13. IPRs AND TECHNOLOGICAL DEVELOPMENT IN PHARMACEUTICALS
Who Is Patenting What in Brazil After TRIPS?

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I. INTRODUCTION

The adoption of the TRIPS Agreement—and, more generally, the global tendency to strengthen intellectual property rights—has raised a heated debate regarding the relationships between stronger intellectual property rights (IPRs) regimes, innovation, and development. After years of stagnation, the economic analysis of the patent system is experiencing a substantial revival. Interestingly, most of the new contributions to the literature are of an empirical nature. Indeed, the economic theory of patents was often deemed to be inconclusive by many economists, given that radically different results could be obtained by slight changes in even ancillary assumptions. Above all, the empirical evidence was so flimsy that it was hard to discriminate against alternative conclusions.

The debate has been particularly virulent with respect to the pharmaceuticals industry. Indeed, this sector brings the trade-offs and issues involved in patent theory to their extreme consequences. Pharmaceuticals is one of the few industries in which patents are unambiguously recognized as being key instruments for privately appropriating the economic benefits of innovation and, therefore, serving as an important incentive for innovation. In this sector, competition is largely based on innovation, and basic science is becoming increasingly crucial for the

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discovery and development of new products. The pharmaceuticals industry also has many of the characteristics usually associated with "strategic" industries. It is a high-growth and skill-intensive sector, which provides products that are in themselves associated with further growth: Health is a major engine of growth, and growth is associated with higher health standards. The pharmaceuticals industry also occupies an extremely socially sensitive sector: large parts of the population increasingly perceive health care as a fundamental human right. The very definition of what a just society should look like increasingly involves references to health care. For developing countries in particular, health has become a major issue, magnified by the tragedies of pandemics such as HIV/AIDS. Thus, it should come as no surprise that TRIPS—of which the pharmaceuticals industry was a firm supporter—has ignited raging controversies regarding the desirability of property rights in drugs, both between developed and developing countries and within rich countries.

An analysis of the relationships between IPRs, innovation, and growth in the context of pharmaceuticals is made even more difficult and irksome because of the intricate relationships between health and growth, especially for developing countries. Moreover, the pharmaceuticals industry itself is undergoing deep and unforeseeable transformations.

In this paper, we try to provide an introduction to some of the most salient aspects of the debate, reviewing the relevant theoretical issues and, above all, the sparse empirical evidence available. The main thrust of our argument is as follows:

- There are, indeed, profound trade-offs between the incentives to innovate and ensuring public access to medicines for which no obvious and simple solutions exist.
- The effects of strengthening the patent regime depend on a wide variety of conditions in any given country: institutions (antitrust, patent offices, etc.); capabilities; modes of competition; the specific nature of patent laws themselves and court interpretations (scope, novelty, etc.). In the specific case of pharmaceuticals, other complementary institutions play a key role, as do such factors as price controls; health systems, in general; basic research, and so forth.
- Both economic theory and the evidence increasingly suggest that the strengthening of IPR regimes in developing countries is likely to impose upon them a series of negative consequences that probably outweigh any comparable benefits gained from the more robust regime.
- The IPR system governing pharmaceuticals has become increasingly dysfunctional—even in countries like the United States. The efficacy and desirability of extending strong IPR protection in the rest of the world raises very legitimate doubts.

We also emphasize that, despite increased knowledge on the subject, little is known about the relationships between IPRs, innovation, and growth, especially

as developing countries are concerned. Thus, theoretical development and especially new empirical evidence are badly needed.

In this vein, we report on very preliminary research addressing the patenting activities in Brazil using domestic patent data, rather than—as is customary—international (that is, U.S. or European) patents. A first look at these data suggests, indeed, that domestic patents reveal somewhat different and relevant insights into the nature and patterns of innovation in developing countries. In particular, we show that the adoption of TRIPS had a great impact on the number of patent applications in Brazil, and that, after 1996, there was a great inflow of nonresident patents. Importantly, the impact of TRIPS is heterogeneous across different technological fields. In particular, the number of pharmaceuticals patent applications started increasing in 2000, at least three years after the number of patents in other fields, and has kept increasing thereafter.

II. PHARMACEUTICALS: BACKGROUND

Ever since its inception, the pharmaceuticals industry has been dominated by a stable core of large, globalized, innovative firms based in a few countries: the United States, the United Kingdom, Switzerland, Germany, Japan, and France. However, this sector is highly competitive. Concentration is very low as compared to other research and development (R&D)- and marketing-intensive industries, mainly because the market is composed of several independent submarkets (for example, tranquilizers are not substitutes for cardiovascular drugs), economies of scale are not very strong, and innovations tend not to build on preceding work. Discovering and successfully developing a new drug remains a highly uncertain activity, and firms find it difficult to use the knowledge accumulated in developing one product for developing a truly different one. Today, after substantial mergers and acquisitions in the industry, the largest pharmaceuticals company controls a market share lower than 10 percent of the world market. In the United States, the market share of the top five and the top ten firms are, respectively, less than 36 percent and around 60 percent. Moreover, the industry comprises many other types of firms competing and, in some cases collaborating, with the major corporations: small, domestic firms involved in adaptation, manufacturing, or marketing; biotech firms mainly active in the early stages of the research and development process; and producers of generics.

Pharmaceuticals have been systematically characterized by little entry and turbulence: the biotechnology revolution and the diffusion of generics constitute major changes in this respect, but nevertheless, most of the biotech companies do not compete directly on the final-product market, whereas the generics segment is already undergoing a process of consolidation. Schumpeterian competition is, however, a distinct feature of this industry. Firms compete first by trying to discover and develop new drugs. The process is highly costly and risky, and only a very small number of molecules actually reach the market. Innovators, thanks to

patent protection, enjoy high profits after the introduction of a new, successful drug. But quite early, innovative products become exposed to competition from imitators, which provide patented variants of the original drug. After patent expiration, generics enter the market, in some cases substantially eroding the profits of the original innovator.

Finally, the industry is characterized by strong information asymmetries: consumers are typically unable to properly evaluate the quality of a drug before taking it. The prescribing doctor decides which drugs to use, but even doctors often do not know all the properties of a drug, especially a new drug for which much of the available information is provided by the company itself. Given the value users may attribute to the product, especially in extreme cases, demand price elasticity tends to be low. Moreover, most consumers are insured (privately or publicly) against at least a part of the cost of prescription drugs, so they are only partially interested in drug prices. The prescribing physicians are, likewise, not completely sensitive to prices, both because they will not pay for the prescribed drugs and because professional norms make them more attentive to the safety and therapeutic value of medicines than to their prices.

The industry has undergone deep transformations in the past 25 years. First, the data gleaned via the veritable molecular-biology revolution has substantially changed the relevant knowledge base and drug research procedures. Chemical analysis and molecular synthesis based on randomized trials now inform the drug-discovery process. Today, it is guided by the understanding of the intrinsic biological bases of diseases, drugs, and cures. Second, the organization of the industry and of individual firms is profoundly changing through the entry of specialized "biotechnology companies," and, more generally, through processes of partial vertical disintegration spanning not only pre-clinical research but also clinical trials. Thus, drug discovery and development now rely on a dense web of interactions between universities, biotech companies, hospitals, firms, organizing trials, and so forth, although large corporations still maintain key positions as integrators of the whole process (Orsenigo et al. 2001).

However, the new opportunities promised by the new technologies do not appear to have materialized. Between 1978 and 2003, research "productivity," measured by the number of patents per dollar of R&D expenditure, in fact, fell: R&D expenditures increased tenfold, whereas patenting output increased only sevenfold (Nightingale and Martin 2004). This data is further corroborated by the number of New Chemical Entities (NCE, a much more demanding measure of innovative activity than is patent assignation) approved by the FDA in the United States between 1983 and 2003. Some increase was displayed until the mid 1990s, followed by a sharp decline in the years since. In 2002, U.S. R&D expenditures in pharmaceuticals were 30 times greater than in the early 1980s, whereas roughly the same number of drugs were approved annually. At the same time, marketing expenditures also increased substantially, reaching more than one-third of sales (Orsenigo et al. 2006).

To some extent, the productivity paradox in pharmaceuticals can be attributed to more demanding regulation. Over time, the regulatory system for product approval has become more stringent, before and after product approval, increasing the cost and the time for launching a new drug on the market.[1] In addition, cost-containment policies have put pressures on the price of drugs in many countries and, with considerable differences across countries, have stimulated the diffusion of generics. The generics industry is growing and is already undergoing a consolidation phase.

It is important to emphasize, though, that the opening and growth of the generics market has also changed the geography of the industry. As in other industries, entry of new companies and new countries occurs in lower value-added segments of the industry and/or in specific niche markets. Indeed, countries like India, Israel, Thailand, and Brazil have been able to develop lively domestic industries in this segment, and some of the firms in these nations have acquired significant positions in the world market. An Israeli company is now among the 20 largest pharmaceuticals corporations worldwide in terms of sales, and there is more than one Indian company among the top 50.

III. STRENGTHENING IPR REGIMES AND TRIPS

A further important change in the industry is linked to the progressive tightening of the IPR regime. In the United States, in particular, various actions and court decisions have introduced reforms essentially aimed at saving the cost and time linked to patent procedures, extending patent duration for some classes of products, and encouraging "non-profit research institutions" to patent and market technologies developed with public funding. Moreover, a series of court cases in the mid-1990s overturned previous practices, granting patents on upstream research and significantly extending patents' scopes, even to cases where the practical application of the patented invention had not been clearly demonstrated. Just to recall a few important steps in this direction, in 1980, the Bayh-Dole act was introduced, which greatly facilitated the patenting and licensing of the results of publicly funded research; in the same year, the U.S. Supreme Court ruled in favor of granting patent protection to living organisms (*Diamond v. Chakrabarty*). These two decisions practically gave birth to the biotechnology industry. In 1982 the Court of Appeals for the Federal Circuit (CAFC) was created. As a result, the whole "inventing system" became more homogeneous (Adelman 1987). Moreover, the CAFC strongly supported the "equivalents doctrine," through which inventors were protected not only from imitative products and processes, but also from

1. However, in more recent years, regulations have become more relaxed and approval times have been shortened (as a result of the Prescription Drug User Fee Act in 1992 and the FDA Modernization Act in 1997).

those substantially similar (or similar in their results), although outside the *literal patent's scope*. Also, the Court strongly encouraged significant compensation for all the damages stemming from the violation of patent protection. In subsequent years, a number of patents were granted establishing the right for very broad claims (Merges and Nelson 1994). Finally, a one-year grace period was introduced for filing a patent after the publication of the invention.

Last, the adoption of TRIPS in 1994 extended and sought to homogenize patent protection in all countries participating in the WTO. Subsequent bilateral agreements even strengthened the TRIPS provisions.

IV. PATENTS AS AN INCENTIVE TO INNOVATE

The debate sparked by TRIPS—and by developments in the United States—touches on a mind-boggling series of difficult questions. In sum, they address the following issues:

- What would be the effects of stronger IPRs on domestic, innovative pharmaceutical-development activities in the southern hemisphere?
- What would be the effects of stronger IPRs on innovative pharmaceutical-development activities in the northern hemisphere?
- Would stronger patent protections induce higher levels of Foreign Direct Investment (FDI) and, thereby, higher rates of R&D and innovation in the southern hemisphere?
- What are the effects on drug prices and public access to drugs?
- How can the negative effects of stronger patent protections be offset? In particular, are price discrimination and parallel trade viable solutions for granting access to drugs at lower prices in poorer countries?
- Are alternative mechanisms for incentivizing and funding research possible and viable?

To introduce discussion on these issues, it might be worthwhile to go back to the basics.

The first, fundamental motivation for patents is that they provide an incentive for private agents to engage in innovative activities. Thus, theory predicts that stronger IPRs should increase the propensity for R&D and, therefore, for innovation. Yet, neither the theoretical nor the empirical literature clearly shows how big this incentive is or should be. Results depend critically on a series of variables, some of which are extremely hard to measure. For example, effects depend on the curvature of the innovation function and/or the probability distribution of innovating for any given dollar spent in R&D (the space of innovative opportunities); on the composition of the population of potential and actual innovators (Baumol 1990, Murphy et al. 1991), and, in particular, on their technological competencies; on the cost structure of R&D; on the costs of imitation with respect to the costs

of innovation; on the actual patterns of imitation (how much does imitation erode innovators' profits?); and, of course, on the specifics of the R&D decision-making process.

Moreover, stronger patent protection might actually hinder technological progress. This is the case whenever incentives for innovation under a monopoly are lower than in more competitive markets. Earlier, theoretical literature suggested that the threat of a new firm entering the market would "force" the incumbent monopolist to have a high rate of innovation (Arrow 1962, Dasgupta and Stiglitz 1980a and 1981, Gilbert and Newbery 1982). But then it was recognized that, given the "sunk cost" nature of research expenditures, an incumbent could deter competitive entry with only a limited amount of research, so that innovation under a monopoly could be substantially lower than with more competition (Dasgupta and Stiglitz 1981 and 1982, Dasgupta et al. 1982, Farrell et al. 2003). Even more important, strong patent protection can significantly slow technological progress when innovation is sequential or cumulative—that is, when it builds on previous innovations (Scotchmer 1991, Merges and Nelson 1994, Bessen and Maskin 2000). Strategic use of patents and litigation costs further deters innovation. Finally, strong patents can distort the direction, in addition to the rate, of innovation. To the extent that patents imply higher prices, research will be focused on diseases with patients who are typically rich enough to pay for prescriptions, and, more generally, on patentable cures and treatments (excluding, for example, nutrition, exercise, environment, etc.). Moreover, to the extent that firms engage in patent races (winner takes all), duplication of effort may occur.

The empirical evidence on these issues is surprisingly thin. A few studies have tried to measure the impact of patent protection on innovation in pharmaceuticals. Scherer (2001) finds evidence of cyclical co-movement in pharmaceutical-industry gross margins and R&D outlays. Schankerman (1988) estimates the value of patent rights using data on patent renewal rates and fees for France and computes the equivalent cash subsidy to R&D, obtaining a value of only 4 percent. However, this result might depend on the fact that, in France, drug prices are very low. Indeed, a similar exercise for Germany yields a value of 15.2 percent (Lanjouw 1998b). These studies focus on the impact of patents on R&D or on innovation as measured by patents themselves. Arora et al. (2005) uses survey data to estimate the so-called patent premium—that is, the proportional, incremental increase in the value of an innovation that is realized by patenting it. A value of the premium less than 1 would, therefore, imply a loss. Results indicate an expected patent premium around 1.3 in biotechnology and 1.05 for drugs. However, these values increase considerably—to 2.45 and 2.3, respectively—if the patent premium is computed conditionally on having actually patented the innovation. These results imply that a 10 percent increase in patent premium increases R&D by 10.6 percent in biotech and by 8.9 percent in drugs, corresponding to an equivalent subsidy rate equal to 22 percent.

Moreover, a 10 percent increase in patent premium increases patent applications by 14.3 percent in biotech and by 12.5 percent in drugs. These results are broadly in line with the findings by Acemoglu and Linn (2004), who estimate that, in pharmaceuticals, a 1 percent increase in the size of the market for pharmaceuticals products raises the number of new drugs by 4 to 6 percent, implying an elasticity of innovations to R&D ranging from 0.8 to 0.85.

These results confirm that patent protection is important in pharmaceuticals, but said results refer to highly developed countries and do not consider the effects of changes in the strength of the patenting regimes. Moreover, critics maintain that the degree of innovativeness of the pharmaceuticals industry might be overstated, because only a few of the new drugs are really innovative—many only introduce minor modifications (for example, in terms of dosage) to existing products.

In this respect, it is important to recall that, throughout the history of pharmaceuticals, the scope and efficacy of patent protection has varied significantly over time and across countries. The United States has provided relatively strong patent protection in pharmaceuticals. Yet many other European countries—including Germany, France, Italy, Japan, Sweden, and Switzerland—traditionally did not offer protection for pharmaceuticals products: only process technologies could be patented. France introduced product patents in 1960; Germany in 1968; Japan in 1976; Switzerland in 1977; Italy, Netherlands, and Sweden in 1978; and Canada and Denmark in 1983. In many cases, as in Japan and Italy (and possibly France), the absence of product patent protection induced firms to avoid product R&D and to concentrate instead on finding novel processes for making existing molecules. In these countries, the development of "me, too" drugs, or inventing around and getting licenses from other companies, became the main research activity.

In other cases (primarily Germany and Switzerland, but also Denmark and Sweden), the absence of product patent protection did not seem to produce such negative effects. Similarly, the reforms of patent laws do not appear to have had a visible and significant impact on the innovative capabilities of industries such as the Italian or Japanese pharmaceuticals industries. If anything, it has been argued that according patent protection to pharmaceuticals products might have had a negative effect, further weakening national industries mainly composed of generic producers (Scherer and Weisburst 1995).

Conversely, in India, pharmaceuticals product patents were abolished in 1970. After this reform, tremendous growth in the domestic generics industry was observed. India became an exporter of bulk drugs and final therapeutics, providing them to many parts of the developing and developed world at lower costs. Almost all the empirical studies on the Indian case agree that a weaker intellectual protection system encouraged the development of indigenous technological capabilities and catching up (see, among others, Lanjouw 1998a, Kumar 1998 and 2002, Ramani and Maria 2005, Chaudhuri2005).

The effects of TRIPS-compliant patent protection[2] on the Indian industry are not clear yet. However, the available evidence suggests that, indeed, a few Indian companies are trying to enter the club of innovative firms, raising their R&D intensity significantly with mixed results thus far. On the other hand, although evidence does not yet show any dramatic shake-out of local producers of generics, most analysts seem to agree that a substantial restructuring is bound to occur. In the best scenarios, most local generics-producing firms would become intermediate-product manufacturers or service providers to larger foreign companies or would continue as generics producers but with much higher costs linked to access to licenses, litigation, and so forth.

These insights are confirmed by other, more recent studies on the effects of strengthening patent protection on innovation. Theoretical analysis suggests that when patents are already strong, increasing patent protection further may actually depress the level of innovation (Gallini 1992, Cadot and Lippman 1995, Horowitz and Lai 2006). Similarly, in countries lagging behind the technological frontier and with low per capita income, stronger patent protection has little effect on the rate of innovation (Deardorff 1992, Helpman 1993, Lall 2003).

Empirically, various studies have confirmed these predictions. Examples include studies of the broadening of the scope of Japanese patents (Sakakibara and Branstetter 2001), the establishment of the Court of Appeals for the Federal Circuit in the United States (Kortum and Lerner 1998, Hall and Ziedonis 2001), and statistical analyses of episodes of strengthening IPR over a 150-year period (Lerner 2005). Moser (2003) examines data constructed from the catalogues of two 19th-century world fairs: the Crystal Palace Exhibition in London (1851) and the Centennial Exhibition in Philadelphia (1876). She also finds no evidence that patent laws increased overall levels of innovative activity but strong evidence that patent systems influenced the *distribution* of innovative activity across industries—that is, the direction of innovative activity.[3]

In sum, there are strong reasons to doubt that strengthening IPRs in developing countries would have a positive impact on domestic innovative activities. Such effect presumes sufficient scientific and technological capabilities, access to knowledge and active participation in research networks, and large domestic markets and/or the ability to export. If anything, stronger IPRs might possibly make life more difficult for local brands and generics producers, especially

2. India signed the Uruguay round of GATT in 1994, but it availed itself of the complete term of the transition period (i.e., 10 years), which was accorded to developing countries to set up a TRIPS-compliant IPR system.

3. In this respect, it has sometimes been argued that stronger IPRs in developing countries could introduce incentives for developing drugs for local diseases—for example, malaria. However, there seems to be no evidence that this is, or could actually be, the case. Decisions concerning the direction of innovative activities would still be influenced by considerations of profitability, by both local and foreign innovators.

if data-exclusivity agreements and patentability for second-use provisions are enforced.

It is even harder to evaluate the effect on R&D and innovation in companies located in rich countries. This will depend on how big the increase in sales and profits might be (which depends also on the resulting price increase), on how much of that will be translated into higher R&D, and on the elasticity of innovation to R&D.

V. PATENTS AS INCENTIVES TO COMMERCIALIZE INNOVATIONS

One finds less skepticism toward the effects of IPRs on innovation when a second set of arguments concerning the role of patents is advocated—namely, that patents disclose information. In the absence of patents, innovations are much more likely to remain secret. Moreover, patents may induce the commercialization of innovation and the development of markets for technology (Arora et al. 2004, Lamoreaux and Sokoloff 1999, Kahn and Sokoloff 1998). The establishment of property rights on research outcomes facilitates the economic exploitation of such knowledge (in the absence of patents, firms would not invest in R&D based on new discoveries because anyone could have access to it) and allows an "ordered" path of exploitation of such knowledge, avoiding the wasteful duplication of effort. The Bayh-Dole Act is clearly based on these assumptions, and the boom in biotech companies (often founded by university scientists) is typically cited as an example of the positive effects of the "new" IPR regime on the commercial exploitation of basic scientific research.

In sum, one finds less skepticism when patents are conceived not so much as an incentive to innovate but as a mechanism for creating markets for technologies. Several objections, however, have been raised against this argument. First, this incentive is not needed in the case of publicly funded scientific research: The invention has already been paid for (by the public), and it has already been realized. Moreover, the argument in favor of the imposition of property rights on otherwise open science rests on a series of specific assumptions about the mechanisms of generation and economic exploitation of knowledge that, as argued by Mazzoleni and Nelson (1998), makes it very hard to accept that argument, in general. In particular, the argument for patenting implies that no further mechanisms of protection are available in the development process.

Indeed, broad patents on basic inventions might hinder further innovation, especially if licenses are given on exclusive terms or at very high prices. First, bringing science into the "market" is likely to distort incentives away from basic research and into specific practical areas that promise commercial rewards. Second, science "*proceeds most effectively and cumulatively when those who do science are part of a community where open publication and access to research results is the norm, and rewards are tied to recognized contributions to the communal scientific*

effort" (Nelson 2004). But widening the scope of discoveries allowed to be kept as proprietary runs precisely against this principle. Other sources of worry relate to the "anticommons problem" (Heller and Eisenberg 1998), which concerns the possibility that the extension of patents into research tools will limit innovation as a result of numerous property-rights claims to the separate building blocks of some product or line of research.

In this case, the evidence is mixed. First, various studies have shown that the Bayh-Dole Act did not give birth to technology transfer from university to industry and that the surge in university patents and licenses predates Bayh-Dole (Mowery et al. 2001). Rather, university patenting seems to be triggered by new technological opportunities (biotechnology, software, etc.) and from improvements in the management of the innovative processes (Kortum and Lerner 1998). Moreover, patents are just one instrument of technology transfer, nor are they the most important one (Cohen et al. 2002, Agrawal and Henderson 2002). Second, there is contrasting evidence that university scientists may shift their focus from basic to applied research. Indeed, much of the research conducted in universities is located in the so-called Pasteur's quadrant (i.e., it is at the same time basic and use-inspired [Stokes 1997]), and, if anything, the evidence seems to indicate strong correlations between patenting and publishing (Agrawal and Henderson 2002, Azoulay et al. 2004, Geuna and Nesta 2006, Breschi et al. 2005). Walsh et al. (2003), in a survey of biomedical researchers in universities and private companies, find no major delays or abandonment of projects as a result of transaction costs, but some evidence of increasing obstacles and delays in securing material transfer agreements for research purposes. Other studies, however, find evidence for a quantitatively modest, but statistically significant, anticommons effect (Murray and Stern 2006) and document solid evidence on publication restrictions for sponsored research in the life sciences (Thursby and Thursby 2003 and 2006).

In the case of developing countries, stronger IPRs might hinder the development of domestic scientific capabilities if royalties on basic research tools are too expensive. However, for these countries, the argument that well-defined IPRs may contribute to the development of markets for technologies and to the commercialization of inventions has a further facet: they could attract foreign direct investment (FDI) and, possibly, related R&D. This argument has some empirical support (Maskus 2001), particularly as it concerns clinical trials and market-development activities. Yet it is also widely recognized that IPRs are only one of the motivations leading to FDI. Other considerations—the availability of local skills, research infrastructures and capabilities, and demand characteristics, as well as other institutional and legal preconditions—are usually more important.[4]

4. A counter-argument is that increased foreign direct investment might produce a crowding-out effect on skilled labor and local researchers for domestic companies.

VI. IMPACT ON PRICES

The obvious cost of stronger IPRs is higher prices. In turn, the impact on prices depends on a series of variables, such as market structure before and after the new patent regime (including the number of domestic and foreign firms, the nature of competition, the ease of market entry and exit, quality differentiation among products, openness to trade, and wholesale and retail distribution mechanisms); demand elasticity; and pricing regulations and competition policies (in particular as it concerns parallel imports and sole distributorship laws [Maskus 2001, Nogues 1993]).

Once again, it is very difficult to evaluate, in general, the effects of TRIPS on drug prices. Scarcity of data and the extreme difficulties in computing comparable price indexes (Danzon 1997, Danzon and Kim 1998) prevent systematic analysis. Clearly, such effect will be different across countries. The evidence surveyed by Maskus (2001) suggests, however, a substantial impact. Price increases after the introduction of patents were estimated by Watal (2000) and Fink (2000) to range from 50 percent to 200 percent in India, whereas Baker and Chatani (2002) suggest that the average increase in price for pharmaceuticals as a result of patent protection is probably close to 400 percent. More specific analyses of specific drugs report that, in Brazil, free-market versions of AIDS drugs were available at $200 as opposed to $10,000 a year for patent-protected versions (Coriat et al. 2006).

Two issues deserve specific attention. First, price regulations certainly have a large role to play in limiting price increases. However, patent holders may choose not to supply the local market at the regulated prices. Moreover, when price regulations are based on "cost-plus" formulae, firms are encouraged to set high transfer prices on imported ingredients, leading to potentially higher prices (Lanjouw 1998a). Conversely, when prices are defined on the basis of reference indices of prices in other markets, firms have an incentive to bargain for the highest possible prices in the low-price economies in order to gain a higher set of global reference prices (Maskus 2001).

Second, price discrimination is often considered as a possible counterbalance to unaffordable drug prices in poor countries. However, this implies banning parallel imports, an important source of low-price drugs in many countries (and a source of exports for producers in developing countries). Further, price discrimination is often viewed as anticompetitive because it allows firms to set prices according to market power in each country. Indeed, Maskus (2001) shows that prices are often higher in developing nations than would be expected under a simple price-discrimination equilibrium and, indeed, are at times higher than in the rich nations.

VII. THE TRIPS AGREEMENT AND PATENTING ACTIVITY: THE CASE OF BRAZIL

Given the complexity of the relationship between the strength of IPR protection and innovative activities (and access to medicines), it is increasingly important to

be able to collect reliable and disaggregated patent data from national patent offices in developing countries. In this section, we focus in particular on the Brazilian case and show some preliminary evidence.

A. Data Analysis

Typically, international patent databases (the European Patent Office [EPO] and the U.S. Patent and Trademark Office [USPTO]) have been used to assess the technological activity and specialization of developing countries (Montobbio and Rampa 2005, Huang and Miozzo 2004) because they allow for international comparability (Pavitt 1988). Because patenting abroad is expensive, patents at the EPO and USPTO should also have the highest perceived economic value by applicants and inventors. However the use of EPO and USPTO patents is not particularly appropriate for the analysis of the economic impact of IPR reinforcement in developing countries—in this case, Brazil.

In the first place, the analysis of international patenting activity can only be based on patents whose applicant or inventor is Brazilian. In principle, one could argue that, if reinforced IPRs in Brazil really constituted an incentive to perform more R&D, this would be observed in patenting activity abroad. Still, the analysis of patenting activity by foreign companies in Brazil would remain out of the picture. Second, a small number of Brazilian (owned or invented) EPO and USPTO patents exist, relative to the overall economic and technological activity of the country (Montobbio 2007, FAPESP 2005, Albuquerque 2000). Brazilian patents numbered 1,715 at the USPTO from 1968 to 2001 and 1,244 at the EPO from 1978 to 2001. Thus, Brazilian firms (in particular, the small and medium ones) do not patent systematically abroad, and international patents provide only a partial view of the nation's inventive activities. International patents mainly reflect the activities of exporters, and, in many cases, they are the results of technological cooperation between Brazilian and U.S. or EU inventors. In fact, the important Brazilian actors involved in international patenting are mainly U.S. and German companies with a foreign address, or their foreign subsidiaries with a Brazilian address. The main Brazilian patenting company is Petrobras, with patents in a set of heterogeneous sectors of economic activity (oil, glass, electric, metals, and machinery).

In particular, in the pharmaceuticals sector between 1975 and 2001, 190 USPTO patents document Brazilian inventions with widely dispersed ownership. Only one-third of the applicants have a Brazilian address, and the top patentees are (excluding 57 patents that are "individually owned") Johnson & Johnson (10), Fond. Osvaldo Cruz (5), and St. Jude Medical (4).[5]

5. Consistent with what is observed above, it can be noted that most of the 10 patents by Johnson & Johnson are related to a specific project and reflect the activity of a specific team of inventors on different types of sanitary napkins and absorbent articles. Finally, it can be noted that 19 USPTO patents with a Brazilian inventor are owned by U.S. universities or medical schools.

Thus, analysis of the data from the national patent offices is more appropriate if the research question concerns the effects of strengthening patent protection within a country. Domestic data provide a much more accurate description of the nature of patenting activity in a developing country, and they allow for investigating the impact in changes in legislation. Typically, these data are very hard to obtain, coverage is partial, and not all the information contained in a patent is available. We provide here an introductory picture of the patenting activity at the domestic patent office in Brazil, using the PATSTAT database.[6] The database contains 442,070 patent applications between 1972 and 2006; 342,453 patents are from firms and other institutions, and 62,162 are from individual applicants (but 37,445 patents' applicants are not identified).[7] Moreover, the database contains 155,871 applicants, including 47,037 individuals. Among the 110,008 applicants with an address (most of them are companies), 68,176 are from Brazil (i.e., 62 percent). However the share of patents of Brazilian applicants of those with an address is only 41 percent.

B. Findings

Inspection of these data suggests a number of findings.

1. The number of patents increased rapidly after 1996. Figure 13.1 shows the total number of patent applications at INPI[8] between 1974 and 2004 from PATSTAT and from the official data provided by INPI through WIPO.[9] The coverage of the PATSTAT database is good, and, particularly in recent years, the numbers of patents in the two databases are very similar. In the PATSTAT database, the total number of patents remained stable between 1974 and 1991; it declined sharply between 1992 and 1996; it increased significantly after 1996.

In fact, between 1996 and 2001, we observe a fourfold increase in the number of patents. The new Industrial Property Law 9.279/96 was approved in 1996 and, in accordance with the TRIPS, introduced patent protection for pharmaceuticals, biotechnological products, and chemical products and processes that were excluded from patentability in the previous 1971 IP code. At the same time, data also show a declining trend between 2001 and 2003. This may suggest that the impact of the legislative change is temporary, even if there is another sharp increase in 2004.

2. The sectoral composition of patenting activity does not vary substantially, except for the increased weight of chemicals and pharmaceuticals after 2002. This aggregate trend covers a heterogeneous sectoral dynamic. Figure 13.2 shows

6. PATSTAT is the OECD and EPO Worldwide Patent Statistical Database.

7. The dataset also contain utility-model applications.

8. The law of creation of the INPI (Instituto National de Propriedad Industrial) was approved in 1970, and the law on industrial property is 5,772, on December 1971.

9. The PATSTAT database provides the publication date of the patent; for WIPO data, see http://www.wipo.int/ipstats/fr/statistics/patents/.

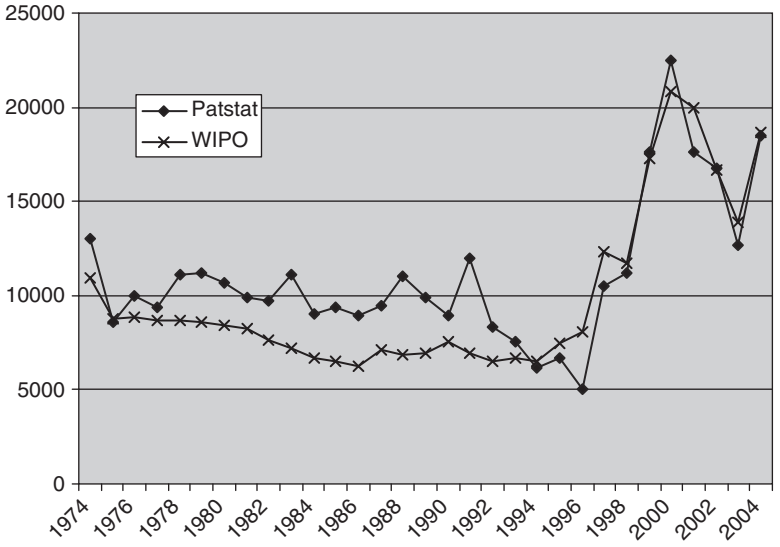

FIGURE 13.1 NUMBER OF PATENT APPLICATIONS IN BRAZIL.
Source: Our elaboration on PATSTAT data.

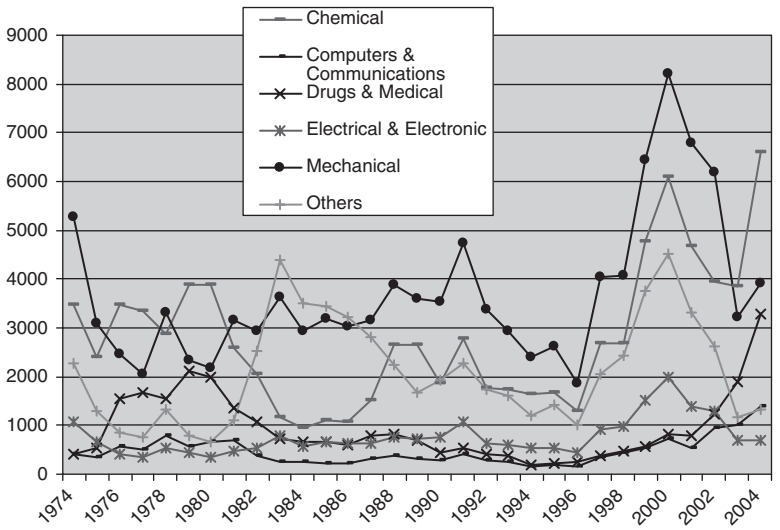

FIGURE 13.2 NUMBER OF PATENT APPLICATIONS IN BRAZIL IN SIX SECTORS.
Source: Our elaboration on PATSTAT data.

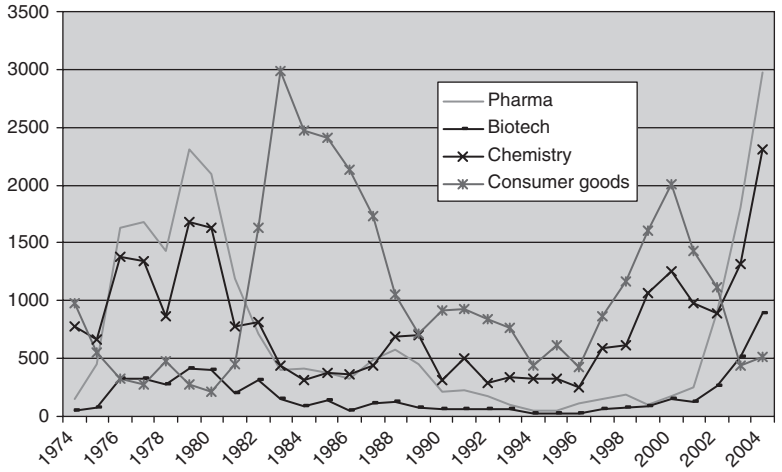

FIGURE 13.3 NUMBER OF PATENT APPLICATIONS IN BRAZIL IN FOUR TECHNOLOGICAL CLASSES.

Source: Our elaboration on patstat data.

the breakdown by six broad sectors; Figure 13.3 shows a more detailed picture of four smaller technological fields.[10] In Brazil, 40 percent of all patents come from the mechanical sector. This share was substantially constant until 2002. Patents in all sectors increased proportionally after 1996, with the exception of a sharp increase in patenting activity in the chemical and pharmaceuticals sectors between 2002 and 2004. In particular, in the pharmaceuticals sector in 2004, the number of patent applications is more than four times as big as the 2001 figure (from 778 to 3,271).[11] However, this trend reflects, in all likelihood, that pharmaceuticals were not patentable (nor were products, nor processes) from 1971 to 1996. Thus, this increase is likely mainly the result of the extension of foreign patents.

Some other relevant facts emerge from these figures. First, there was substantial patenting activity in Brazil between 1974 and 1979 in the pharmaceuticals field. Questions arise: What types of technological activities does this indicate? Which are the main economic actors? Second, throughout the 1990s, very few patents in pharmaceuticals were granted, with only 30 patents in 1994.

3. Nonresident patents increased much faster than resident patents. Figure 13.4 shows that the increase in the number of patents between 1996 and 2000 was mainly the result of patent applications filed by nonresidents, with a more than threefold

10. The different IPC classes have been reaggregated into economic sectors and technological fields following OECD (1994). The sectoral classification is available from the authors upon request.

11. We define pharmaceutical patents as all the patents corresponding to the class named "pharmaceuticals and cosmetics" of the classification OST30. The IPC four-digit codes corresponding to such class are A61K and A61P.

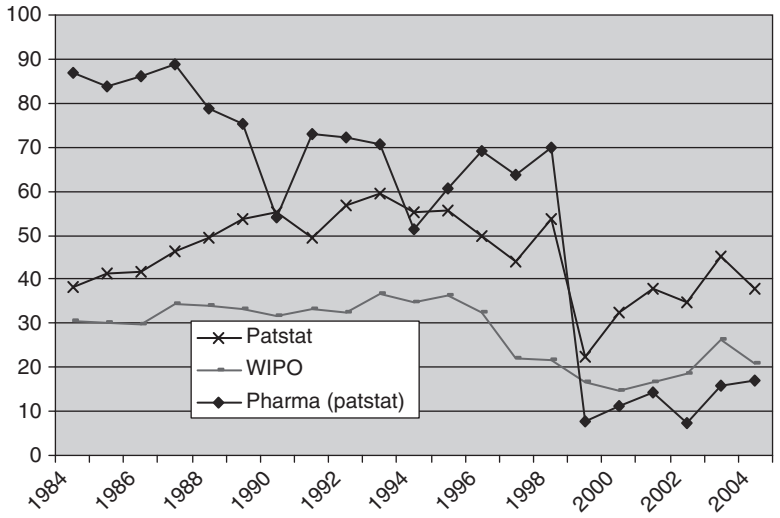

FIGURE 13.4 RESIDENT SHARE OF TOTAL PATENTS.
Source: Our elaboration on PATSTAT data.

increase (from 5,446 in 1996 to 17,741 in 2000, according to WIPO). In the same period, patents by residents increased by 50 percent. After 1999, according to the PATSTAT database (and after 2000, according to WIPO), the ratio of resident patents to total patents started rising again. Note that in the PATSTAT databases, on average, the percentage of resident patents is lower. This is probably because we do not have the addresses for all the applicants. Overall, these data show that there was a massive inflow of patent applications after the introduction of the law 9.279. Many of these applications were probably patents already filed abroad and extended to Brazil.

Moreover, Figure 13.4 shows a sudden drop in the share of patents applied for by Brazilian residents, particularly in pharmaceuticals. As pharmaceuticals patents grew rapidly after 2000, the shares of patent applications from Brazilian residents dropped from 66 percent between 1993 and 1998 to 15 percent from 1999 to 2004.

Finally, Table 13.1 shows that all the top pharmaceuticals companies are multinational, foreign-owned corporations. After 2001, the top five companies accounted for more than one-fifth of the total number of patents in the pharmaceuticals sector, and the top 10 companies accounted for 27 percent of pharmaceuticals patents.[12] In particular L'Oreal, Astrazeneca, and the group Pfizer-Pharmacia have 19 percent of all pharmaceuticals patents in Brazil.

12. However, it is important to note that the number of firms increased substantially with the number of patents. From 1993 to 1996, the pharmaceutical sector comprised 249 patents and 114 patenting firms (2.18 patents per firm); from 2001 to 2004, the sector comprised 4,583 patents and 848 firms (5.4 patents per firm). Moreover, in the sub-periods

TABLE 13.1 TOP 10 PATENTING PHARMACEUTICAL COMPANIES IN BRAZIL IN THREE SUB-PERIODS

	1993–1996	Country	Patents	% of total patents
1	L'OREAL	FR	34	13.65
2	PFIZER	US	13	5.22
3	GLAXO	GB	12	4.82
4	ASTRAZENECA	SE	7	2.81
5	GRUNENTHAL	DE	7	2.81
6	BAYER	DE	7	2.81
7	NOVARTIS	CH	6	2.41
8	BRISTOL-MYERS SQUIBB	US	6	2.41
9	AVON PRODUCTS	US	6	2.41
10	EMISPHERE TECHNOLOGIES	US	5	2.01
	TOTAL PATENTS IN THE SUB-PERIOD		249	100
	TOTAL FIRMS IN THE SUB-PERIOD		114	
	1997–2000			
1	L'OREAL	FR	26	5.46
2	COLGATE PALMOLIVE	US	20	4.20
3	NOVARTIS	CH	18	3.78
4	HOFFMANN LA ROCHE	DE	18	3.78
5	ASTRAZENECA	SE	13	2.73
6	GRUNENTHAL	DE	11	2.31
7	HOECHST	DE	10	2.10
8	NIPPON SHINYAKU	JP	9	1.89
9	EISAI CO	JP	7	1.47
10	HENKEL	DE	7	1.47
	TOTAL PATENTS IN THE SUB-PERIOD		476	100
	TOTAL FIRMS IN THE SUB-PERIOD		224	
	2001–2004			
1	PFIZER	US	358	7.81
2	L'OREAL	FR	297	6.48
3	ASTRAZENECA	SE	178	3.88
4	BASF	DE	71	1.55
5	HOFFMANN-LA ROCHE	DE	69	1.51

2001–2004

6	ELI LILLY	US	60	1.31
7	AVENTIS	DE	60	1.31
8	JOHNSON & JOHNSON	US	53	1.16
9	PHARMACIA	US	50	1.09
10	NOVARTIS	CH	48	1.05
	TOTAL PATENTS IN THE SUB-PERIOD		4583	100
	TOTAL FIRMS IN THE SUB-PERIOD		848	

Source: Our elaboration on PATSTAT data.

4. The increase in the number of pharmaceuticals patent applications lags other sectors' by at least three years. The number of pharmaceuticals patents granted is still very low. The substantial take-off of pharmaceuticals and biotech patents took place in 2000. These numbers refer, however, to patent applications, and not to granted patents. The number of patents granted is still very low.[13] These observations are probably the outcome of some specific features of the process through which TRIPS was implemented in Brazil, in particular as it concerns pharmaceuticals.

First, according to the Brazilian Government, article 65(2) of TRIPS is applicable to Brazil as a developing country, and, therefore, the transitional period of four years (which ended in 2000) may have created uncertainty about the validity of some pharmaceuticals patents. Moreover, the highly disputed 1999 Provisional Measure 2014—transformed into law 10.196 in 2001—conditionally grants pharmaceuticals patents on ANVISA's approval (Agência Nacional de Vigilância Sanitária[14]) and rejects applications for some substances, matters, and products

1997 to 2000 and 2001 to 2004, no decline in the concentration rate occurred even though the number of companies was almost four times higher.

13. See, for example, INPI statistics on www.inpi.gov.br or EFPIA (2004). According to EFPIA (2004), Brazil has only issued 428 non-pipeline and 628 pipeline pharmaceuticals patents between 2000 and 2004. Unfortunately, we do not have data on the number of patents granted in different sectors.

14. The National Health Surveillance Agency (ANVISA), established in 1999, is an independent and financially autonomous regulatory agency that exercises sanitary control over production and marketing of products and services subject to sanitary surveillance (http://www.anvisa.gov.br).

related to pharmaceuticals inventions that lack pipeline protection.[15] In general, since the ratification of TRIPS, Brazil has imposed relatively more restrictions on pharmaceutical-related patents than have other countries. This particularly concerns the issues of compulsory licensing; high fees and obligations for pipeline applications; international exhaustion and parallel imports; and a permissive attitude toward actions intended exclusively to produce information, data, and test results by unauthorized parties (e.g., Provisional Measure 2014 claims that these actions, aimed to obtain marketing approval for a patented pharmaceuticals product, are not considered infringement of the patent). Thus, the data suggest that the inflow of foreign pharmaceuticals patents was delayed until 2000 by the actions of Brazilian authorities who sought to soften the actual strength of patent protection in this sector.

VIII. CONCLUSION

The available evidence, including Brazilian patent data, although difficult to assess, would seem to suggest that the links between patent protection and innovative performance are less direct than is usually assumed, even in the pharmaceuticals sector and especially in the short-to-medium run. Strong patent laws do, indeed, confer an advantage to innovators in the pharmaceuticals industry, but they may not be enough to promote innovation in contexts where innovative capabilities are low or missing altogether.

In particular, our preliminary analysis of Brazilian data suggests that the adoption of TRIPS had a substantial positive impact on the number of patent applications in Brazil. However, the great majority of these new patent applications have come from nonresidents, most likely as extensions of foreign patents. Thus, it is too early to assess whether this substantial increase in (foreign) patents is the result of pipeline patents under the TRIPS mailbox provision, or whether it will become a permanent characteristic of patenting activity in Brazil.

Second, the impact of TRIPS is heterogeneous across different technological fields. In general, the introduction of TRIPS does not seem to have changed the pattern of technological specialization in Brazil, with one major exception: the growth of the share of the chemical and pharmaceuticals patents, especially after the year 2000—three years *after* the upsurge of patenting in other fields. After

15. A pipeline protection is available as an "extension" of the patent granted in some other country. Any Brazilian patent granted on such a pipeline application must be identical to the foreign patent on which it is based and will expire on the same date as that foreign patent. No patents shall be issued, however, for inventions (a) that were already commercialized in any market by the holder or with his or her consent, (b) that were already worked by third parties in Brazil, or (c) that any third party in Brazil has been engaged in serious and effective undertakings with a view to start working the invention.

2000, pharmaceuticals patents continued to grow, and five big, foreign industrial groups have accounted for more than one-fifth of all the pharmaceuticals patents after 2001.

These data also show that domestic patent statistics are very sensitive to changes in the legislation and administrative procedures of the national patent office. Still, they provide a crucial source of information for evaluating the impact of TRIPS and for appreciating how relative specific national provisions may expand or reduce effective patent protection.

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