

# 11 Intellectual Property Rights and Inequalities in Health Outcomes

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## INTRODUCTION

The intensification of economic globalization that has taken place in recent decades has been facilitated by the internationalization of intellectual property institutions. Although this process started at the end of the nineteenth century, it was accelerated in the twentieth century by the adoption of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) developed and negotiated in the context of the General Agreement on Tariffs and Trade (GATT) Uruguay Round (1986–1994) (World Trade Organization, 1994). The internationalization of intellectual property rights (IPRs) regimes has increasingly limited the room left to countries to exercise their sovereign rights and discharge their obligations in public health, including those subsumed under the right to health (Cullet, 2003; Yamin, 2003; Reinharz & Chastonay, 2004). On the one hand, IPRs promote innovation in pharmaceuticals but, on the other hand, they limit access to the resulting products. In addition, such rights only promote certain types of research and development (R&D)—those addressed to the most profitable markets.

This chapter explores inequalities in health outcomes emerging from the existing IPRs regime. First, it considers the internationalization of the IPRs system and in particular the issues arising from the adoption of minimum standards of IPRs protection contained in the TRIPS Agreement. Second, it briefly examines some features of innovation in the pharmaceutical field and the changes underway in the predominant business model for R&D. Third, it discusses the role of patents in pharmaceutical R&D, particularly with regard to diseases prevailing in developing countries. Fourth, the chapter explores issues relating to IPRs and access to medicines. These include how policy interventions can improve such access through compulsory licenses, as well as the limitations of the existing international framework on the matter. Finally, the implications of recently negotiated free-trade agreements are briefly discussed.

## INTERNATIONALIZATION OF INTELLECTUAL PROPERTY

Historically, countries developed their IPRs regimes in accordance with their own interests and levels of development. However, the system gradually began to be internationalized in the late nineteenth century, when two groundbreaking international conventions were adopted: the Paris Convention on the Protection of Industrial Property (1883) and the Berne Convention for the Protection of Literary and Artistic Works (1886). The Madrid Agreement for the Repression of False or Deceptive Indications of Source on Goods was adopted in 1891. With the exception of revisions of the Paris Convention, several decades passed with little change.

During the 1970s, in the context of new perspectives on development, developing countries sought to reverse the trend towards the expansion of IPRs and proposed a revision of the Paris Convention. A major goal of the revision was to amend Article 5A to promote use of the patented inventions in the countries of registration (Roffe & Tesfachew, 2001, p. 388). Not only did this initiative fail; it also caused developed countries to take the offensive once again and propose a new and ambitious instrument in the framework of GATT which eventually led to the adoption of the TRIPS Agreement in 1994. This was followed by the adoption of the Trademark Law Treaty (1994), WIPO Copyright Treaty (1996), WIPO Performers and Phonograms Treaty (1996), and Patent Law Treaty (2000). This new wave of agreements confirmed that the move towards trade liberalization and an increasingly intensive use of knowledge in all spheres of human activity was “accompanied by a heretofore unrecognized rise in ‘entry barriers’ that impede access to knowledge” (Coriat, 2002, p. 1).

Although after the year 2000 no new international agreements on IPRs were adopted, efforts to create international standards have continued in the area of patents through a World Intellectual Property Organization (WIPO) initiative to develop a Substantive Patent Law Treaty (Correa & Musungu, 2002) and rights related to copyright in the area of signal-based broadcasting through the adoption of a new treaty on the matter under the auspices of WIPO.<sup>2</sup> In addition, a number of free-trade agreements (FTAs) that contain high levels of IPRs protection have been adopted since then. Negotiating such agreements has allowed the United States to gain concessions on a bilateral basis that were unlikely to be reached in a multilateral framework where developing countries have become increasingly reluctant to support a further elevation of IPRs standards (World Intellectual Property Organization Secretariat, 2004).

## FROM DOMESTIC FLEXIBILITY TO INTERNATIONAL AGREEMENT—THE NEW SCENARIO

The adoption of the TRIPS Agreement represented a significant step in the internationalization of the IPRs system, because all World Trade Organization (WTO) members are bound to comply with the minimum standards the

agreement set forth in the main areas of IPRs protection (Howse, 2007). The TRIPS Agreement introduces for the first time in an international treaty an obligation to protect efficacy and safety data against unfair commercial use (Article 39.3) (Howse, 2007). With regard to patents, the agreement obligates members inter alia to grant product patents in all fields of technology (including pharmaceutical), specifies the exclusive rights to be granted, sets out conditions for exceptions to exclusive rights and compulsory licenses, and strengthens process patents through the reversal of burden of proof. It also contains some flexibilities, such as the possibility of determining what qualifies as an invention, how compulsory licenses are granted, and the allowance for parallel imports.

The agreement put an end to the significant leeway countries had to design their national systems under those international conventions established between the end of the nineteenth century and the 1980s. When today's industrialized countries were in the process of development, they enjoyed great flexibility in designing their own IPR systems. Mark Twain's personal fight to have his copyright recognized internationally provides a telling example. Twain tried to register his name as a trademark in order to prevent his novels being freely copied; the books of British authors, in particular, were legally copied during most of the nineteenth century. In 1842, Charles Dickens toured the United States pleading for international copyright, and in 1843 he published *American Notes* in which he expressed his frustration with U.S. law. Fifty thousand pirated copies were sold within three days in the United States. His *A Christmas Carol* sold at that time for the equivalent of \$2.50 in London and for six cents a copy in the United States (Vaidhyathan, 2001).<sup>3</sup> Foreign authors did not receive copyright protection in the United States until 1891.

In the case of patents, as a net importer of technology between 1790 and 1836, the United States restricted the issue of patents to its own citizens and residents. Even in 1836, patent fees for foreigners were fixed at ten times the rate for U.S. citizens. In many European countries (such as France, Germany, and Switzerland) that are proponents of strong patent protection today, pharmaceutical product patents were only recognized after the 1960s. Portugal, Spain, and the Nordic countries waited until the 1990s.

Under the Paris Convention for the Protection of Industrial Property, contracting parties were permitted to exclude patent protection in certain sectors (such as pharmaceuticals), determine the duration of patent rights, limit the exclusive rights conferred, and grant compulsory licenses for a variety of reasons, including lack of local working of a patent, that is, the patent holder not industrially executing the invention in the country of grant. In fact, the most successful cases of industrial and technological development in recent history took place in a flexible framework of IPRs protection, such as witnessed in Japan and Korea. The more recent robust development of the Indian pharmaceutical industry, which has become a major world supplier

of cheap generic medicines and active ingredients, was also possible in the absence of pharmaceutical product patents (Chaudhuri, 2005).

This flexibility was reduced dramatically with the adoption of the TRIPS Agreement, which is essentially the outcome of well-organized campaigns by a few industries, notably pharmaceutical, entertainment, software, and semiconductors (Sell, 2003). In particular, the TRIPS Agreement represented a major victory for the pharmaceutical industry, which had worked hard to expand the patent protection of products that were excluded from patentability in most developing countries at the time the TRIPS Agreement negotiations were launched in GATT in 1986—a time at which over fifty countries did not recognize patent protection for pharmaceuticals.

Under the TRIPS rules much of the flexibility that developed countries enjoyed to design their own systems of IPRs is no longer permitted for developing countries. Although arguments about increased technology transfer, foreign direct investment to, and innovation in such countries were made during the negotiations by the proponents of the agreement, it was obviously intended to benefit those countries and industries with greater capacity to generate new knowledge and information. An early study concluded that

patent harmonization has the capacity to generate large transfers of income between countries, with the USA being the major beneficiary . . . These transfers significantly alter the perceived distribution of benefits from the Uruguay Round, with the USA benefits substantially enhanced, while those of developing countries and Canada considerably diminished. (McCalman, 1999, p. 30)

McCalman's findings have been widely confirmed by recent statistics. Although there is no conclusive evidence of an increase in the flows of production technologies to developing countries, there has been an impressive rise in world royalty payments. North America and Europe account for more than two-thirds of all payments, followed by Asia and Latin America; royalty payments grew from \$61 billion in 1998 to \$120 billion in 2004, of which the United States was the main beneficiary (World Bank, 2000, 2007).

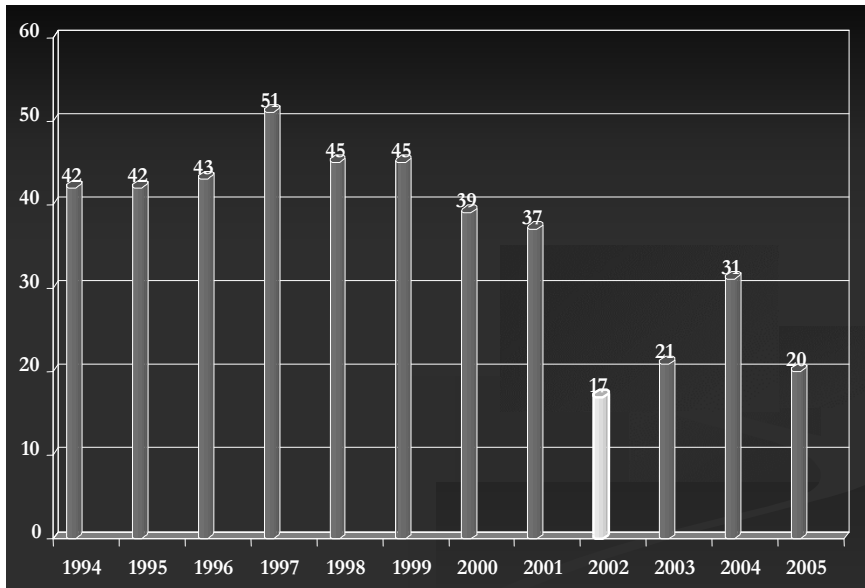
## INNOVATION IN PHARMACEUTICALS

While public R&D institutions have been the main source for discoveries of potential pharmaceutical use, the pharmaceutical industry has mainly funded and carried out the development phase of pharmaceutical products, including costly and lengthy clinical trials. The public sector accounts for around 44 percent of the total funding for health research, while the private for-profit sector funds around 48 percent (Burke & de Francisco, 2004).<sup>4</sup>

Much incremental innovation takes place in the industry by way of (often marginal) modifications of existing processes or products or the ways products are administered. Patents on these minor modifications are generally applied for as part of a strategy to delay generic competition that is often referred to as “evergreening.” The industry’s innovation performance is measured, however, by the new chemical entities it is able to develop and have approved by health authorities.

The development of new chemical entities for pharmaceutical use as indicated in Figure 11.1 presents a worrisome picture. The number of such entities delivered per year has fallen substantially since the 1990s,<sup>5</sup> thereby increasing the average cost of developing new drugs. That decline seems paradoxical for three main reasons. First, since the 1980s and particularly as the implementation of the TRIPS Agreement was completed in developed and developing countries,<sup>6</sup> patent protection allowed companies to increase income generation worldwide through the exercise of stronger and, in some cases, longer patent rights and data exclusivity.<sup>7</sup> Second, a new set of scientific and technological tools—such as genomics, proteomics, and combinatorial chemistry—has the potential to speed up drug discovery. Mass screening of potential drug candidates has been substituted by more efficient methods enabling the rational design of drugs. Third, the pharmaceutical industry continues to be one of the most profitable sectors of the global economy, fourth only after mining, crude-oil production, and commercial banking (Angell, 2004; Commission on Intellectual Property Rights, 2006). Moreover, funds allocated to R&D have increased since the last decade. The fall in innovative productivity may indicate a crisis in the model of drug development carried out by large pharmaceutical companies: while the overall level of investment has risen dramatically, the number of new products has not increased (Charles River Associates, 2004; Commission on Intellectual Property Rights, 2006). Large firms find it more difficult to maintain a continuous pipeline of new and commercially viable products. Instead, they depend for new drugs on advances made by small biotechnology companies, while certain segments of biomedical research are undertaken in cooperative ways following an “open-access” model, and many of the clinical studies are done by specialized contractors. Open-access models of innovation may be increasingly applicable to biomedical research as computational models utilizing genetic information become more important as part of the product development process (Maurer, Rai, & Sali, 2004).

In response to the decline in innovative performance, some pharmaceutical companies are moving towards a disaggregated business model focusing on a few areas of core competence (discovery, development or marketing). At the same time, they are outsourcing other activities with biotech companies, contract research organizations, independent drug-development firms, and freelance sales organizations (*Economist*, 2007). Companies are streamlining their pipelines, focusing on fewer



*Figure 11.1* Development of new chemical entities for pharmaceutical use, 1992–2004.

Source: US FDA

diseases, and licensing in (i.e., obtaining from other companies under license agreements) more drug candidates. Thus, many large pharmaceutical companies have introduced drastic reorganization of their R&D activities. Years ago, GlaxoSmithKline took the lead by dividing R&D into therapeutic areas and setting up seven Centres of Excellence for Drug Discovery (CEDDs). Roche will also create five Disease Biology Areas (DBAs) for oncology, virology, inflammation, metabolic diseases, and central-nervous-system disorders, which will cover everything from drug discovery to medical proof of concept to marketing (Nagle, 2007). The biggest pharmaceutical company, Pfizer, recently announced up to five R&D site closures and an increasing reliance on outsourcing and in-licensing (Nagle, 2007). Once believed to hold unique competence to develop new drugs, large firms may still retain an unparalleled financial capacity to bear the cost and risks of drug development. However, new actors have emerged that can make better use of new scientific and technological tools, and more efficiently carry out preclinical and clinical trials as well as the complex procedures of marketing approval.

There are other challenges to the existing model of drug development. One is the growing concern about the conflict of interest underlying the development of data regarding drug efficacy and safety. Lewis, Reichman, and So (2006, p. 1) have observed that

[S]o long as drug companies retain primary responsibility for conducting or funding clinical trials, they will be tempted to selectively disclose information and to avoid research programs that could reveal unfavorable outcomes. Nor would a disclosure requirement alone ensure that the stakeholding company will conduct all the tests deemed most beneficial to public safety. . . . There are few incentives to undertake costly testing (phase IV clinical trials) if the results might only serve to narrow use of the drug to a smaller subgroup of patients or prove unfavorable to its continued use.

For this reason, these authors suggest the “establish[ment of] an independent testing agency to conduct clinical trials under specified conditions of transparency. . . . This separation of clinical trials from sponsorship could attenuate the conflict of interest problem” (Lewis et al., 2006, p. 1).

Another effect attributable to the decline in innovative capacity is the proliferation of secondary patents (such as on polymorphs, isomers, formulations, new uses, etc.) relating to existing drugs which are strategically used to keep competitors out of the market through administrative measures or costly litigation (Federal Trade Commission [FTC], 2002).<sup>8</sup> Through the acquisition of such patents—in some cases fraudulently<sup>9</sup>—companies are often able to significantly delay the entry of generic competition and maintain high profits on old drugs, to the detriment of consumers and governments.

In sum, there are important changes in the innovation path and in the R&D model for pharmaceutical products. Such changes do not affect the industry’s significant reliance on patents for funding R&D and setting limits to generic competitors. On the contrary, they have increased the value of patents, including those on minor developments, as income-generating tools.

## PATENTS IN THE PHARMACEUTICAL INDUSTRY

The pharmaceutical industry, with sales exceeding US\$400 billion annually, is highly globalized. The major companies operate through subsidiaries and trade in active ingredients or formulated products in many countries, while some also hold R&D facilities in several countries. Large pharmaceutical companies acquire patent rights globally, including in poor countries, with few exceptions made in the case of the least developed countries (LDCs).<sup>10</sup> The advantages of a global patent regime for the industry are obvious; under patents and other forms of IPRs, such as trademarks, they can charge prices substantially higher than marginal costs.

There seems to be little doubt that patents play a key role in funding the activities of the industry and particularly that they provide a stimulus for R&D. However, this statement needs to be qualified in two respects.

On the one hand, innovation essentially depends on the outcomes of commercial activities in developed countries. Although industry has relentlessly sought to ensure patent protection for its products in developing countries, these countries account for only about 10 percent of global sales (in value) and for 5 to 7 percent of the global industry's profits (Pharmaceutical Research and Manufacturers of America, 2005). The extension of pharmaceutical patents to developing countries under the TRIPS Agreement is likely to have no significant impact on the development of new medicines (Scherer, 2004). Scherer examined whether global welfare is better served by a uniform worldwide system of pharmaceutical product patents or by international rules allowing low-income nations a "free ride" on the discoveries of firms in rich nations. Key variables included the extent to which free riding reduces the discovery of new drugs, the rent potential of rich as compared to poor nations, the ratio of the marginal utility of income in poor as compared to rich nations, and the competitive environment within which R&D decisions are made. Scherer found that, under plausible conditions, global welfare would be better served by allowing free riding by poor countries (Scherer, 2004).

On the other hand, patents foster R&D relating to diseases that predominantly affect rich countries. Patents only work as incentives where profitable markets exist. As noted in the report of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPRH):

Where the market has very limited purchasing power, as is the case for diseases affecting millions of poor people in developing countries, patents are not a relevant factor or effective in stimulating R&D and bringing new products to market. . . . For developing countries, where the demand is weak—but not the need—there is little incentive to develop new or modified interventions appropriate to the disease burden and conditions of the country. (Commission on Intellectual Property Rights, 2006, pp. 34–6)

This is the logical consequence of the nature of patents. They confer an incentive that may only be realized when the appropriate conditions exist in terms of human resources, capital, and expected returns.

There have been expectations about the new impetus to R&D, especially in the area of Type II and III diseases,<sup>11</sup> which may emerge in innovative developing countries such as India. However, available evidence indicates that, despite an increase in R&D expenditure by large local pharmaceutical companies, their effort is small compared to large multinational companies and is concentrated on drugs of interest in rich markets. Moreover, the model that Indian companies have adopted is to develop new molecules and license them out to large pharmaceutical companies at an early stage of development in order to avoid the heavy costs of clinical trials and regulatory approvals (Chaudhuri, 2005).

In brief, patents do contribute to the development of new treatments where large profitable markets exist. Lack of demand to treat the diseases of the poor makes patent protection irrelevant for Type III diseases and only relatively important for Type II diseases. Hence, patents may deepen the existing inequalities between rich and poor, as they generate an incentive to develop and market profitable drugs and not those badly needed to address the health problems of the greatest portion of the world population. Alternative mechanisms to promote pharmaceutical innovation are needed, especially for diseases of the poor.

Several public-private partnerships (PPPs) have been established to develop products needed in developing countries. For example, a partnership between Drugs for Neglected Diseases Initiative and Sanofi-Aventis, which has developed a fixed-dose combination of artesunate-amodiaquine, has submitted the drug for registration in twenty-three sub-Saharan African countries with current registration in twelve of these countries (Drugs for Neglected Diseases Initiative [DNDi] & Sanofi-Aventis, 2008). There are, however, serious concerns about the sustainability of such initiatives (Commission on Intellectual Property Rights, 2006), and a discussion of alternative mechanisms to promote innovation has been started by the World Health Organization (WHO). In 2008, the World Health Assembly adopted a draft global strategy and plan of action on public health, innovation, and intellectual property that, *inter alia*, encourages governments to consider new ways to stimulate research and development into health treatment for diseases that disproportionately affect developing countries (ICTSD reporting, 2008). The alternative mechanisms proposed include:

1. Market exclusivity for a limited period modeled on the “orphan drug” scheme applied in the United States under the Orphan Drug Act of 1983. Although this approach apparently has been successful in the United States, it seems to work when purchasing power is high (Commission on Intellectual Property Rights, 2006). In addition, the conferred exclusivity may, unless other measures are implemented, deny low-income patients access to new drugs.
2. Rewards in the form of prizes for the development of medicines to address diseases prevailing in developing countries. Such a scheme might be used more generally to encourage the development of new drugs without subjecting them to exclusive rights under patents. Stiglitz has proposed the establishment of a medical prize fund “for those who come up with a vaccine or cure for the kinds of diseases that afflict those in developing countries” (2007).
3. Advance purchase commitments that guarantee the future purchase of certain quantities of a product to be developed at an agreed price, with further reduction after a period of time. This mechanism is likely to work best when a molecule has already been identified and the risk involved in R&D is relatively low (Barder, Kremer, & Levine, 2005).

4. Open source schemes, particularly for the identification of new candidate molecules (Kepler et al., 2006). This approach may foster advances in early phases of the R&D cycle of pharmaceuticals.
5. A new international treaty on medical research, proposed by a number of nongovernmental organizations (NGOs) and governments to ensure sustainable funding for R&D in pharmaceuticals (Kepler et al., 2006).<sup>12</sup>

Some of these proposals, particularly the scope for open-access initiatives, may be further explored in the context of the World Intellectual Property Organization (WIPO) Development Agenda originally proposed by Argentina and Brazil in 2004. In September 2007, for example, the WIPO Assembly adopted forty-five of the recommendations under discussion (World Intellectual Property Organization, 2008).

## ACCESS TO MEDICINES

Like any other incentive mechanism, the way patents work depends on the context in which they are applied. In countries lacking capital and required scientific and technological infrastructure, patents operate as a levy collection mechanism and not as a stimulus of local R&D. Patents restrict the extent of the diffusion of innovations by imposing monopolistic prices on consumers and royalties on technology users. The more isolated the product is from competition with possible substitutes, the higher the prices and the charges that can be levied. This obviously reduces the benefits that would have accrued to society at large and to patients in particular had the innovation been made available to competitors to manufacture generic products. The price increases introduced by patent protection may be extraordinarily high. In India, where pharmaceutical product patents came into force only in January 2005, the cost of treatment against leukemia, for instance, might be several times higher if a patent were to be granted on a crystalline form of the main available treatment (imatinib).

Another illustration is found in the evolution of the prices of patented antiretrovirals (ARVs). In 2000, the cost of treatment per patient per year was more than US\$10,000. Competition by Indian generic firms made available the same ARV treatment in 2001 for less than US\$400 and the prices of both the originator's and generic drugs continued to fall thereafter. At the time, this lower cost treatment was possible because India did not recognize pharmaceutical product patents and was able to produce generic versions of products which were under patents elsewhere. However, as of January 1, 2005, India was bound to grant such patents (including for patents validly filed after January 1, 1995). Hence, in the future no alternative supply will exist for new drugs, and patent owners may charge prices that high- and middle-income consumers are able to pay. Unless national

legislation provides for effective TRIPS-consistent mechanisms to control prices of patented medicines, such as compulsory licenses, a large portion of the poor population in developing countries may be deprived of access to drugs.

High pricing of medicines has human rights implications, particularly through the restriction of domestic autonomy to provide access to needed treatments. These implications are increasingly recognized as a core duty under the international human right to health (Hunt, 2006). Indeed, the CIPIH report recognizes this right and the duties it imposes on states with respect to medicines. Similarly the UN Special Rapporteur on the Right to Health issued, in September 2007, draft *Human Rights Guidelines for Pharmaceutical Companies in Relation to Access to Medicines*, which, inter alia, demand that the company's corporate mission statement "expressly recognize the importance of human rights generally, and the right to the highest attainable standard of health in particular, in relation to the strategies, policies, programs, projects and activities of the company" and that the company "should integrate human rights, including the right to the highest attainable standard of health, into the strategies, policies, programs, projects and activities of the company" (p. 4).<sup>13</sup>

Conventional economic theory suggests that, to encourage innovation, competition based on price and quantity may have to be temporarily restrained. This would reduce *static efficiency* but bolster *dynamic efficiency* by increasing the likelihood of innovators recovering their R&D investment (United Nations Conference on Trade and Development Secretariat, 1998).<sup>14</sup> The static-dynamic efficiency rationale applicable in a developed society, however, does not necessarily hold when strong inequalities exist. High levels of IPRs protection may have significant negative *allocative* consequences in developing countries without contributing to, or even impeding, their technological development (Stiglitz, 1999). In the case of pharmaceuticals, while consumers in developing countries contribute to the R&D budgets of pharmaceutical companies, these companies concentrate their research on profitable drugs for developed countries and neglect those needed by the poor in developing countries (Commission on Intellectual Property Rights, 2006). As a result, while patents play an important role in funding R&D for certain types of pharmaceuticals, they significantly affect access to the innovations they promote (Chaudhuri, 2005). The concerns about the implications of patents on access to drugs have been voiced by developing countries and NGOs in many forums.

Such concerns were reflected in the Doha Ministerial Declaration on TRIPS and Public Health (World Trade Organization, 2001). The declaration recognized the "gravity" of the public health problems afflicting many developing countries and LDCs, especially, but not limited to, those resulting from HIV/AIDS, tuberculosis, malaria, and other epidemics. As well, it recognized concerns about the effects of intellectual property protection

on prices (World Trade Organization, 2001). The Doha Declaration confirmed some of the flexibilities allowed by the TRIPS Agreement, such as the possibility of granting compulsory licenses and of permitting the parallel importation of patented products. A key paragraph (Paragraph 4) in the Doha Declaration states:

We agree that the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health. Accordingly, while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all.

Compulsory licenses, as next discussed, may be an important instrument to increase access to medicines under patent protection. Indeed, UN bodies such as the Commission on Human Rights have recognized compulsory licensing as a mechanism for developing countries to fulfill their obligations under the right to health (see, for example, United Nations High Commissioner for Human Rights, 2001).

## COMPULSORY LICENSES

A compulsory license is an authorization given by a government (through the administration or a court) for the use, by a third party, of a patent (or other intellectual property rights) without the consent of the titleholder. The concept of compulsory licenses also encompasses governmental non-commercial use, that is, the use by or under the authority of the government of a patent. In conformity with Article 31 of the TRIPS Agreement, national laws can provide for the compulsory use of a patent by the government or by a third party. Government use and compulsory licenses mitigate the legal power conferred by a patent and can be an important instrument to ensure access to drugs at affordable prices.

Although the granting of compulsory licenses was contemplated in the Paris Convention for the Protection of Industrial Property as early as 1925, few such licenses have been granted, except in the United States, where, despite the US government's active defense of patents held by US companies abroad, thousands of patents have been subject to compulsory use by the government or to remedy anticompetitive practices (Correa, 1999; Reichman & Hasenzahl, 2003).<sup>15</sup> Many developing countries, especially those that followed British patent law, have provided for the granting of such licenses. However, until recently, the compulsory license system remained unused. Many developing countries have been sensitive to pressures from developed countries not to grant such licenses (Outerson, 2005).

While compulsory licensing is compatible with the TRIPS Agreement, provided that the conditions set out in Article 31 are met, developing countries sought to confirm their right to issue them and determine the grounds for their use through the Declaration on the TRIPS Agreement and Public Health (Paragraph 5(b)). This confirmation was likely instrumental in encouraging a number of developing countries to grant compulsory licenses (see Table 11.1). Brazil also threatened the granting of such licenses, which eventually led to a substantial reduction in the prices charged by patent owners for some antiretrovirals (ARVs) (Commission on Intellectual Property Rights [CIPR], 2002).

As indicated in Table 11.1, in some cases compulsory licenses have been granted to allow the local manufacture of patented drugs, while in others the objective is to import cheaper versions of them. Both means are fully compatible with the TRIPS Agreement. Malaysia, for example, was the first country to issue a license and to exercise the “government use” or “Rights of Government” provisions,<sup>16</sup> a special type of compulsory license issued following the adoption of the Doha Declaration on the TRIPS Agreement and Public Health in 2001 (Ling, 2006). In most cases, compulsory licenses or government use have been granted for ARVs. But there is no reason to limit the use of such mechanisms to ARVs. Thailand is the first developing country to target other types of products—those for the treatment of heart diseases (Ministry of Public Health & National Health Security Office, 2007).<sup>17</sup> Remuneration paid to patent owners ranges from 0.5 to 4 percent of the value of the products produced under license. In most cases, the resulting price reductions are significant, thereby allowing governments to increase the number of patients treated.

However, countries in need of cheaper versions of patented pharmaceuticals may increasingly face a situation in which they lack manufacturing capacity to produce them while foreign supplies are unavailable. Due to lack of technical capacity, adequate equipment, human resources, high costs of production, or other obstacles, many developing countries and LDCs cannot produce the active ingredients needed to manufacture pharmaceutical products. While these countries may issue compulsory licenses to import generic versions of patent-protected medicines, TRIPS rules impose constraints on the production and export of products patented in the supplier country. Paragraph 6 of the Doha Declaration recognizes 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. It instructed the Council for TRIPS to find “an expeditious solution to this problem.” After long and difficult negotiations, the council reached a consensus agreement that was adopted as the Decision of the General Council of the World Trade Organization on 30 August 2003 (the WTO Decision). It stipulates several conditions to be met in order to make use of the waivers it provides for exporting and importing countries.

*Table 11.1* Compulsory Licenses and Government Use of These in Developing Countries

Country and Date Compulsory License Adopted	Type of Authorization	Products	Cost Reduction	Remuneration to the Patent Owner
Zimbabwe May 2002	Based on a declaration of emergency, it empowers the minister to authorize the use of patented inventions by any government department or third party, for the service of the state	ARVs	From US\$197–237 per year to US\$180	n.a.
Malaysia November 2003	It authorizes the local distributing agent for an Indian manufacturer to import from India, for the purpose of supplying public hospitals for two years	ARVs	From US\$315 to US\$58 per month	4% value of stocks actually delivered
Mozambique April 2004	Compulsory license to enable local manufacturing	ARV fixed dose combination	2% total turnover	
Zambia September 2004	Compulsory license for local manufacturing	ARV	2.5% total turnover	
Indonesia 2004	It authorizes the minister to appoint a pharmaceutical factory as the patent exploiter for and on behalf of the government	Nevirapine and lamivudine	Fixed dose combination produced for US\$38 per month	0.5% net sales
Ghana October 2005	Government use	ARVs	From US\$495 to US\$235 per year	n.a.
Thailand November 2006 January 2007	Government use	Efavirenz  Plavix Kaletra	From US\$41 to US\$22 per month	0.5% sales value
Brazil May 2007	Public interest	Efavirenz (600 mg)	From US\$1.59 to US\$0.45 per dose (saving of US\$30 million in 2007)	n.a.

Source: Elaborated on the basis of Oh, 2006, and Khor, 2007 (n.a.= information not available).

A few countries have enacted legislation to implement the WTO Decision as potential exporters, namely, Canada, Norway, India, the Netherlands, and Iceland. On 17 May 2006, the European Parliament and Council adopted Regulation (EC) No. 816/2006 on compulsory licensing of patents relating to the manufacture of pharmaceutical products for export to countries with public health problems. Based on a proposal by the European Commission on compulsory licensing of patents relating to the manufacture of pharmaceutical products for export to countries with public health problems (Commission of the European Communities, 2004), the regulation incorporated a number of additional conditions to those already imposed by the WTO Decision, but ultimately took a largely positive approach (Abbott & Reichman, 2007).

A major hurdle in the mechanism set up by the WTO Decision is the need for potential suppliers to undertake prior negotiations with the patent owners (the Canadian and EU implementation regulations, for instance, provide for a thirty-day period for negotiations). This may significantly delay the granting of a compulsory license. In addition, since the simple offer for sale may infringe patent rights (specifically Article 28.1 of the TRIPS Agreement), firms willing to tender for the supply of drugs to beneficiary countries may not do so before obtaining a compulsory license in the exporting and, if needed, the importing countries. Obviously, few firms would be prepared to bear the cost of obtaining such licenses before a firm commitment to purchase their products has been made.

As a condition for use of the WTO Decision, potential importing countries must give notice of their intention to do so (Correa, 2004). So far, no country has done so and the WTO Decision has never been applied. This is a worrisome signal as to the effectiveness and feasibility of the mechanism. Despite this, in December 2005 the WTO Decision was incorporated as a new article (31*bis*) of the TRIPS Agreement, with the intention of it becoming a permanent mechanism. Such incorporation is, however, subject to ratification (in accordance with WTO rules) by member states, which so far have not rushed to do so.<sup>18</sup>

In sum, the Doha Declaration was a politically and socially important initiative that seemed to reaffirm the need to give priority to public health over commercial interests inherent to the acquisition and exercise of intellectual property rights. However, its practical implementation with regard to compulsory licenses has been strongly influenced by the commercial interests it was intended to counterbalance.<sup>19</sup>

## **FREE-TRADE AGREEMENTS**

At the same time the Doha Declaration was negotiated and adopted, the United States initiated negotiations of bilateral and regional FTAs with more than twenty countries. The FTAs incorporate TRIPS-plus requirements. Agreements were entered into with Jordan, Chile, Singapore, Morocco, the

Central American countries and the Dominican Republic, Bahrain, Oman, Peru, and Colombia. Some of these agreements have already been ratified by the US Congress.<sup>20</sup> Other FTAs have been signed by or are under negotiation between developing countries and the European Union (EU) or the European Free Trade Association (EFTA).

The common pattern in these FTAs is that they further elevate the level of protection virtually in all areas of IPRs, notably copyright and patents. In the case of the US FTAs, partner countries are obliged *inter alia* to grant patents on plants, extend the patent term in certain circumstances, and adopt the “utility” standard for patentability (in place of the narrower requirement of industrial applicability<sup>21</sup>). They are also obliged to grant exclusive rights in respect of test data on pharmaceuticals and agrochemicals. In some cases, the protection enforceable under these FTAs is greater than that applicable in the United States itself (Abbott, 2006). Paradoxically FTAs do not seem to generate any obligation within the United States, leading to a situation in which US companies will receive more extensive IPR protection in FTA signatory countries, including many poor countries, than in the United States (Abbott, 2006). These FTAs may have significant implications on access to medicines while, for reasons explained earlier, they are unlikely to have any impact on R&D investment. Governments seek, however, to sign FTAs in order to get permanent free access to the big US market, or retain current preferential conditions of access, with the expectation of gains in other trade areas.

The US FTAs further obligate partner countries to extend patent terms to compensate for delays in marketing caused by approval procedures for medicines and “unreasonable” delays in the examination of patent applications. Most agreements do not mention whether extensions to compensate for delays apply only to the country where the medicine is sought (a seemingly legitimate interpretation) or whether delays in the country where first approval was obtained should also be calculated. No maximum period is provided for the extension, unlike the current law in the United States, where some time limits are provided.<sup>22</sup> As a result of these extensions, which may be cumulative, patents for medicines may last much longer than the twenty years required under Article 33 of the TRIPS Agreement.

In a significant departure from the TRIPS standard,<sup>23</sup> the US FTAs also obligate the parties to grant “data exclusivity” for at least five years starting from the date of approval of a pharmaceutical product. This is granted irrespective of whether or not the product is patented and whether or not the relevant test data are undisclosed. Such exclusivity will also apply irrespective of whether the national health authority requires the submission of the data; that is, even in cases where it relies on an approval made in a foreign country. In addition, the Central America–Dominican Republic–United States Free Trade Agreement (CAFTA-DR) and those signed with Peru and Colombia provide for a five-year waiting period. According to Article 15.10.1(b) of CAFTA, a signatory country may require the person

providing information in another territory to seek approval in that country within five years of obtaining marketing approval in the other territory. If narrowly interpreted, this provision may allow the originator of test data who obtained approval for a medicine in a foreign country to delay up to five years an application for the approval of the same medicine in a country signatory of the FTA.

The implications of data exclusivity will be significant, particularly in countries that only recently introduced patent protection for pharmaceutical products, since medicines that are now off-patent will become subject to exclusive rights. These provisions create an effective barrier to generics competition, since even where a product is off-patent, no marketing approval can be granted to a generic manufacturer unless it replicates the full set of test data necessary to obtain approval. This is costly, time-consuming, and questionable under ethical rules, such as those of the Helsinki Declaration and its amendments (World Medical Association, 2004). A study for Peru relating to forty-three pharmaceutical products estimated that their average price would have been between 94.3 percent and 114.4 percent higher if they were subject to data exclusivity (Apoyo Consultoría, 2005).

The US FTAs also require a *linkage* between drug registration and patent protection that is absent in the TRIPS Agreement. As a result, if broadly interpreted, the national health authority may be required to refuse marketing approval to a generic version of a product if a patent on it is in force, except by consent or acquiescence of the patent owner. In addition, such authority must inform the patent owner about applications for the approval of generic products. Parties may, however, narrowly interpret the “linkage” obligation, for instance, by limiting it to patents over active ingredients (excluding formulations, polymorphs, isomers, doses, etc.), and put on the patent owner the burden to judicially request the suspension of third parties’ approval procedures, as is the case in the United States.

Some US FTAs restrain WTO member states’ freedom, confirmed by the Doha Declaration, to determine the grounds for compulsory licenses. Thus, in the case of the FTAs with Jordan, Australia, and Singapore, such grounds are limited to cases such as anticompetitive practices, public non-commercial use, national emergency, or other circumstances of extreme urgency. This limitation, which openly contradicts the Doha Declaration, did not appear in other US FTAs with developing countries after the adoption of the declaration. US FTAs with Australia, Singapore, and Morocco limit parallel importing of medicines and other products, that is, importing without the consent of the patent owner a patented product that has been legitimately put on the market abroad. Finally, some US FTAs, such as the one with Morocco, require the recognition of patents over the “second indication,” that is, a new therapeutic use of a known medicinal product. This unnecessarily expands the scope of patentability and ignores the right, recognized by the TRIPS Agreement, to exclude the patentability of therapeutic methods.

So far the European Union has included a few provisions in trade agreements with other partners, mainly the obligation to adhere to intellectual property conventions, such as the Budapest Treaty and the international convention establishing the International Union for the Protection of New Varieties of Plants (UPOV). Some bilateral agreements, such as those entered into with South Africa (1999), Tunisia (1998), and the Palestinian Authority (1997), require them to ensure adequate and effective protection of intellectual property rights “in conformity with the highest international standards” (Drahos, 2002, pp. 14–18). Currently the EU is engaged in negotiations with six regions in Africa, the Caribbean, and the Pacific. These include more elaborated chapters on intellectual property, including TRIPS-plus substantive and enforcement provisions. However, unlike the US FTAs, the drafts under consideration do not seem to include higher substantive standards of protection on medicines.

In sum, US FTAs significantly increase the level of IPRs protection for medicines and, hence, the power of large pharmaceutical companies to charge higher prices in signatory countries. There is no justification for this in terms of additional R&D, since the markets of partner countries are relatively small and the additional income will make no difference to the global R&D budgets of these companies.<sup>24</sup> However, the increase in the cost of medicines may have a disproportionately high impact on the population of poorer countries. In some countries, such as Colombia and Peru, the ministries of health, which actively participated in the FTA negotiations without having sufficient power to influence their outcome, requested that their governments provide compensatory funds in order to face the increased costs of medicines. At least in the case of Peru, such measures were never actually implemented.

## CONCLUSIONS

The intellectual property system has undergone a gradual but steady process of internationalization. A web of international treaties today supports global R&D, production, and trade. In the case of pharmaceuticals, such treaties, in particular the Patent Cooperation Treaty (PCT) and the TRIPS Agreement, provide large companies procedural means and substantive rights to exploit their innovations practically worldwide.

The international treaties entered into at the end of the nineteenth century and for most of the last century gave countries leeway to exercise their sovereignty in health-related matters. The TRIPS Agreement has dramatically changed that scenario by imposing a number of minimum standards, particularly in the area of patents.

Patents have played an important role in encouraging investment in pharmaceutical R&D. However, the innovative productivity of the industry is drastically declining, despite new scientific and technological tools available

for drug development. In addition, patents only work as incentives where profitable markets exist. Other mechanisms need to be established and initiatives supported (such as “open-access” models) to encourage more R&D in diseases disproportionately affecting developing countries.

Likewise, policy interventions are needed to mitigate the negative impact of IPRs on access to medicines by the poor. Compulsory licenses provide one such measure. A growing number of developing countries have made use of these licenses, particularly to increase access to HIV/AIDS drugs, but there is nothing in the compulsory licenses system limiting its use to one category of medicines or diseases.

In the future, governments may face difficult challenges to provide access to patented drugs. This is because all WTO member states are now bound to confer product patent protection, and the mechanism set up by the WTO Decision is overburdened by conditions unlikely to encourage the supply of cheap products under patent protection in possible exporting countries.

Finally, despite the moral and political weight of the Doha Declaration, the United States and other developed countries have continued to seek a further expansion of IPRs to the benefit of pharmaceutical companies and other patent holders. The enhanced standards of protection create a disproportionate cost to developing countries that are parties to such agreements.

In sum, the IPRs system does promote research into more effective and efficient treatments. However, its bias is towards diseases of commercial interest. Some developing countries have applied policies to minimize the harm of IPRs, but their capacity to do so is being eroded by the new wave of FTAs. In addition, and most importantly, these countries need to look outside the IPRs system for mechanisms that foster innovation in the treatment of diseases that prevail among their people.

## NOTES

1. The author is thankful for the contribution of Lisa Forman.
2. See <http://www.cptech.org/ip/wipo/bt/>.
3. The arguments articulated during that period in the United States against international copyright may currently suit numerous poor countries. It was argued that expanding literacy demanded cheap yet excellent books; there was no inherent property right in literature; granting copyright to foreigners would give them a monopoly at the expense of US reading public; US publishers and their employees needed the de facto advantage afforded by the absence of protection (Vaidhyathan, 2001).
4. Given the amount of public funding involved in the creation of new patented drugs, including in some cases foregone tax deductions for R&D, at least part of the income obtained by pharmaceutical companies may be regarded as an inequitable windfall.
5. It is also to be taken into account that most new chemical entities are “me toos,” that is, they do not represent a genuine therapeutic innovation. The great majority of new drugs approved annually have therapeutic qualities

similar to those of one or more already marketed drugs. The proportion of drugs considered by the US Food and Drug Administration (FDA) as potentially significant therapeutic advances over existing drugs has declined from 26 percent to 19 percent since the early 1990s (Center for Drug Evaluation and Research, 2005; see also Spector, 2005).

6. Transitional periods were provided for developing countries, economies in transition, and the least developed countries. Developing countries that did not previously recognize pharmaceutical product patent protection could delay its introduction until January 1, 2005, but only a few countries made full use of this possibility.
7. As a result of demands received in the process of accession to the WTO or to satisfy demands of the United States or the European Union, several countries have implemented in the context of FTAs *sui generis* regimes granting exclusivity over the test data necessary to obtain the marketing approval of pharmaceutical products containing new chemical entities.
8. In order to avoid the proliferation of “low quality” or wrong patents, strict standards of patentability should be applied to assess patent applications. See, e.g., Correa, 2006.
9. See, e.g., Federal Trade Commission (FTC), 2003.
10. Occasionally, pharmaceutical companies fail to patent in other developing countries, such as in the case of oseltamivir, prescribed for avian flu and produced by Hoffman LaRoche under an exclusive license from Gilead Sciences (USA). This drug was not patented, for instance, in Argentina, Indonesia, Philippines, and Thailand by Hoffman LaRoche.
11. Type I diseases are incident in both rich and poor countries, with large numbers of vulnerable populations in each. Type II diseases (often termed *neglected diseases*) are incident in both rich and poor countries, but with a substantial proportion of the cases in the poor countries (e.g., HIV/AIDS and tuberculosis). Type III diseases are those that are overwhelmingly or exclusively incident in the developing countries (Intergovernmental Working Group on Public Health, 2007).
12. See, e.g., <http://www.cptech.org/workingdrafts/rndtreaty.html>.
13. Available at [huachen.org/english/issues/health/right/docs/draftguid150508.doc](http://huachen.org/english/issues/health/right/docs/draftguid150508.doc).
14. *Static efficiency* is achieved when there is an optimum utilization of existing resources at the lowest possible cost. Static efficiency may be subdivided into: (i) *Production efficiency*, which includes technical and nontechnical operating efficiencies, together with transaction cost and X-efficiency savings; (ii) *Allocative efficiency*, which is the allocation of products through the price system in the optimum manner required to satisfy consumer demand. *Dynamic efficiency* is the optimal introduction of new products or products of superior quality, more efficient production processes and organization, and (eventually) lower prices over time (United Nations Conference on Trade and Development Secretariat, 1998).
15. A recent US Supreme Court decision that denied a permanent injunction in a case of patent infringement effectively amounts to the grant of a compulsory license on “equity” grounds. In *eBay Inc. et al. v. Mercexchange, L. L. C.* of May 15, 2006, the Court stated that “the decision whether to grant or deny injunctive relief rests within the equitable discretion of the district courts.” This means that an infringement may not necessarily lead to a permanent injunction if the court is convinced, based on equity considerations, that it is not justified.
16. The criteria to determine which patented medicines may be subject to government use are the following: must be listed in the National Essential Drug

List; or necessary to solve important public health problems; or necessary in emergency or extreme urgency; or necessary for the prevention and control of outbreaks/epidemic/pandemics; or life saving; and, if the prices of the medicines are too high to be affordable by the government to supply to the beneficiaries of the national health insurance. The royalties will be between 0.5 percent and 2 percent, depending on the retail value of the products.

17. The Thai decision has been challenged on arguments that the grant of compulsory licenses will jeopardize innovation in pharmaceuticals. The available empirical evidence, however, does not support this contention. Scherer analyzed the extent to which the granting of compulsory licenses in the United States affected R&D expenditures by firms and, particularly, whether such licenses diminished or destroyed the incentives to undertake R&D by patent holders. His statistical findings relating to seventy companies showed no negative effect on R&D in companies subject to compulsory licenses but, on the contrary, a significant rise in such companies' R&D relative to companies of comparable size not subject to such licenses. See Scherer, 2003, p. 107–08; Outterson, 2005, p. 230 (arguing that compulsory licenses need not harm optimal innovation). Indeed, this evidence undermines the argument that no R&D would be carried out if exclusive rights were not granted under patents. Thus, Tandon noted that “firms spend large sums of money on efforts to ‘invent around’ the patents of their competitors. Under generalized compulsory licensing, these expenditures would be unnecessary, which might increase the welfare benefits” (Tandon, 1982, p. 485).
18. Only sixteen members and the European Union (out of 150 members) have so far accepted the amendment. They are: United States (December 17, 2005); Switzerland (September 13, 2006); El Salvador (September 19, 2006); Rep. of Korea (January 24, 2007); Norway (23 May, 2008).
19. As evidenced, for instance, by the statement read by the chair of the WTO General Council as a condition for the approval of the WTO Decision by the United States. The statement overstated the need for measures to prevent the diversion of cheap drugs from poor to rich countries, and unjustifiably extended differential coloring and shaping conditions to active ingredients. See [http://www.wto.org/english/tratop\\_e/trips\\_e/gc\\_stat\\_30aug03\\_e.htm](http://www.wto.org/english/tratop_e/trips_e/gc_stat_30aug03_e.htm).
20. United States–Jordan Free Trade Agreement (2001); United States–Chile Free Trade Agreement, signed at Miami June 6, 2003, and entered into force January 1, 2004 (Chile FTA); United States–Singapore Free Trade Agreement, signed at Washington May 6, 2003, and entered into force January 1, 2004 (Singapore FTA); United States–Morocco Free Trade Agreement, signed at Washington June 15, 2004 (Morocco FTA) and entered into force on July 1, 2005; United States–Dominican Republic–Central America Free Trade Agreement, signed at Washington May 28, 2004, and entered into force August. 5, 2004 (CAFTA-DR FTA). Parties to the CAFTA-DR FTA are Costa Rica, Dominican Republic, El Salvador, Guatemala, Honduras, Nicaragua, and the United States.
21. Under this “utility” standard, any invention which is useful may be patentable, even if not industrially applicable (e.g., business methods, research tools). The “industrial applicability” standard is narrower, as it requires that the invention be usable in an industry (broadly understood).
22. The extension in the United States to compensate for delays in the marketing approval process shall not exceed five years and, in no case, shall exclusivity exceed fourteen years from the date of approval by the Food and Drug Administration (35 U.S.C. § 156). In addition, the extension applies to only one patent per product.

23. The TRIPS Agreement requires members to protect *undisclosed* test data of pharmaceutical (and agrochemical) products against unfair competition (Article 39.3). Under this rule, correctly interpreted, members are not obligated to grant exclusive rights over test data.
24. In May 2007, a bipartisan agreement was reached at the U.S. Congress to amend some of the provisions of the FTAs signed by the United States with Peru and Panama in order to reduce negative impacts on public health.

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