sum taxation. Indeed, governments in the developed and developing world sponsor pharmaceutical R&D. According to a recent estimate, the public sector accounted for 45 percent of the US\$ 125.8 billion global spending on health-related R&D in 2003.³⁷ However, publicly sponsored medical R&D typically does not result in patent-free medicines coming onto the market. Most public sector funded R&D focuses on basic research, rather than developing promising molecules into marketable medicines. This pattern partly reflects the incentives of academia, which reserves rewards for scientific discovery, and the lack of expertise and financing to engage in resource-intensive clinical trials.

Research-based pharmaceutical companies, in turn, draw on scientific research to develop commercial products. However, they usually require promising discoveries to be patented, for otherwise they would not invest in the still risky development of marketable products. As a result, universities and public research institutes have aggressively sought out patents for the fruits of their research efforts. While these patents generate royalty income for scientific research laboratories, they also imply that taxpayers pay twice for medical R&D: first through government-sponsored scientific research and then through above marginal cost pricing of patented medicines.³⁸

In sum, unless governments are willing to finance the full R&D cycle, the commercialization of medical products will invariably involve patent ownership. Yet full public funding of the whole R&D process is unlikely to be a viable option—not least because governments are usually less well informed about society’s innovation needs than private markets. That said, a greater role for the public sector in drug development is desirable for those diseases for which the patent system fails to offer adequate incentives, especially the “type 2” and “type 3” diseases described above. Economists have developed several mechanisms in this regard, some of which have already been implemented.

First, publicly-funded research institutions may enter into collaborative agreements with private pharmaceutical companies for the development of treatments against a specific disease. *Public-private partnerships* (PPPs) may still involve the patenting of research outputs, but up-front contractual arrangements can provide for the distribution of medicines at preferential or cost-based prices to low-income countries.³⁹ An example of a PPP is the Global Alliance for Tuberculosis Drug Development, funded by the Bill and Melinda Gates Foundation, the Rockefeller Foundation, and a number of bilateral government donors. Three drugs are currently

³⁷ See De Fransisco and Matlin (2006).

³⁸ In the United States, the Bayh-Dole Act expressly encourages the private commercialization of publicly funded scientific research. In principle, the federal government retains so-called “march-in” rights to license inventions of government-contracted research institutes to third parties without the consent of the patent holder if it determines that such inventions are not being made available to the public on “reasonable” terms. However, the government has so far not made use of this “march-in” clause.

³⁹ The model adopted by several of public-private partnership ventures has some similarity to the ‘opt-out’ proposal by Lanjouw (2001). Under that proposal, pharmaceutical companies are forced to elect between developed or developing countries for exploiting their market exclusivity.

undergoing clinical trials under this initiative, with Bayer, Novartis, and biotechnology company Chiron as private partners.⁴⁰

Second, governments or aid agencies may make advance commitments on minimum purchases for new vaccines or drug treatments that meet certain pre-defined standards. The rationale for such guarantees is to reduce the uncertainty about future demand and thereby lower the risk of investments in relevant lines of R&D.⁴¹ Like the patent system, *advance market commitments* (AMCs) are a “pull” mechanism, seeking to create incentives for private R&D (as opposed to the “push” provided by a PPP). In fact, drugs benefiting from an AMC would normally be patented. However, as in the case of PPPs, up-front contractual arrangements can specify price ceilings and other conditions favoring drug access in developing countries. A pilot AMC project to develop a vaccine for pneumococcal disease is currently being tested by the Global Alliance for Vaccines and Immunization (GAVI) and the World Bank, with \$1.5 billion in funding from Italy, the United Kingdom, Canada, Russia, Norway, and the Gates Foundation.⁴²

Third, governments may create monetary prizes, which reward private companies for inventing drug treatments of benefit to society. In return for the prize money, companies would make their inventions freely available to the public, not involving any patents.⁴³ *Innovation prizes* are also a “pull” mechanism. Their main attraction is the avoidance of market exclusivity. Once approved by a regulatory authority, drugs would be supplied competitively, driving prices towards marginal costs. In addition, the absence of patent rents would reduce inefficiencies resulting from “excessive” investments in marketing and associated distortions in R&D incentives (see the discussion above). The idea of offering prizes for technological innovation goes back several centuries and has found application in many fields of technology.⁴⁴ Some promising prize initiatives already exist in the field of biomedical research.⁴⁵

While AMCs and innovation prizes offer solutions to some of the deficiencies of the patent system, it should be pointed out that they also come with certain drawbacks. Chiefly, in designing AMCs and innovation prizes, governments have to deal with the uncertainty of R&D undertakings. If purchase commitments or monetary rewards are overly generous, companies will generate large rents. If they are too small, companies may not be willing to invest. In addition, if complete contracting is not possible, problems of time consistency may well arise. Once a company has sunk its R&D investment and developed a new vaccine or drug treatment, governments have an incentive to renegotiate their original commitment. The history of similar incentive mechanisms in the defense industry illustrates that serious problems of incomplete

⁴⁰ See <http://www.tb Alliance.org/home/home.php>. Other public-private partnerships include the International AIDS Vaccine Initiative, the International Partnership for Microbicides, the South African AIDS Vaccine Initiative, the European Malaria Vaccine Initiative, the Malaria Vaccine Initiative, the Medicines for Malaria Venture, the Areas Global Tuberculosis Vaccine Foundation, the Foundation for Innovative New Diagnostics, and the Drugs for Neglected Diseases Initiative (WHO, 2006).

⁴¹ See Kremer (2002) for a more detailed discussion of this mechanism.

⁴² See http://www.vaccineamc.org/media/launch_event_01.html for more information.

⁴³ See Love and Hubbard (2007) for a more detailed treatment of innovation prizes.

⁴⁴ See the article “How prizes pushed progress,” available at <http://www.msnbc.msn.com/id/5191763>.

⁴⁵ See, for example, the Archon X Prize for Genomics (<http://genomics.xprize.org>).

contracting could emerge. Notwithstanding these drawbacks, there is substantial scope for these alternative “pull” mechanisms to create R&D incentives consistent with access considerations—particularly for “type 2” and “type 3” diseases.

4. Policy options

Section 2 argued that the coming years will likely see a larger number of innovative medicines receiving patent protection in developing countries, thus amplifying concerns about their affordability in those countries. At the same time, addressing the health burden in rich and poor countries will continue to require substantial investments in medical R&D. In this section, I put forward several suggestions for policy that seek to reconcile access and innovation objectives. I divide these suggestions into those applicable to developing country policymakers and those specific to the US.

The developing country agenda

To begin with, many developing countries have not implemented available flexibilities under the TRIPS Agreement in their national laws and regulations.⁴⁶ This deficit should be remedied. Of particular relevance are laws enabling governments to make effective use of compulsory licenses. In this context, it is surprising that many developing countries invested significant negotiating resources in the August 2003 Decision, but so far only 14 countries have ratified the subsequent amendment of the TRIPS Agreement (of which 10 countries are high income countries).⁴⁷

From an economic and equity viewpoint, a case in favor of compulsory licenses can be made. Limited health insurance coverage and the incomplete reach of public health programs mean that prices have important ramifications for poor people’s access to medicines. Even if compulsory licenses are rarely used, a credible threat to issue them can be an important bargaining tool for governments in price negotiations with patent-holding firms. Since most developing countries represent tiny shares in global pharmaceutical sales, their use of compulsory licenses is unlikely to have a significant effect on global incentives for R&D into “type 1” diseases. In addition, the size of developing country markets is too small to offer incentives for R&D into “type 2” and “type 3” diseases, warranting alternative incentive and funding mechanisms.⁴⁸

Admittedly, free use of compulsory licenses raises a collective action problem. Even though most developing countries are individually too small to materially affect the bottom-line of

⁴⁶ See Musung and Oh (2005).

⁴⁷ See http://www.wto.org/english/tratop_e/trips_e/amendment_e.htm (visited February 7, 2008). The amendment will only come into force once it has been ratified by two thirds of WTO members.

⁴⁸ Compulsory licenses may raise the concern of harming a developing country’s attractiveness to foreign direct investment (FDI). At the end of the day, this is an empirical question. However, it is worth noting that rational investors are unlikely to interpret a compulsory license to address a specific health need as a broader signal towards weaker protection of property rights. In addition, since pharmaceutical R&D is a global public good, one country’s compulsory licensing decision should not have an effect on a companies global R&D location decisions.

research-based pharmaceutical companies, as a group they do. Since developing countries benefit from new treatments against “type 1” diseases, it seems only fair—and indeed, economically desirable—for at least the middle income countries to share the burden of R&D costs. In an ideal world, such burden sharing would be effectuated through Ramsey pricing, whereby prices depend on local demand elasticities (see Box 3).⁴⁹ Even though the evidence discussed in the previous section points to substantial price variations, it does not lead to the conclusion that current international pricing structures approximate a Ramsey scenario. In the absence of any international framework outlining what would be considered Ramsey-type price levels, it seems hard to deny individual countries the right to determine for themselves whether free-market prices imply the right level of burden sharing. That said, it would be desirable in the longer term to develop an international framework that could lead to more objective criteria triggering the use of compulsory licenses.

The same type of reasoning applies to price control policies. Like compulsory licenses, they are an effective tool to reduce prices for patented medicines from the free-market levels. Indeed, the majority of countries—both developed and developing—regulate pharmaceutical prices in some form. However, some developing countries do not (e.g., Malaysia). While often seen as inimical to a market economy, price regulations for pharmaceuticals can be justified on economic grounds. As explained in Box 2, Ramsey prices are, in fact, regulated prices, not free-market prices. Of course, uncoordinated national price controls are unlikely to lead to a pattern approximating a global Ramsey price structure.⁵⁰ From this view, it would again be desirable to develop an international framework guiding countries on what such a structure might look like.

In implementing compulsory licensing and price control policies, developing country policymakers should comprehensively review their national health burden, available financing mechanisms for pharmaceuticals, and the cost effectiveness of drug treatment programs. Much attention has centered on the three killer diseases—HIV/AIDS, tuberculosis, and malaria. As described in Box 1, almost all of the post-Doha compulsory licenses have pertained to antiretroviral drugs and have been confined to government use. While the high incidence of HIV/AIDS in large parts of the developing world appears to justify this focus, there is still debate among economists about the cost effectiveness of treatment programs for HIV/AIDS, even at the lowest prices.⁵¹ In any case, other communicable and non-communicable diseases such as heart diseases and diabetes account for significant parts of the health burden in most developing countries. Governments need to carefully analyze the effects of drug prices on medicines access and health outcomes in both private and public markets and act accordingly.⁵²

⁴⁹ Jack and Lanjouw (2003) show that distributional concerns can be incorporated into a Ramsey pricing approach, such that prices in the poorest countries could even be below marginal production cost.

⁵⁰ Having said this, in the European Union, price ceilings tend to be lowest in the relatively poorer member states where market demand is likely to be more elastic (Stegemann, 2007).

⁵¹ Some economists argue that scarce financial resources should be directed mainly at prevention efforts. See Fink and Bell (2005) for a review and Over (forthcoming).

⁵² Such analyses should also take into account the effect of medicines access on drug misuse and the development of drug resistance, as discussed by Laxminarayan, Over, and Smith (2005) for the case of malaria treatment.

One critical question raised in Section 2 is how developing countries can make effective use of compulsory licensing in a situation where there may be no supplies of quality-certified generic drugs available anywhere in the world. Small scale production for selected markets may be associated with increased manufacturing cost and substantial business risk. It is too early to tell to what extent these commercial obstacles prove to be prohibitive. One way of making compulsory licensing more attractive to generic suppliers may be to pool the demand for drugs from different countries, using regional procurement systems or bulk orders from international development agencies.⁵³ However, such an approach could necessitate the coordination of compulsory licenses among developing country governments.⁵⁴

Finally, developing countries should have an interest in promoting alternative R&D mechanisms for developing drugs treating “type 2” and “type 3” diseases. Indeed, research institutes from larger developing countries already participate actively in some of the existing initiatives.⁵⁵ Strategies towards addressing health conditions disproportionately affecting developing countries are currently being discussed in a WHO Intergovernmental Working Group on Public Health, Innovation and Intellectual Property. This Working Group offers developing countries an opportunity to raise the profile of alternative R&D mechanisms and, in the longer term, mobilize financial support for existing and new programs.

The US agenda

The United States plays a crucial role in the global pharmaceutical market. As pointed out in the previous section, the US market accounts for nearly half of global sales and, as such, shapes R&D incentives for “type 1” diseases. Drug prices in the United States are not controlled, leading price levels to exceed those of most other nations in the world. High US prices have the potential to undermine discriminatory pricing strategies, as pharmaceutical companies fear direct or indirect price spillovers from low price jurisdictions.

High drug prices are also a significant concern in the US domestic healthcare system, with significant numbers of Americans being uninsured and employers cutting back health insurance in light of rapidly increasing healthcare costs. Healthcare reform is high on the US political agenda, with presidential candidates putting forward different visions for reform. The pros and cons of different proposals involve complex trade-offs, which go beyond the scope of this paper. I focus here on two issues that have potential implications for developing countries.

First, there seems substantial scope to improve the allocation of R&D investments by promoting a more rational selection of drugs. As discussed in Section III, information asymmetries and the presence of large patent rents have led research-based pharmaceutical companies to invest heavily in marketing their patented medicines. While marketing activities offer certain benefits in providing market participants with critical information about drugs, they also create a severe

⁵³ The United Nations Children’s Fund (UNICEF) and the Clinton Foundation already offer this possibility.

⁵⁴ Abbott and Reichman (2007) discuss possible mechanisms through which such coordination could be achieved.

⁵⁵ For example, the founding partners of the Drugs for Neglected Diseases Initiative include the Oswaldo Cruz Foundation from Brazil, the Indian Council of Medical Research, Malaysia’s Ministry of Health, and the Kenyan Medical Research Institute.

principle agent problem when doctors prescribe medicines to patients. There are several options for promoting a more rationale selection of drugs. One is to more tightly regulate the marketing activities of companies. Another is to promote independent assessments of the cost-effectiveness of alternative treatments. Canada, Australia, New Zealand, and the UK possess institutions that perform such a task and their evaluations often serve as an input into reimbursement policies under government-sponsored health insurance plans.⁵⁶

On balance, more rational drug choices would help contain drug prices. In addition, it would offer incentives away from R&D for treatments that offer only minor improvements over already existing drugs towards more risky lines of R&D that have the potential to yield more radical pharmaceutical breakthroughs. Given the size of the US market, such an outcome would be of benefit to other developed and developing countries as well.

Second, seeking to lower prices of prescription medicines, the US Congress has in recent years considered legislation to authorize parallel imports, mainly from Canada and other developed countries. From a purely economic point of view, such a move seems questionable. The main source of lower prices in the relevant foreign countries is drug price regulation. In other words, parallel imports would import foreign price controls into the US. In this case, why not establish price controls in the United States—especially if parallel imports raise additional regulatory issues and may lead to curtailed supplies in the exporting country?⁵⁷ The answer appears to be political feasibility: there may be a Congressional majority for allowing parallel imports, but not for introducing domestic price controls. It is likely that developing countries would at least initially be excluded from any move permitting parallel drug imports. However, once implemented, pressure may well arise to expand the list of beneficiary countries to include poorer nations as well, which would severely undermine any differential pricing strategy of pharmaceutical companies.⁵⁸

Turning to US trade policy, the US Government should not stand in the way of countries seeking to use the flexibilities of the TRIPS Agreement. Even though the United States agreed to the Doha Declaration in 2001 confirming these flexibilities, it has undermined them through TRIPS-plus provisions in FTAs. In addition, the United States has put political pressure on countries not to grant compulsory licenses and has sent ambivalent messages to countries that have done so. For example, even though USTR acknowledged that Thailand's recent compulsory licenses

⁵⁶ See Faunce (2006). In 2004, Germany created a similar agency—the Institute for Quality and Efficiency in Healthcare (see <http://www.iqwig.de>). The United States Congress has recently considered the creation of a 'Center for Comparative Effectiveness,' as part of the Children's Health and Medicare Protection Act of 2007. However, this Act was vetoed by President George W. Bush.

⁵⁷ Pharmaceutical companies would likely respond to the opening of parallel importation by raising prices in relevant foreign countries. If price controls prevent such a move, they may attempt to curtail supplies to a level which just meets the demand of the foreign country in question. Indeed, concerned about the possibility of drug shortages have led the Canadian pharmacists to call for a ban on parallel drug exports to the U.S. See "Canada pharmacists seek ban on drug exports to U.S.," *Reuters*, January 15, 2007.

⁵⁸ The proposed "Pharmaceutical Market Access and Drug Safety Act of 2007" put forward by a number of US Senators foresees imports from Australia, Canada, the European Union, Japan, New Zealand, and Switzerland, though additional countries could be added to this list provided they meet certain regulatory standards. See <http://dorgan.senate.gov/documents/newsroom/drugimportation.pdf>.

complied with WTO rules, it later elevated Thailand to the Priority Watchlist in its Special 301 Report, alleging “*lack of transparency and due process*” in the issuance of the compulsory licenses.⁵⁹ Similarly, the US ambassador in Thailand complained that “*we did not have any advance notice at all that Thailand was going to go ahead with compulsory licensing.*”⁶⁰ However, it is not clear in what way Thailand’s compulsory licenses lacked transparency or did not follow due process under the rules of the TRIPS Agreement. Since the licenses were for government use, Thailand was not even required to first seek a voluntary license from the patent holder—though the Government had engaged in extensive discussions on pricing with the patent holder before issuing the compulsory licenses.⁶¹ The TRIPS Agreement also does not require the notification of compulsory licenses to other governments. Lastly, in a meeting with the Thai Health Minister, US Commerce Secretary Carlos Gutierrez expressly demanded that Thailand abandon the issuance of the compulsory licenses.⁶²

Building on the May 2007 Bipartisan Agreement between the Administration and the Congressional leadership, the United States should issue its own “Domestic Doha Declaration” encompassing at least the following elements:

- A mandate to amend all ratified FTAs to incorporate the flexibilities of the Bipartisan Agreement.
- Implementation of the August 2003 Decision to allow US generic companies to export to countries with insufficient manufacturing capability wishing to make use of compulsory licenses.
- A call for all US government agencies and diplomatic missions to respect the rights of WTO members under the TRIPS Agreement and, in particular, not to interfere with countries’ compulsory licensing policies.⁶³

Interestingly, such a Declaration has a precedent in US trade policy. In 2000, Bill Clinton issued an Executive Order effectively prohibiting the US Government from seeking any TRIPS-plus standards in Sub-Saharan African countries, which could interfere with access to treatments for HIV/AIDS.

As the largest bearer of the global R&D burden, the United States should have an interest in developing an international framework for promoting Ramsey-type pricing of patented pharmaceutical products. Such a framework would establish a set of criteria for calculating “fair” and economically efficient price levels for countries at different levels of development. It would not take the form of a negotiated international treaty, but a set of recommendations

⁵⁹ See the letter by Susan Schwab to Congressman Thomas Allen, January 17, 2007 and the 2007 USTR 301 Report.

⁶⁰ See “US envoy wants to heal rift,” *Bangkok Post*, May 22, 2007.

⁶¹ See “Facts and Evidences on the 10 Burning Issues Related to the Government Use of Patents on Three Patented Essential Drugs in Thailand.” White Paper by the Ministry of Public Health and the National Health Security Office of the Government of Thailand.

⁶² “Drop drug policy, US tells Thais,” *Bangkok Post*, May 23, 2007.

⁶³ Such a call has already been proposed by several US Congressmen. See Senate Resolution 241 of June 20, 2007.

drawing on expert advice from economists and pharmaceutical experts. The recommendations could also address obstacles in implementing such a pricing regime, such as the avoidance of price spillovers through parallel trade or cross-country reference pricing.

Finally, the United States should support and contribute financially to initiatives seeking to promote R&D into “type 2” and “type 3” diseases. So far, support by the US Government for such initiatives has been lackluster.⁶⁴ Stronger leadership by the United States at the World Health Organization in this area could make an important difference. In the longer term, alternative R&D mechanisms—such as AMCs and innovation prizes—could also find application in the United States to foster innovation in areas currently neglected by private R&D efforts.

⁶⁴ Levine (forthcoming).

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