New Suppliers & New Markets: Essays on the Global Pharmaceutical Industry

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By

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Introduction

The Global Pharmaceutical industry has been witnessing tectonic shifts in the last two decades. The burden of chronic diseases globally keeps rising and healthcare stakeholders are increasingly mandating and/or influencing doctors on what they can prescribe. This is occurring in tandem with markets of the developing world rapidly gaining pace, and pharmaceutical regulators increasingly becoming risk-averse in approving new drugs. Such trends become increasingly complex to analyze especially more so in a new world order, where the World Trade Organization and treaties like the Trade Related Intellectual Property Rights are redefining the terms of trade between nations, more specifically in R & D intensive industries like pharmaceuticals. Sloan et.al argue that critics of the pharmaceutical industry evaluate the functioning of this extremely important sector on the basis of four ‘high’s; High R&D costs, High Marketing Expenditure, High Prices, and High Profits.

This dissertation proposal argues that perhaps this paradigm of ‘Highs’ is changing - especially with the emergence of New Suppliers (like Pharmaceutical Industries in the Developing World) and New Markets (with the global rise of generic medicines). Chapter 1 of this dissertation is a prelude to further analysis conducted in Chapter 2. We lay out background policies and case studies relevant to India’s growing drug and pharmaceutical industry that influenced its evolution in the last half century. The Indian pharmaceutical industry has off late captured global attention more so, after India implemented the WTO-TRIPs agreement and domestically enforced stronger patents in the country since 2005. Unlike

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pharmaceutical industries from other developing countries, India’s domestic pharmaceutical firms seem to have adapted well to this shift in intellectual property regime. With our backgrounder and case studies in place, we proceed to investigate this particular issue in Chapter 2. We document increasing R&D and increasing private returns to R & D for especially the modern Indian pharmaceutical firms as the country adopted stronger patents between 1990 and 2005. But beyond that, we also argue that there were broad macro-level shifts, like India’s overall economic reform process and the growth of US generic markets since the mid 1980s, that were important cogs in explaining the rise of the Indian pharmaceutical industry. As a logical extension of this investigation, Chapter 3 proposes to connect the emergence of these New Suppliers, with New Markets – generic medicines in the United States. Using US pharmaceutical sales data from 1997 to 2008, we propose to estimate consumer surplus generated in US markets with the entry of generics. Alongside this chapter also intends to touch on important policy, managerial and international trade related issues while wrapping up the dissertation.
Chapter 1:

Abstract

This essay takes an institutional and political-economy perspective and documents shifts in policies across four distinct periods in the evolution of the modern Indian pharmaceutical industry. A *Pre-history period* marked initial forays of domestic entrepreneurs in the industry before India’s independence. A *MNC period* till around 1970s marked the predominance of multinationals in post-Independence India; this after the country had adopted product patents and therefore accorded market power to global pharmaceutical firms with monopolies in globally held drug patents. An *Intervention period* marked governmental intervention and re-aligning of the industrial policy regime, bringing alongside a growth of domestic firms in the industry. Finally, a *Liberalization period* has been well and truly underway for the industry (as well as the overall Indian economy) since the early 1990s. This has come with an overhauling of protectionist policies that kept domestic firms at bay from the forces of the global market economy. Our attempt in documenting shifts in institutions and the policies during these four periods is interwoven with their impact over the industry’s evolution. In the concluding section of this chapter we report our learnings from firm case studies, covered as part of a field trip to India in December 2008. The case studies of 14 Indian firms form the basis of our subsequent econometric investigations in Chapter 2.
Introduction

The history of the modern pharmaceutical industry in India could be broadly categorized into four periods. A pre-history period marked the advent of some nationalist Indians spearheading early efforts to develop the industry before India’s independence in the early 20th century. A subsequent MNC period marked the entry of global pharmaceutical firms in India after 1947, the year when the country got independence from British rule. This was the period when the country adopted the British Patents Act 1911 and recognized product patents. MNC firms subsequently held sway in domestic markets with globally held drug patents. The MNC preeminence however meant that drug prices in India were high during the post 1947 phase, something which was realized to be of national importance after the Indo-China war of 1962. Around that time, the Government of India (GoI) started taking active interest in developing the domestic drugs and pharmaceutical industry, especially to ensure self-sufficiency in public health, for example in areas of antibiotics and vaccines manufacturing. The result was the ushering in of what can be called an Intervention period from around the 1970s. Especially in its early phase during this period, India’s patent laws were reformed encouraging process patents (and abolishing product patents) with the Indian Patents Act 1972 being put in place. Further, price controls were imposed on drug products, and foreign ownership restrictions (with the Foreign Exchange Regulation Act of 1973) were laid out to encourage domestic firms in overall Indian industry as much as in drugs and pharmaceuticals. The intervention period was also one when there was considerable governmental control imposed on overall industry in general. The Industries Act 1951 had already ushered in a period of protectionist sentiments after India got independence in 1947. This was whetted up around the 1970s, with firms in India subject to stricter licensing requirements from the government. The period was also marked by a progressive discouragement of large firm activity in India with special reservations and incentives being promoted for small scale industries, entrepreneurship suffering as a result. Further, protectionist policies in trade and foreign investment along with distortions in currency regimes kept the global markets at bay from the Indian economy and its constituents. Some of these started changing between 1985 and 1990, the latter half of the intervention period. Under the stewardship of the then Prime Minister Mr. Rajiv Gandhi, the folly of protectionism for long run capability and competence building of domestic firms was realized – and some reforms were initiated by stealth\(^3\) (Panagariya 2008). Such attempts were however minimal and further dismantling of the licensing regime and

\(^3\) Stealth because Mr Rajiv Gandhi had to initiate economic reforms while keeping in minds the constraints of coalition politics that was prevalent then, and has been prevalent in India for a major part of the last 2 decades.
corrections to take care of distortions in the trade policy and currency regime were much needed for the economy\(^4\). Such an impetus for large scale reforms came in the early 1990s. This phase which could be called the *Liberalization period* for the Indian industry (and also for the Indian economy at large) came about as the Indian economy faced a severe balance of payments crisis in 1991 with both high fiscal and current account deficits as it relied on external borrowing from the IMF to finance the deficits. This apart rising debt service obligations, peaked out rates of inflation and inadequate exchange rate adjustment made the situation dire. That was when the GoI aggressively pursued large scale economic reforms and policies related to trade liberalization in India. Indian industry was substantially deregulated with the New Industrial Policy of 1991, the external sector was radically liberalized with the rupee being made convertible on the current account and capital account convertibility was introduced gradually. This apart, trade in services was liberalized with policies like allowing of private banks and phased reduction of customs duties and tariffs brought into place.

The liberalization period had its effects on the overall Indian industry, the pharmaceutical industry being no exception to this rule. The industry in particular also faced the winds of global trade with India acceding to the WTO-TRIPs regime and committing to implement product patents by 2005 in the country. This was a key shift for an industry as R & D intensive as pharmaceuticals. More so, because traditionally, Indian drug makers relied on complementary capabilities and a weak patent regime to reverse-engineer and sell cheaper quality globally patented drugs, both in domestic and weakly patented markets of the world. Alongside patent regime changes, price controls on drug products were also relaxed and restrictions on foreign ownership were also withdrawn. The fourth period thus has marked an onset of forces of global competition for Indian pharmaceutical industry, as it has tried to reorient itself in the value chain of the global pharmaceutical industry. This essay outlines the above four periods in the history of modern Indian pharmaceutical industry. We outline specific policies relevant to each period and where possible, use anecdotal and ongoing empirical findings to substantiate the effects of these policies on the industry at large. Our conclusion charts a picture of guarded optimism that lies ahead for the pharmaceutical industry in India. It recognizes the role of its origins and strength of its

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\(^4\) The latter half of the intervention period also witnessed some shifts in global policies which created opportunities for the domestic pharmaceutical industry in India. Foremost among these changes was the opening of the generic markets in the US, brought about by the Drug Price Competition and Restoration Act of 1984 – commonly termed the Hatch-Waxman Act. The opening of the US generic markets in the US brought about a substantial market opportunity to Indian drug makers who with close to 2 decades of protectionism had developed enough of imitative skills to market reverse-engineered generic formulations to these markets.
complementary capabilities but also sounds a caution for the domestic Indian drug firms to recognize the winds of change from global forces of demand-supply in realigning itself with the world’s pharmaceutical markets.

**Pre-History (pre 1947)**

The modern history of Indian pharmaceuticals dates back to the late 1800s and early 1900s. That was roughly also the time when India during its last half a century of colonial rule was witnessing a rise of nationalist individuals in the society. Despite a rich, more than a millennia old history of traditional Hindu medicine, some of them during early 1900s, had started making forays into science and technology at large and pharmaceuticals more specifically. This came about as influences of modern medicines started to bear its first imprints in India through the advent of the British, Dutch and French scientists and pharmacists travelling to India. The domestic industry however could be traced to the earliest manufacturers who relied on self production rather than imports. Two firms essentially (still in existence in modern day India) mark the start of the industry’s modern history. One was The Bengal Chemical and Pharmaceutical Works (BCPW) Ltd set up in Kolkata, Eastern India by a nationalist scientist Acharya P. C. Ray and the other was Alembic Chemical Works Co. Ltd in the modern day city of Vadodara, in the Western Indian state of Gujarat. BCPW mostly was into manufacturing of drug products using indigenous materials while Alembic started off with production of tincture iodine and formulations⁵, a product portfolio it stuck with till the 1960s. In the 1970s, Alembic was among the first domestic firm entering into a technology transfer agreement with Eli Lilly-USA to manufacture Erythromycin. Beyond BCPW and Alembic, this period between 1904 and 1907 also saw the establishment of four research institutes -- the Haffkine Institute in Bombay, Central Research Institute in Kasauli, Kings Institute in Madras, and Pasteur Institute in Coonoor – to work upon sera and vaccines. All these institutions, sought to harness insights from a global revolution in pharmaceuticals and drugs-making going on during that period, trying to bring in more rational design of drugs

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⁵ We use the word Bulks/API/Formulations liberally in this essay. Bulk drug makers specialize in producing chemicals that go into the production of drug formulations. Advanced intermediates or advanced bulk makers also do that just at a further specialized stage of production. Formulation makers are firms who make the final drug products in various medicinal forms like tablets or capsules using the chemicals supplied by bulk makers and adding excipients. Formulation makers could opt to be generic makers if they decide to use an off-patent going drug originally produced by another firm and enter the market with a product of similar chemical composition but a different brand name. Bulk (also called active pharmaceutical ingredients or APIs), advanced intermediates, or formulations could be one vertically integrated operation within a pharmaceutical firm coupled with its R & D divisions who might specialize not only in generic R & D but also R & D for new drug molecules.
manufacturing rather than relying on traditional and random search processes for chemical combinations to treat human ailments.

**The MNC Period (1947 - 1970s)**

Much of the industry landscape started changing after India achieved independence in 1947. India adopted the British Patents and Design Act of 1911 which in its essence granted product patents. The British Act allowed a firm to patent a product or process with the life of a drug patent being 14 years. There was also a provision of the Act to patent all processes for drug manufacturing. Such a regime stunted the growth of local firms, as global pharmaceutical firms established their monopolistic presence in the domestic markets with pre-established global patents on drugs and manufacturing processes (Chaudhuri 2005). The MNC presence in Indian pharmaceutical industry came about also as an extension of their earlier entry during the colonial period. Serving mainly through exports, earliest representation of foreign drug firms in the Indian markets came from Parke Davis’ representatives who had come to India in 1899 and had set up a branch in 1907. Burroughs Wellcome and Ciba too had set up a branch in the year 1912 and 1928 respectively (Chaudhuri 2005). Some others also had entered into partnerships with local firms or licensed importers – notable ones being Cyanamid (then Lederle), Sandoz and Merck & Co.

By the time, India got independence, the government was keen to ensure that MNC firms in India do indeed continue their activities in India, albeit starting their production from the basic stages – hoping that this would ensure domestic firm capability building in the process. However, such efforts were unsuccessful, especially since the country moved into a patent regime that recognized both processes and products since 1947 and also because foreign ownership of domestic firms were unregulated till the early 1970s. Both together ensured that MNC firms continued their commercial presence in the country with drug products for global patents which also meant that drug prices were high in India. For the consumer, alternatives were few, not being able to afford MNC manufactured drugs domestic consumers relied still on spurious/traditional medicines. Table 1 below outlines the evolution of MNC firms within India and their stages of entry into the business value chain. With respect to MNC activities in the value chain, it is worth noting that by the early 1950s, only 7 firms (Boots, Burroughs Wellcome, Ciba Geigy, Cyanamid, Glaxo, May & Baker and Parke Davis) had commenced some initial manufacturing (Chaudhuri 2005). Such activities mainly involved processing of imported bulk drugs into formulations. A report from the Committee on Drugs and Pharmaceuticals (1975) substantiates this, that MNC firms at that time were not keen to produce bulk drugs from initial stages – especially since it required
substantial investments. N H Israni, the first Indian Managing Director of Pfizer India noted the following about MNC firm activities during that period: “The MNCs considered the Indian market too small for setting up separate plants in the country. They were also not keen to lower the prices of drugs and try to enlarge the market, fearing adverse impact in their home countries. Content with small markets that could be captured at higher prices, they preferred imports to local production. Even when they started production, they were keener to formulate imported bulk drugs or those bought from others rather than to produce the bulk drugs themselves.” (Chaudhuri 2005).

It thus became increasingly clear to domestic policy makers that Western drug firms would be hard pressed to start manufacturing from the initial stages, perhaps this was the motivation for thinking differently on improving domestic drugs manufacturing capability. This resulted in a few initiatives on the GoI’s part. The most notable among this was an initiative to develop the public sector in the industry, and for this the Indian Government looked for assistance from the Soviet Union. In 1956, after some preliminary back and forth negotiations and travel by Indian scientists to Soviet Union and vice versa, GoI was ready with a proposal to overhaul the public sector drug enterprises existing at that time. Notable steps that were reflected upon during that period included, extension of the antibiotics plant of the Hindustan Antibiotics Ltd, the only public sector firm existing in pharmaceuticals at that point of time. This apart, there were thoughts on setting up new plants to produce antibiotics, synthetic drugs, and drug intermediates. All of these initial policy reflections resulted in setting up of the second public sector pharmaceuticals firm in India – the Indian Drugs and Pharmaceuticals Ltd in 1961 – mainly to produce sixteen bulk drugs at that point of time.

Table 1 – Representative MNCs in Indian Pharmaceutical Industry

<table>
<thead>
<tr>
<th>Name of MNC</th>
<th>Year of Earliest Establishment</th>
<th>Year of Commencement of Formulation Production</th>
<th>Year of Commencement of Bulk Production</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott Laboratories</td>
<td>1946</td>
<td>1960</td>
<td>Not produced</td>
</tr>
<tr>
<td>Anglo French Drug Co. (Eastern)</td>
<td>1923</td>
<td>After 1955</td>
<td>Not produced</td>
</tr>
<tr>
<td>Bayer (India)</td>
<td>1958</td>
<td>1967</td>
<td>1968</td>
</tr>
<tr>
<td>Boehringer Knoll</td>
<td>1959</td>
<td>1960</td>
<td>1962-63</td>
</tr>
<tr>
<td>Burroughs Wellcome</td>
<td>1912</td>
<td>1949</td>
<td>1965</td>
</tr>
<tr>
<td>Ciba Geigy of India</td>
<td>1928</td>
<td>1947-1951</td>
<td>1957</td>
</tr>
<tr>
<td>Cyanamid</td>
<td>1947</td>
<td>1953</td>
<td>1961</td>
</tr>
<tr>
<td>E. Merck (India)</td>
<td>1967</td>
<td>NA</td>
<td>1973</td>
</tr>
<tr>
<td>German Remedies</td>
<td>1949</td>
<td>Early 1960s</td>
<td>1962</td>
</tr>
<tr>
<td>Glaxo Laboratories (India)</td>
<td>1924</td>
<td>1947</td>
<td>1956</td>
</tr>
<tr>
<td>Hoechst Pharmaceuticals</td>
<td>1956</td>
<td>1958</td>
<td>1959</td>
</tr>
<tr>
<td>Organon (India) - Parent Company Akzo</td>
<td>1967</td>
<td>1973</td>
<td>1970</td>
</tr>
<tr>
<td>Company</td>
<td>Year 1</td>
<td>Year 2</td>
<td>Year 3</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>--------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>Parke Davis (India)</td>
<td>1907</td>
<td>1954</td>
<td>1961</td>
</tr>
<tr>
<td>Pfizer</td>
<td>1950</td>
<td>1952</td>
<td>1956</td>
</tr>
<tr>
<td>Roche Products</td>
<td>1958</td>
<td>1961</td>
<td>1962</td>
</tr>
<tr>
<td>Roussel Pharmaceuticals (India)</td>
<td>1956</td>
<td>NA</td>
<td>Not produced</td>
</tr>
<tr>
<td>Sandoz (India)</td>
<td>1947</td>
<td>After1958</td>
<td>1959</td>
</tr>
<tr>
<td>Smith Kline and French (India)</td>
<td>1950</td>
<td>1963</td>
<td>Not produced</td>
</tr>
<tr>
<td>Wyeth Labs</td>
<td>1960</td>
<td>1963</td>
<td>1963</td>
</tr>
</tbody>
</table>

Source: Chaudhuri 2005

The MNC firms during this period of Indian leaning towards Soviet technology transfer in the sector did not sit idle. First, they lobbied hard to ensure that domestic manufacturing did not infringe on their product portfolio and second, they also gave in during this process of negotiations with the Indian government, committing to step up ante and enter serious manufacturing. Ten MNCs (including some from the 7 mentioned above) entered into bulks manufacturing – though at that point - they were still picking up bulks imported from the intermediate stages. This trend continued till the mid 1970s, when it was found (from a study by Ministry of Petroleum, Chemicals and Fertilizers, 1978) that out of the total bulk drugs consumed by MNCs in India for formulations, 22.3 % came from imports, 31.8% were supplied by domestic Indian firms, while the rest 46% was accounted by own production. The MNC firm strategies thus were clear and consistent during the 1960s and 1970s in sync with Mr Israni’s observations above, though slowly they were conceding to the Indian government demands for entering pharmaceutical production from the basic stages.

Two aspects need to be understood in more careful details to wrap up this discussion on the MNC period in Indian pharmaceuticals. The first was the question of market power and in that, the accompanying role of the prevalent patent regime between 1947 and early 1970s. The Patents and Design Act of 1911 which was in force till 1972 did not categorically state on what was patentable (Patents Enquiry Committee 1950 and Ayyangar, 1959). However Indian patent office followed the interpretation that a ‘new process for manufacturing a drug – whether old or new – was patentable, and also, a new drug product was patentable provided the process of manufacturing was described in the patent. The process, however, in such a case, was not required to be new’ (Chaudhuri 2005). MNC firms around the world had already started manufacturing new drug products around the mid-1930s – at a time when the antibiotics revolution was touching global pharmaceutical industry. Thus, while, domestic firms after Indian independence of 1947, concentrated on developing manufacturing processes, MNC firms could easily exert market power by claiming ‘product patents’ for globally patented drugs that they had developed in the earlier decades in Western markets. In Indian markets specifically, MNC firms ensured
that their patents were all consuming, listing out all processes possible for a single drug product, thereby creating entry barriers for a domestic firm with process capabilities to enter the industry. There are existing anecdotes of this strategy being used extensively by MNC firms during the post 1947 period in India – however one rather illuminating example of this comes from the annual reports of The Hindustan Antibiotics Limited (HAL) – the only public sector pharmaceutical firm in India during the 1950s: “HAL developed an indigenous process for manufacturing oxytertracycline hcl. A plant was set up and production began in 1961, this without any external help. The same year though, Pfizer started manufacturing the same drug and HAL had to suspend production as Pfizer took legal action alleging infringement of patent rights.” (Chaudhuri 2005). MNC firms during this period also took action for patent infringement by domestic firms in the manufacturing of chloramphenicol and metronidazole. Domestic firms thus restricted themselves to working with licenses from MNC firms for their patented products, or in some rare cases they tried to develop relatively innovative drug products with new processes of manufacturing – though even there, delaying tactics were suitably adopted by MNC firms albeit with lax interpretation of patent claims from the Indian patent office and the courts (see Chaudhuri 2005 for an example of this in the Hoechst versus Haffkine Institute and Unichem case for manufacturing tolbultamide in 1968 which went in favor of Hoechst).

The other aspect about the MNC period in Indian pharmaceuticals relates to prevalent drug prices. In what is perhaps the most comprehensive study of drug prices available during that period (Tariff Commission, Govt. of India Report, 1968), eighteen bulk drugs and related formulations were selected to understand their pricing structure. While one cannot rule out biases in this selection process itself, broad results from that study points out that Indian formulation prices when compared with other developed countries were similar, and in terms of prices of bulk drugs, they were actually higher in India than other advanced countries of the time. An impartial evidence of this also comes from a US Senate Committee report (Kefauver Committee): “India is among nations with the highest drug prices in the world” (Kidron 1965).

In a nutshell the MNC period in Indian pharmaceutical industry was thus marked by MNC firm monopoly presence with imports and hardly any manufacturing, establishment of two public sector firms with Soviet assistance to spur up domestic drugs making capabilities, market power for MNC firms with globally held patents, and high drug prices for consumers in the domestic market. MNC firms thus by early 1970s held close to a 70% market share in the industry, as one can see in Table 2 below.
The MNC hegemony however was a worry for the GoI, more so since the country’s war with China in 1962. For the first time, GoI considered seriously on policy interventions in domestic pharmaceutical settings. The earliest ramifications of interventions thus came about in the form of the first controls on prices of drugs and pharmaceuticals in India, introduced in the wake of the Chinese aggression and declaration of emergency during the latter half of the MNC period. The Drug (Display of Prices) Order of 1962 and the Drug (Control of Prices) Order, 1963 were thus issued under Defence of India Act. In 1966, GoI further introduced a system of allowing increases in prices by issuing Drug Prices (Display and Control) Order making it obligatory for the manufacturers to obtain price approvals from GoI before increasing prices of any formulation. But these initial steps on price controls were soon realized to be not effective enough. If at all, GoI realized the need to take a closer look at the existing patent regime as also regulating foreign ownership of domestic firms. In sum, this ushered in the Intervention Period in the Indian pharmaceutical industry. We discuss this period in more details in the next section.

**The Intervention Period (1970s – early 1990s)**

The intervention period for the Indian pharmaceutical industry is worth a discussion both at the macro and the sector-specific level. At both these levels, a host of policies were implemented during this period to guide firm trajectories as local firms registered a substantial presence in domestic markets. We will first take up sector-specific policies related to patent regimes and drug price controls, moving on next to economy level policies that were implemented during this period. The latter would include government intervention for the overall Indian industry, specifically by implementation of a licensing regime that promoted the existence of subscale local firms protected from global competition.

Beyond the License Raj\(^6\), the GoI also put in place restrictions on foreign ownership of domestic firms and ensured that trade and foreign direct investment policies along with the exchange rate regimes –

\(^6\) The term License Raj was coined in the late 1950s by Indian statesman Chakravarthi Rajagopalachari who later became the second Governor General of independent India. It refers to the elaborate licenses, regulations and accompanying red tape that were required in
were not only sufficiently distorted but also biased towards local entities. Towards the end of our discussion on the *Intervention period*, we note the advent of a latter half, around 1985 onwards, when the central government started realizing the folly of protectionism and made its first forays in liberalizing the Indian economy and the industry. We also note here that for the pharmaceutical industry specifically, this was also the period when with the passing of the Drug Price Competition and Patent Restoration Act in 1984 in the United States, generic markets appeared as an opportunity for Indian drug makers endowed with process capabilities and skilled in making generic formulations. As we discuss the policies, we will also note its effect on firm scale and scope in the pharmaceutical industry during the industry and note trends in R & D intensity and exports to get a sense of the industry’s evolution.

*Sector-Specific Interventions - Patent Regime Changes:* One of the key policy interventions during this period after the 1970s was the enactment of the Indian Patents Act (1970) which was implemented in 1972 with the Indian government abolished the existing patent regime inherited from the British Patents Act 1911. The 1972 Patent Act ensured that a firm could now patent only a method or a process. The patent life was reduced to 5 to 7 years (the former from the date of sealing or the latter from the date of filing of complete specifications, whichever was shorter) from that of the earlier 14 years. Further, for a particular drug only one method or process was now patentable. The Indian Patent Act 1972 was restrictive in other aspects as well. The provisions on “local working” and licensing of rights contained in the Act limited the scope of process patents (Fink, 2000). The Act provided that any pharmaceutical process on which a local patent was obtained, had to be “worked” in India within three years from the date of sealing of the patent. After three years of sealing, the patent owner was subject to the provision on “licensing of rights”, i.e., the patent owner was obliged to license his process to a local manufacturer in cases where the patent was not locally worked for a royalty not exceeding 4%. The government also had the authority to grant a compulsory license on a process after three years from the date of sealing of the patent, if the product was not available locally at “reasonable” rates. The Drug Price Control Order (we discuss price control regimes subsequent to this discussion on patent regimes) was primarily responsible for determining these rates and when a compulsory license was granted, the royalty rate for such a license was to be set by the government in all cases where the process patent owner and the

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India to set up business since 1947, but more so since the 1970s. This was something of a conscious decision by India to move into a planned economy. But in turn this also meant that the center or the state had to be approached for each and every industrial activity, almost, ranging from capacity expansion to product diversification.
licensee could not agree upon a rate between themselves. The Act also provided that the burden of proof in cases of patent infringement rested on the patent owner.

The 1972 laws on intellectual property rights (IP) were effective for three decades in India till 2005. In three decades of a patent regime sans product patents, domestic Indian drug makers registered their presence vis-à-vis foreign firms not only in home but also in some export markets. The industry flourished on what is loosely termed as *reverse engineering*. A drug like Ranitidine (brand name: Zantac) could be introduced globally by the original innovator GlaxoSmithKline in 1983 with a worldwide product patent. But this only to see an Indian firm making a cheaper generic version of it within 2 years time by 1985 (See Table 3 for other such examples). Essentially the period during 1970 onwards ensured that lax IP laws fostered firm competencies in imitative R & D and manufacturing such that local firms could manufacture knock-off drugs from patented molecules by global firms.

**Table 3: Time Lag of new drug introduction by local Indian firms**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year Introduced abroad</th>
<th>Year Introduced in India</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salbutamol</td>
<td>1973</td>
<td>1976</td>
</tr>
<tr>
<td>Methyldioxy</td>
<td>1974</td>
<td>1976</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>1974</td>
<td>1980</td>
</tr>
<tr>
<td>Naproxen</td>
<td>1978</td>
<td>1982</td>
</tr>
<tr>
<td>Captopril</td>
<td>1981</td>
<td>1985</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>1984</td>
<td>1988</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>1983</td>
<td>1988</td>
</tr>
<tr>
<td>Acriflavine</td>
<td>1985</td>
<td>1988</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>1985</td>
<td>1989</td>
</tr>
</tbody>
</table>

Source: Chaudhuri 2005 and Kenla 2002

*Sector-Specific Interventions – Price Controls:* We have noted in the discussion of the *MNC period* that prices of drug products were high in India after independence. Perhaps on the imperative of taking care of consumer welfare, and also with rising awareness to become self-sufficient in public health needs ever since the Indo-China war of 1962, the GoI took its first steps to implement price controls on drug products in the early 1960s – this with the implementation of the first Drug Price Control Order of 1963. Subsequent versions of price control orders till 2005 were implemented in 1966, 1970, 1979, 1987 and 1995 (See Table 4). Broadly speaking, the Indian government has attempted a 3-tier control on bulk drug prices, formulation prices and overall profitability. This has meant that the government does not fix/revise prices for all the drug products – it does so only for scheduled drugs, that is, those listed in the Drug Price Control Orders (DPCO). The non-scheduled drugs are exempted from price controls. Also, the retail prices of scheduled formulations are calculated on the basis of mark-ups over material and other costs. Further, while fixing the maximum selling prices of scheduled bulk drugs, the government
takes into consideration specified rates of return on net worth/capital employed. Since, the basic
structure of DPCO was largely determined during the 1979 order, and it has remained mostly unaltered
since then (the only changes has been on the number of scheduled drugs, the degree of markup over
costs permitted for formulation pricing and the rate of return allowed on bulk drug pricing), we will base
our discussion mostly with DPCO 1979. Before that however, it is important to understand the genesis
of DPCO 1979 in lieu of DPCO 1970. In suppression of all orders issued earlier, The Drug (Price
Control) Order, 1970 (DPCO,1970) was issued under The Essential Commodities Act, 1955 with an
objective to bring down prices of essential drugs, curbing excessive profit, promoting R&D and
diversification of future development of the drug industry. It came at a time, when along with changes in
patent regime, GoI seriously started contemplating accompanying policy interventions to tilt the scales
of protectionism towards domestic drug firms.

Table 4: Drug Price Control Orders in India over the decades

<table>
<thead>
<tr>
<th>Year</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1962</td>
<td>The control on prices of drugs and pharmaceuticals in India was introduced for the first time in the wake of the Chinese aggression and declaration of emergency and accordingly the Drug (Display of Prices) Order, 1962 and the Drug (Control of Prices) Order, 1963 were issued under Defence of India Act.</td>
</tr>
<tr>
<td>1966</td>
<td>The Govt. introduced a system of allowing increases in prices by issuing Drug Prices (Display and Control) Order making it obligatory for the manufacturers to obtain price approvals from Govt. before increasing prices of any formulation.</td>
</tr>
<tr>
<td>1970</td>
<td>In suppression of all orders issued earlier, The Drug (Price Control) Order, 1970 (DPCO,1970) was issued on 16th May 1970 under sec 3 of The Essential Commodities Act, 1955 with an objective to bring down prices of essential drugs, curbing excessive profit, promoting R&amp;D and diversification of future development of the drug industry.</td>
</tr>
<tr>
<td>1979</td>
<td>DPCO 1979 was issued empowering Govt. to fix maximum sale price of 347 indigenous manufactured scheduled drug, new bulk drugs, imported scheduled drugs and to fix retention price, common sale price and pooled price of scheduled bulk drug and to fix leader price of specified formulations as per schedule I &amp; II.</td>
</tr>
<tr>
<td>1987</td>
<td>On the basis of Drug policy 1986, DPCO 1987 was issued where no. of bulk drugs under control was reduced to 142. The leader price concept in 1979 was renamed as Ceiling Price. The power to recover overcharged amount from the companies was also incorporated.</td>
</tr>
<tr>
<td>1998</td>
<td>DPCO 1998 (at present in force) was introduced under which the no. of drugs under price control was reduced to 76 (2 omitted and at present 74) and the GoI has been empowered to fix and revise the price of non-scheduled formulation also.</td>
</tr>
</tbody>
</table>

Source: Pharmaceutical Exporters Council of India, Pharmaceuticals-India.
DPCO 1970 was thus implemented to ensure two objectives, first among them being reasonable prices at which drugs were available in India. The second was to create an incentive structure for the domestic producers so as to encourage them to produce new formulations and to use, as active ingredients, new drugs that were products of original research in India. Besides covering the above-mentioned formulations, DPCO 1970 also gave the Government the power to fix the minimum price of essential bulk drugs. When DPCO 1979 came into action, it had three significant changes from DPCO 1970. These were: (i) the number of bulk drugs under price control was reduced from 347 to 163; (ii) non-essential formulations were excluded from price control; and (iii) all small-scale units with an annual turnover of less than US $ 1.22 million (Rs. 10 million) were exempted from the purview of price control. The last one was critical, because it was part of an overall economy-level drive to introduce reservation for small scale industries within the country. One can infact find that ever since DPCO 1979 small-scale sector expanded in the Indian pharmaceutical industry with some 8,000 small-scale units in operation according to the GoI Annual Report of 1999-2000. The next revision of price controls came in the form of the National Drug Policy of 1986 (there was also an earlier National Drug Policy of 1978 that looked at the reformed patent regime and the DPCO 1979) and a new DPCO was introduced in 1987. DPCO 1987 reduced the number of drugs under price control: the number of bulk drugs under price control was reduced from 163 to 145. A subsequent version, DPCO 1995, further brought about the following changes:

- New drugs, developed through indigenous R&D efforts were excluded from price control for 10 years from the commencement of commercial production;
- The scope of price control was limited to two categories of drugs: (i) those for which there were at least 5 bulk drug producers and 10 formulation producers, with none having a market share exceeding 40 per cent, and (ii) genetically engineered drugs produced by recombinant DNA technology.

The policy regime related to price controls thus evolved substantially over time, moving from absolute intervention to gradual relaxation of products under controls. This can be best understood by the sharply declining number of bulk drugs under price control, 347 in 1970, 163 in 1979, 145 in 1987 and 74 in 1995. To conclude, price controls have played an important role during the intervention period to give domestic firms a level playing field against MNCs. They have been introduced as part of the overall National Drug Policies of 1978, 1986 and 1994, broad elements of which we discuss in the section after the one that follows on foreign ownership regulations.
Foreign ownership restrictions were a key element of overall macroeconomic intervention of the Indian government during the 1970s and 1980s. The key act in this regard was the Foreign Exchange Regulation Act - FERA 1973, and this along with the National Drug Policies of 1978, 1986 and 1994 were influential in guiding the pharmaceutical industry’s trajectory. With an aim to regulate foreign capital in India, Section 29 of FERA made a distinction between firms with foreign equity of more than 40% (an arbitrary number), the FERA companies - and others, so that one could restrict the activities of the former. FERA companies were also not allowed to have foreign equity participation in excess of 74% and for the range of 40%-74% participation in equity; they had to take permission from the Reserve Bank of India for operations in India. The New Drug Policy - NDP 1978 was announced close to FERA 1973 following the recommendations of the Committee on Drugs and Pharmaceutical Industries, 1975. It was critical of MNC activities in the domestic markets, especially for not taking initiative to develop the domestic drugs industry from the basic stages. NDP 1978 had the objective of developing a strong public domestic sector playing a leading role in drugs production while channeling priorities of foreign firms in line with national priorities. It also wanted to deepen the production base of domestic firms so that they could undertake drugs production from the basic stages. For this, it encouraged R & D in concomitance with the requirements of the Patents Act 1970 and also wanted to ensure that consumers get reasonable prices as per DPCO 1970. Implemented in tandem, FERA 1973 for the overall Indian industry as applied to the pharmaceutical sector and NDP 1978 guided key policy interventions to tilt scales towards domestic manufacturers:

- First, FERA companies which were manufacturing formulations or bulks not involving 'high technology' were required to reduce foreign equity to less than 40%. The criterion for 'high technology' stemmed from the governmental committee set up in 1978, which imposed 12 aspects (mostly related to the physical and chemical laws of drugs manufacturing) to identify the nature of drug production in India. This committee allegedly found that less than half of the bulk drugs produced by FERA companies involved high technology and thus imposed the above requirement.
- A number of drugs as per NDP 1978 were then reserved for production by the public sector that is for those companies with less than 40% foreign equity.
- NDP 1978 also made the following announcement: licenses to FERA companies would be restricted to high technology bulk drug production and related formulations provided (a) 50% of
These strict licensing requirements for foreign firms were continued in the subsequent NDP of 1986, with even more restrictions imposed, the ratio 1:5 as stated above being reduced to 1:4 for FERA companies for example. Further NDP 1986 also ensured that MNC companies were denied access to the scheme of de-licensing introduced for 94 bulk drugs. Taken together, NDP 1978, NDP 1986 and FERA 1973 were influential in guiding the industry’s evolution – especially the role of MNC firms. It might be instructive here to take a look at MNC firm reactions during this phase. They had the option of either reducing the foreign equity participation to less than 40%, or withdraw manufacturing operations in India, or to continue manufacturing in India as FERA companies accepting the restrictions. The reactions were not uniform. From 1970s onwards new MNCs entering the Indian domestic pharmaceutical industry was minimal if not zero. Some MNCs like Bristol Myers Squibb did not enter at all, while some others wound up operations like Sterling - Winthrop Company which sold off their shares to Dey's Medical Company in Calcutta. Smaller ones like Abbott Labs, Fulford, and Knoll reduced their foreign equity participation. Only thirteen MNCs still retained greater than 40% equity participation, some of them being Hoechst, Burroughs Wellcome, Bayer, Ciba Geigy, Johnson & Johnson, Pfizer and Sandoz. The two policies also resulted in MNCs (which were more keen on formulations productions than bulk) setting up bulk manufacturing plants from the basic stages rather than from the intermediate stage. After mid 1990s these regulations were done away with and many such manufacturing plants set up by MNCs for bulk production were sold off as MNCs again started disinvesting in manufacturing operations. FERA 1973 has ever since been done away with progressively in the 1990s and then has been replaced with the Foreign Exchange Management Act (FEMA) 1999-2000, that has eased out investment by MNC firms in domestic Indian drug makers as much as relaxing out foreign investment norms by Indian firms in the form of joint ventures or acquisitions.
Economy level Interventions – Licensing, MRTP Act, Customs duties, FDI regimes, Exchange rates, Corporate taxes

Till now, we have focused on the sectoral-level policy interventions that guided the evolution of the pharmaceutical industry in India during the 1970s to the early 1990s. One must also bring into the picture at this point the role of overall economy-level interventions in India during this period – especially with relation to licensing requirements, competition acts, trade barriers and distorted exchange rate regimes.

License Raj in India has been a much studied area in the literature (see Aghion et.al 2008 for a latest work). In general industrial licensing enacted under The Industries Act 1951 required all kinds of enterprises to seek governmental licenses at either the state or central level to start any kind of business operations and also for expansion of scale or scope. Further imports were also brought under licensing requirements through an elaborate mechanism. Imports licensing divided imports into three categories in ascending orders of essentiality – consumer goods, intermediate goods (raw materials, components and parts), and capital goods. Imports of non-essential consumer goods were banned whereas those seen essential (food grains, edible oils, sugar, and certain drugs and pharmaceuticals) were imported exclusively through state agencies. All other imports were categorized into: non permissible (banned), limited permissible (with mandatory certification from another agency regarding essentiality as well as a mandatory clearance from Controller General of Imports and Exports CGI&E), automatic permissible (without mandatory certification for essentiality but clearance from CGI&E) and Open General License (without certification or clearance from CGI & E). The imports licensing system also brought about associated trade barriers, with peak tariff rates reaching close to 300% during this period. Add to that, an elaborate administrative machinery deployed for the allocation of permissible imports by sector of use (public or private), by type of goods (consumer, intermediate, capital) and by industries and categories of firms within industries – the environment was tailor-made to make firms thrive with enough of governmental protection. Not surprisingly, a substantial number of Indian pharmaceutical products, in formulations as well as bulks came under the licensing requirements with domestic firms benefiting as a result. While all of this was only relaxed towards the mid 1990s, such an elaborate interventionist mechanism along with reservation for small scale firms, ensured that the industry never realized the

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7 We document much of these reforms by going through 20 year (1985-2005) budget documents and economic surveys, available at the Government of India’s website of the Finance Ministry.
importance of a globally competitive minimum efficient scale remaining within its own frog-in-a-well paradigm.

The other aspect of economy-level intervention came from India’s own version of competition act, which dated back to the Monopolies and Restrictive Trade Practice Act (MRTP) of 1969. MRTP was enacted to control the establishment, expansion and structure of large enterprises to prevent the concentration of economic power and to curb restrictive practices. The Act discouraged growth of large industries and thus prevented economies of scale being realized. MRTP 1969 along with FERA 1973 (discussed above) discouraged not only large firm formation/agglomeration but also entry into any industry. For example, MRTP Act required companies to obtain government permission to expand production or establish new capacity if the company had assets over 20 million rupees, was financially connected with a company of that size, or sold more than 60% of any product or service produced in India. Together, MRTP and licensing, only added to the travails of a firm seeking a Darwinian growth guided by market forces. Infact, with corporate tax rates of 40-50% during this period, a Foreign Direct Investment (FDI) regime that required surmounting extensive bureaucracy to get a go-ahead and also strenuous access to foreign exchange in what was a distorted fixed exchange rate regime – made the situation difficult even for the ambitious firm, thriving in domestic protectionism seemed to be the only recourse. Thus during this period, the pharmaceutical industry (like many others in the overall manufacturing sector), only saw what was inevitable – a growth of the industry true, but populated with sub-scale firms fragmenting out the market, limited R & D, and survival based on products from process capabilities that were exported to countries with weaker patent protection. Hardly any attempts to invest in drug discovery or basic research were registered ala a Western drug firm during this intervention period.

It might worthwhile here to note the effect of sectoral and economy-level interventions on the growth of the domestic Indian pharmaceutical industry. A looser patent term up after 1970, resulted first in the growth of the domestic bulk manufacturing industry, alongside also came about a rise of formulation makers in the industry. As Figure 1 shows below, both bulk and formulations manufacturing were on the rise during this entire intervention period growing substantially from around a paltry $0.1 billion around the 1970s. Much of the products produced though were more imitative in nature than innovative. An oft cited example in this regard comes
from what happened to drug price competition in global ARV markets with the entry of Indian drug firms. ARV therapy stands for Anti-Retro Viral therapy to treat viral infections like HIV with drugs, not to kill the virus, but to slow down its growth. When the virus is slowed down, so is HIV disease, researchers claim. Antiretroviral drugs are thus referred to as ARV and ARV therapy is referred to as ART. Alarmed at Africa’s situation in HIV, in 2000-2001, under the Acceleration Access Initiative, The United Nations and World Health Organization came together with global pharmaceutical firms like Abbott, Boehringer, Bristol Myers, GSK, F Hoffman La Roche and Merck to bring into global markets, currently the world’s most used ARV cocktail combination of drugs, that of stavudine, lamivudine and nevirapine. But the package was exorbitantly priced at $10439 in late 2000 with global monopoly of this drug lying with Hoffman La Roche. Doctors and policy experts dealing with Africa’s AIDs situation complained of this price point given Africa’s general purchasing power parities. In 2002, Indian pharmaceutical firm Cipla Ltd entered the ARV markets with a cheaper generic version. A few others from India, namely Hetero Drugs & Aurobindo Pharma followed suit, resulting in generic ARV price points reaching $159– a 98.5% price reduction from the starting price of the original innovator Hoffman La Roche, that too in just a span of 5 odd years. And while by 2008 the original innovator too had managed to slash its prices by about 97%, the ARV story is illustrative of the potential impact of Indian pharmaceutical industry in global drug markets – endowed in process competencies and offering stiff price competition in markets of global diseases, especially in economies with weak patents.
Incentives for growth since mid 1980s – Interventions easing and Hatch-Waxman Act

Till now, we have discussed how patent regimes, price controls and economy-level interventions had created an environment of protectionism within the domestic economy of India during the substantial portion of the 1970s and 1980s. But this web of protectionism slowly started untangling around the latter half of the intervention period, during the Prime Ministership of the Late Mr Rajiv Gandhi. This was the period when the Indian economy first witnessed, what can be termed as the initial tentative steps towards easing of protectionism. This came about with initial efforts to liberalize the economy as interventions were eased and policy corrections were initiated with respect to import de-licensing, creation of export incentives, relaxation of controls over the industry and some initial steps in correcting the overvaluation of the Indian rupee. Some notable measures during this era that started around 1985 included liberalizing the imports of capital goods and intermediate inputs by expanding the list of items under open general license, reduction of the share of canalized imports – import items in which the government had monopoly rights for imports and extension of replenishment licenses to exporters to get access to imports of goods for production in the domestic market. Further, interest rates on export credit were reduced and foreign exchange for exporters was given easier access. In particular, 25 industries were de-licensed in 1985 including some bulk pharmaceuticals and the asset limit for firms which came under the Monopolies and Restrictive Trade Practices Act (MRTPA) was raised from INR 200mn to INR 1bn in 1986, thereby enhancing product market competition. Also, broad banding permitted firms in some industries to switch production between similar product lines. Between 1985 and 1989 efforts were also taken to depreciate the exchange rate at an accelerated pace with exporters being allowed to
retain 5-10% of their foreign exchange earnings with an eye on promoting exports. All of this was good news for the domestic pharmaceutical industry, more so, since accompanying global policy legislations were opening up export market opportunities for them. The most notable among these legislations was the approval of the Drug Price Competition and Patent Restoration Act in 1984 in the United States. Often called the Hatch-Waxman Act, this law permitted manufacturers to file Abbreviated New Drug Applications (ANDAs)\(^8\) for generic versions of all post-1962 approved pharmaceutical products. The Hatch-Waxman Act opened the floodgates for generic competition in the pharmaceutical industry. Since 1984, the US generic industry has grown to more than $16 billion in annual sales, representing more than 53% of all prescriptions filled in 2004. As the US generic markets grew it also provided an opportunity for India’s new generic makers (like Cipla and Aurobindo above in the ARV example) during the late 1980s and early 1990s. “It helped that the Indian pharmaceutical industry had built its generic capabilities by then and could be the first mover in the US markets,” notes Mr. D G Shah, Secretary General of the Indian Pharmaceutical Alliance. As Scherer and Weisburst (1995) document, the rise of Indian drug exports in US markets came along during this period of the opening of US generics markets, and further with Italy’s decline in generic exports to the US. From around $ 96 million in 1980-81, exports of Indian drugs and pharmaceuticals had increased to $ 1.9 billion in two decades by 2000-01 (Chaudhuri 2005). By 1988-89 India was already a net exporter of drugs and pharmaceutical products, with more than 3/4th of the bulk drugs produced and 1/4th of the formulations produced being exported out of the country (Source: Organization of Pharmaceutical Producers of India, 2004)\(^9\). Thus, in a nutshell while the early 1970s and 1980s resulted in sectoral and economy level interventions to create a strong pharmaceutical industry endowed with process capabilities, a sudden easing of interventions during the latter half along with generic market opportunities in the US saw the hitherto

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\(^8\) ANDAs could be filed under 4 categories, depending on whether the required patent information has been filed or not, whether the patent has expired, whether the patent has not yet expired and approval is sought after patent expiration or if the patent is invalid and the generic drug will not infringe with its ANDA. These 4 categories are called as para I to para IV ANDAs a term we use during the course of our discussion in the paper. Indian generic makers have mainly looked at Para IV ANDAs which has also given them the desired holy grail of the generics drug industry, the 180 day exclusivity to market their product during which no other generic maker can enter the markets. Para IV ANDAs are a costly option though and the counts of such ANDAs being approved for Indian generic makers have been decreasing. Bulk drug makers intending to supply active pharmaceutical ingredients (APIs) to generic manufacturers for US markets have to file a Drug Master File, or DMF detailing manufacturing details and chemistry composition with the FDA.

\(^9\) FDA data supplied to us by John Dietrich, Food and Drug Administration, USA also shows that bulks and formulations manufacturing for exports also brought about global standards of excellence for Indian drug firms, by 1999, 193 manufacturing plants in India –41% of all complying plants from inspections in Japan, Taiwan, Korea and India - complied with FDA regulations.
developed process manufacturing skills in Indian pharmaceutical industry increasingly becoming complementary capabilities in global pharmaceutical markets – such that they started offering generics market competition to the advanced drugs markets of the world.

The Liberalization Period (1990s – till date)

A spate of reforms marked India’s transition into an open economy in the early 1990s. While the Intervention period of the 1970s-1980s certainly had its effects on promoting subscale firms, liberalization opened the world economy to the Indian industry, no less for its pharmaceutical sector. In this section we discuss this Liberalization period. First, we outline in brief, various economy-level reforms that the Indian government engaged in during the early 1990s. Next, we outline specific sectoral – level policies for the pharmaceutical industry, the most notable among them being India’s signing into the World Trade Organization and acceding to its Trade Related Intellectual Property charter in 1995. Having documented the economy-level and sectoral-level policy changes, we note their effects on the domestic pharmaceutical industry – this in terms of firm capabilities as witnessed through rising R & D intensity, sales and market structure.

Economy-level liberalization

In 1991, after 3 decades of protectionism, the Indian economy faced a classic external payments crisis with both high fiscal and current account deficits. It relied on external borrowing from the IMF to finance the deficits but with it came the rider of opening up the economy making it integrated with global markets as per the obligations of the IMF’s Articles of Agreement. Thus started a phase of serious economic reforms in India’s liberalization experience under the stewardship of the then finance minister, Dr Manmohan Singh, who is also the current prime minister of India. Perhaps the most influential step in liberalizing the Indian industry (and off course alongside its economy) came from the charter of The New Industrial Policy of 1991 (NIP 1991). The NIP 1991 trimmed the need for industrial licenses as was needed during the intervention period to just five industries. Further, public sector monopoly was restricted to just eight sectors and the remainder was opened to the private sector. A policy of automatic approval for foreign direct investment - FDI up to 51% was also initiated for 34 industries. In terms of economy-level changes, substantial shifts occurred in the external sector. The requirement to get imports licenses on intermediate and capital goods was removed in July 1991, (for consumer goods this was removed a decade later in 2001) and peak import tariffs were lowered progressively from what was in
excess of 300% in 1991 to 10% by the time the 2008 budget was approved by the Indian parliament (Figure 4). The rupee was devalued by 22% in 1991 and was made convertible on the current account in 1994.

Figure 3: Trends in Rupee versus the dollar and the Real Effective Exchange Rate

Source: Panagariya (2008) & RBI

Exchange rate regimes in fact saw a substantial transition during this period and merit a separate discussion in themselves. Suffice it to note here that in 1992, the Indian economy witnessed the introduction of the partial convertibility of the rupee with a dual exchange rate system being introduced. This was termed the Liberalized Exchange Rate Management System or LERMS. LERMS meant that quite a few systematic shifts occurred in the manner in which foreign exchange was dealt with in India. First, all foreign exchange receipts on current account transactions (exports, remittances etc..) were required to be surrendered to authorized dealers (ADs) in full. Next, the rate of exchange for conversion of 60% of the proceeds of these transactions was the market rate quoted by the ADs, while the remaining 40% was converted using the central bank, Reserve Bank of India’s (RBI) official rate. The ADs were in turn to surrender to the RBI, 40% of their purchase of foreign currencies representing current receipts at the official rate of exchange announced by the RBI. They were free to retain the balance 60% of foreign exchange for being sold in the free market for permissible transactions. Scholars and policy debaters argued that LERMS was only a transitional system that was implemented to provide stability to the rupee – rationally however, the LERMS gave way to a convergence of the dual rates as a unified exchange rate market was introduced involving no legal requirements for surrender of foreign exchange earnings to the RBI. This transition of the Indian rupee into what has been termed a ‘managed or dirty float’ regime starting with the 1991 reforms, resulted in both the REER (real effective exchange rate) and the NEER (export-weighted nominal exchange rate) depreciating through the major portion of
the liberalization period with some appreciation seen in the later years, between 2001 and 2005. That it has had its effects on increasing the competitiveness of Indian exports in global markets, as much so for its pharmaceutical products, is a truism accepted by the industry and scholars working on the Indian economy.

**Figure 4: Customs Duty – Peak Rate over the years**

![Customs Duty - Peak Rate (%)](image)

Source: Reserve Bank of India Website (On Non-Agricultural Goods reduced to 20% in 2004).

Exchange rate reforms came under the broader set of current and capital account convertibility. Current account convertibility allowed residents to make and receive trade-related payments in foreign currency by themselves, be that for exports or imports and was applicable for all kind of transactions except for capital purposes. Also, capital account convertibility was introduced gradually, based on the recommendations of the Tarapore Committee, with greater liberalization for companies and financial institutions. There was further liberalization of trade in services with introduction of items like The Insurance Regulatory and Development Authority (IRDA) bill in 1999. Further, private banking was allowed and 74% FDI was permitted under an automatic route in private banks. In matters of infrastructural reforms, 100% FDI under automatic approval in infrastructure was allowed along with the passing of the 2003 Electricity Act to de-license generation and freely permit captive generation.

Reforms in India at this time also witnessed considerable financial sector reforms. The National Stock Exchange was established in 1994, and lending rates of commercial banks were deregulated. Stock Index Futures were introduced in 2001 and Foreign Institutional Investors (FIIs) were permitted to invest in government securities. The statutory liquidity ratio (SLR) – that specifies the amount a bank has to maintain in the form of cash, gold or approved securities and is quoted in terms of the total demand and time liabilities of the bank - was cut from a peak of 38.5% to 25% in 1998. This was a substantial tool to regulate banking by the RBI, but its slashing down of rates meant that interest rates in the economy moved towards a market-determined regime. Additionally, the Foreign Exchange
Management Act introduced in 1999 was made consistent with the unified exchange rate system since 1993 and the liberalized market determined exchange rate system operational at that time. It also replaced FERA 1973 and was also a key financial sector reform at the economy-level. Finally, Indian firms were allowed progressively during this period to raise money in financing overseas acquisition using standard international financing routes like External Commercial Borrowings (ECBs), Foreign Currency Convertible Bonds (FCCB), Global Depository Receipts (GDR) or American Depository Receipts (ADR). One of the key sectors that benefited from such an allowance was Indian pharmaceuticals, we outline in Table 5 below Indian pharmaceutical firms representative list of overseas acquisitions to illustrate the same.

Table 5: Select ADR/GDR/FCCB by Indian Pharmaceutical

<table>
<thead>
<tr>
<th>Year</th>
<th>Firm Name</th>
<th>Amount ($ millions)</th>
<th>ADR / GDR / FCCB / ECB</th>
<th>Stock Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
<td>Ranbaxy Laboratories</td>
<td>100</td>
<td>GDR</td>
<td>Luxembourg Stock Exchange</td>
</tr>
<tr>
<td>2004</td>
<td>Orchid Chemicals and Pharmaceuticals</td>
<td>75</td>
<td>FCCB</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>Wockhardt Ltd.</td>
<td>100</td>
<td>FCCB</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>Sun Pharmaceutical</td>
<td>225</td>
<td>FCCB</td>
<td>Singapore Stock Exchange</td>
</tr>
<tr>
<td>2004</td>
<td>Glenmark Pharmaceuticals</td>
<td>100</td>
<td>FCCB</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>Sun Pharmaceutical</td>
<td>350</td>
<td>FCCB</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>Glenmark Pharmaceuticals</td>
<td>70</td>
<td>FCCB</td>
<td>Singapore Stock Exchange</td>
</tr>
<tr>
<td>2005</td>
<td>Orchid Chemicals &amp; Pharmaceuticals</td>
<td>100</td>
<td>GDR</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>Lupin Limited</td>
<td>100</td>
<td>FCCB</td>
<td>Singapore Stock Exchange</td>
</tr>
<tr>
<td>2006</td>
<td>Ranbaxy Laboratories</td>
<td>400</td>
<td>FCCB</td>
<td></td>
</tr>
</tbody>
</table>

Source: Analyst Reports, Annual Reports of Respective Companies from their website financial information archive, validated with news item on web archives of The Economic Times, India. Not all acquisitions are listed, this is a sample representative list.
The Indian liberalization experience also occurred concomitantly with export promotion policies. While the first Export-Import Policy was drafted during the latter half of the intervention period, in 1985, the Export-Import Policy of 1993 (EXIM 1993) took active steps to provide a thrust to exports especially in the agricultural and labor intensive sectors where the country was perceived to have a comparative advantage. EXIM 1993 also had some other significant policy announcements. It significantly pruned the negative list for exports. A new Export Promotion Capital Goods Scheme permitting import of capital goods at a concessional 15% duty rate was introduced for the services sector. Export Oriented Units and Export Promoting Zones, EOUs and EPZs in agriculture and allied sectors were allowed to sell up to 50% of their produce in domestic markets. Interest rates on pre and post shipment export credit in rupee were also reduced from 11 to 9%. The final aspect of economy-level liberalization came from corporate tax policies – Indian corporate tax rates were some of the highest in the world at around 40% in the mid 1980s along with additional surcharge that was payable by large firms. In the 1990s however, this was progressively brought down to 30% by 2007-2008, reflecting in lower tax provisions for corporate India as reported in Figure 5 below.

**Figure 5: Tax Provision for All of Corporate India**

Source: Reserve Bank of India Analysis on all Indian Companies from the 50th Annual Report on the Working and Administration of the Companies Act, 1956 published by the Department of Company Affairs, Government of India.

*Sectoral liberalization - WTO-TRIPs and R & D in Indian pharmaceuticals*

Alongside economy-level reforms, the pharmaceutical sector during the liberalization period also witnessed some key sectoral-level changes. We have documented earlier the gradual relaxation of the number of bulk products that remained under price controls and further, the doing away with FERA-1973 that affected foreign ownership of firms in India with FEMA 1999-2000. Further, a depreciated rupee during the early 1990s along with relaxed norms for overseas investments and FDI related
policies, both for inward and outward investments also influenced the trajectory of firm strategies and the industry’s contours during this period. But perhaps the foremost among all changes came from India’s signing of the WTO-TRIPs agreement in late 1994 – committing to overhaul its patent regime that recognized process patents (and hence imitative skills in firms) by 2005. This was a radical shift especially for an industry as dependent on R & D as pharmaceuticals – the TRIPs signing infact slowly changed the regulatory environment for firms, conventional norms of appropriating rents out of process innovation was slowly made decadent with implementation of the new IP regime. No wonder, firms could foresee that no longer could they use mere process skills to survive in the industry, instead the focus shifted towards R & D, both in absolute and qualitative terms. We discuss all of that in this section starting with an outline of India’s signing of the WTO-TRIPs charter.

India’s signing of WTO-TRIPs came not without intense lobbying and negotiations between developed world and its own policy makers. Given the precedence of severe price competition offered by Indian firms like Cipla in the anti-retroviral case as documented above, firms from Western countries were particularly keen to reverse India’s existing process patent regime that was in place with the Patents Act 1972. Indian negotiators on the other hand voiced concerns should stronger IP laws be introduced, citing welfare effects and rising drug prices domestically as well as in the developing world, where Indian pharmaceutical exports had a significant presence. India finally did accede in 1995 however, perhaps in an environment of overall macroeconomic reforms. Following up on the Uruguay round of WTO negotiations India signed the WTO-TRIPs agreement in late 1994 committing to implement a globally consistent product patent granting regime within the country by 2000. Subsequently it started amending its own patent laws. As Table 6 outlines below, the new Patent Amendment 1995 bill allowed filing and handling of product patent applications for pharmaceutical and agricultural chemical products and marked a full-circle in the Indian experience with Intellectual Property laws. Patent Amendment 1995 bill also granted facilities for Exclusive Marketing Rights (EMR) and mailbox applications for drug products that will be due for review of their patents once the new patent was fully active in India. The new patent term was for 20 years from the grant date.

Between 1995 and 2000 the industry witnessed stormy times – both with international organizations, MNC firms as also US and EU slugging it out with Indian counterparts on the correct and consistent implementation of TRIPs. Between 2000-2001 India signed the Patent Cooperation Treaty ratifying the
Paris Convention. There were also legal disputes being fought out by MNC drug firms as to the correct application of the EMR provision in India\(^{10}\).

### Table 6 – Reforms in Intellectual Property Laws in India

<table>
<thead>
<tr>
<th>Year</th>
<th>IPK events in India</th>
<th>Implications</th>
</tr>
</thead>
</table>
| From Pre’72 to Post ’72 | British Patents and Design Act, 1911 - Patents Act 1970                            | • Pre 1972: A product and process patent regime: Life of drug patents 14 years; One could patent all processes for drug manufacturing.  
• Post 1972: Product patent regime abolished, patent only a method or a process. Life reduced to 5 - 7 years, for a particular drug only one method or process patentable. |
| 1994-1995          | Signing of the WTO TRIPs treaty by India as a result of the 1986-1994 Uruguay Round of negotiations | • Dec 31st, 1994: The Patents (Amendment) Ordinance allowing filing and handling of product patent applications for pharmaceutical and agricultural chemical products, as well as the granting of exclusive market rights. EMRs on those products. The Ordinance became effective on January 1, 1995.  
• The Patents Amendment Bill 1995 was introduced. |
| 1998-1999          | Transition period                                                                   | • Indian Patent office keeps receiving product patent applications.  
• Meanwhile disputes with US and EU at WTO related to violation of product patents.  
• WTO asks GoI to complete institutional reform on new IPR laws by April 1999. |
| 2000-2001          | India signs and ratifies Paris convention and PCT                                  | • WTO reviews the TRIPs terms and grants an extension to India beyond 2000 but before January 1st 2005 – the new deadline to implement product patents. |
| Dec 2004 – 1\(^{st}\) of Jan 2005 | Amendments to Patents Act before deadline of Jan 1st 2005 as set by WTO | • Product patent regime in place finally. From 1\(^{st}\) of Jan 2005 a firm could also now file for a product patent within India, and granted the same. |


In sum, implementing product patents in India even after the country’s signing of WTO-TRIPs had its own share of controversies and took a rather long transition period. Finally, on Jan 1st 2005, India implemented product patents within the country. The new patent laws, as per the 3rd amendment to the new Indian Patent Act implemented product patents for drugs and pharmaceuticals in 2005. While

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\(^{10}\) A much highlighted case internationally has been the tussle between Indian drug firm Natco Pharma managing to get a stay order from the Chennai High Court on EMR granting of Novartis’s cancer drug Glivec.
ensuring it was consistent with the TRIPs requirement the 2005 Patent Act tried to retain competitiveness of Indian firms in the global generics industry by introducing subtle nuances to the new IP laws. First, India’s new patent laws did not provide for patent term restoration, so that an Indian product patent was likely to expire a few years before the same patent expired in the main generics markets. Also, a Roche-Bolar provision was introduced in 2002, which facilitated R&D and lab scale production before patent expiration (Section 107A of the Patents Act). Finally, the strict patentability requirement introduced in the 2005 Act could also be used to reject some patent applications on incremental innovations, such as new uses for existing drugs and new forms of a known compound (Section 3(d) of the Patents Act). These aspects of the patent legislation were expected to shorten the exclusivity period of drug products in India, allowing early entry by Indian firms to maintain their competitiveness in the generics industry of global pharmaceutical markets, but in all probability this got giving the domestic firms a head start only in domestic markets.

The liberalization period thus marks a competitive reinvigoration and transformation of the pharmaceutical industry in India, not only in the face of overall macro-economic reforms but beyond that revised patent laws that changed the appropriability environment under which firms could adopt strategies to seek rents from innovation. There has been a wide distribution in firm-level responses to the TRIPs transition during this period. While one would have expected past capabilities to act as a deterrent in the reformed patent regime, in some sense those precisely have acted as a key source of comparative advantage at least in the medium term. If not the entire industry, at least its 30 to 40 of modern firms have actually started investing in R & D and reaping statistically significant increasing (private) returns from them. As the final subsequent section in this discussion on liberalization period documents, a substantial component of pharmaceutical R & D in India during the 1990s was perhaps aimed towards a policy of medium term survival - catering generic markets – only few moving up on the R & D continuum.

**Industry Response to Indian Economic Reforms**

Let us now summarize the industry response to the liberalization period at various levels. While some firms have taken to adopting the generics route as a medium term survival strategy, taking advantage of its early entry in US generics markets aided with the Hatch-Waxman Act of 1984, a few others, have indeed stepped up R & D investments as part of an overall trend marking the industry’s moving up the R
& D continuum in the global pharmaceutical industry. Further, it must be noted that TRIPs has also brought in some amount of R & D tax credits given by the Indian government to sectors engaging in research and development\textsuperscript{11}.

The fact that the pharmaceutical industry in India has upped its R & D ante is an interesting trend given the history of stronger patent regimes in various economies around the world. To start with some background, Lerner (2002) documented over 60 patent reform cases in the course of 150 years and found little evidence of a strengthening of local patent law significantly increasing local invention. When one looks at further empirical evidence, this finding is validated out. Historically, stronger IP hasn’t had much impact on domestic R &D behavior of industries in local economies where stronger patents were implemented. If at all, it only encouraged technology transfer (Branstetter, Fisman & Foley 2006) or have induced governments to actually dole out R & D subsidies for supporting local innovation, as in Korea (Choi, 2007). In most other cases, like in Italy (Scherer & Weisburst, 1994) stronger IP has resulted in a wiping out of the local industry, pharmaceuticals especially in the context of this discussion. This is perhaps expected given that this industry is predominantly an R & D intensive one, relying substantially on innovation outputs like patents to grab a share of the market rents. Qian (2007) documents this more systematically finding in a sample of 26 countries that establishment of formal pharmaceutical IP laws, in the period 1978-2002, induced no further incentive to innovate for the respective industries. From the theoretical standpoint, these empirical findings conform to a seminal theoretical paper (Grossman & Lai, 2004). They predict that imposition of stronger patents in local economies would generate little additional incentive for local firms to conduct R & D. This especially given that in a global economy, local firms always had access to larger foreign markets that were protected with product patents. The argument also looks intuitively elegant, how can a smaller domestic-market accession to stronger patents induce incentives to innovate and engage in R & D, especially when these firms always had access to advanced markets with the security of stronger IP?

In the case of Indian pharmaceuticals however, it seems to be emerging as an counterintuitive evidence to this assertion. To investigate further at the firm-level our research team conducted a field trip to India in December 2008. Learnings from this trip are documented in the following section.

\textsuperscript{11} It must be mentioned here that after signing of TRIPs, the Indian government has made specific policy announcements with respect to R & D tax credits, details on this are included in a Table in the appendix.
Learnings from Firm Case Studies

This section documents summary of conversations with firms, the interviews being part of a field-trip undertaken in India during December 08. Our overall goal was to understand the evolution of firm capabilities in the Indian pharmaceutical industry. The 14 firms covered in the trip were selected to represent the wide spectrum of capabilities in the industry. We interviewed 5 firms (Suven Labs, GVK Biosciences, Aurigene Technologies, Advinus Therapeutics and Jubilant Organosys) specializing in contract and/or collaborative drug discovery research with Western partners. 5 more were Indian generic firms, 2 among which Ranbaxy and Dr Reddy’s were early leaders in drug discovery in the industry, setting up their R & D centers in early 1990s. The other 3 among these five, Glenmark, Sun Pharmaceuticals and Zydus Cadila entered drug discovery in the last decade with different business models to fund NCE (New Chemical Entity) and NBE (New Biological Entity) research. We also spoke to 4 other firms, 1 of which was a MNC with a 50 year presence in India, Novartis’s India subsidiary; 2 firms focusing on India’s growing domestic markets, USV Limited and Emcure Pharmaceuticals. The other remaining firm in the sample was Avesthagen, a fledgling biotech entity in the industry. The field trip was undertaken in a tumultuous time in India’s recent history; a fortnight after the Mumbai terror attacks riddled and shocked the country’s financial center, leaving the world dismayed. Over a span of 12 odd days we crisscrossed 5 Indian cities of Mumbai, Hyderabad, Bangalore, Delhi and Ahmedabad talking to the 14 Indian firms and getting a sense of entrepreneurship, firm capabilities and industry evolution to get a sense of the industry’s responses to macro and micro level changes in the last decade.

We gratefully acknowledge funding from the Alfred P. Sloan Foundation.

Before we proceed to discuss the findings of the field trip, some background might be in order. The project team’s past work had carefully documented that ever since India signed the WTO-TRIPs agreement in 1994, firms in the industry had witnessed not only rising R & D investments but also increasing (private) returns to investments in R & D (Arora and Branstetter and Chatterjee, 2007 & 2008). Further investigation also showed that the trend of rising R & D investments (and returns to the same) was more significantly evident in the technologically progressive firms than others in the industry. A closer look at the outputs of the R & D process, through investigation of firm’s yearly patents filed at the US Patent Office and regulatory filings at the US Food and Drug Administration, showed however that the nature of R & D being engaged in by Indian pharmaceutical firms, were more process than product oriented. In other words one could observe that the industry was able to survive at least in the short term through ‘exploitative’ rather than ‘explorative’ research. Theoretically, this
finding was hard to justify. As discussed in the previous section, a famous model in international economics and IP (Grossman and Lai 2003) shows that firms in a Southern (or developing/emerging) economy are always incentivized to conduct basic R & D as long as there is access to market for the outputs of such R & D work in Northern markets protected with stronger IP. In other words, Indian firms could always have done drug discovery work even before the country signed WTO-TRIPs and committed to implementing stronger patent laws from 2005. This was because, should they have succeeded, the output of such work could always have been sold as a blockbuster drug in the world’s advanced pharmaceutical markets in US and Western countries. How might then one justify firm-level response to the advent of stronger intellectual property as we witnessed through rising R & D investments in Indian pharmaceutical firms?

Our field trip conversations broadly were thus structured in order to understand the evolution of firm capabilities in response to the three broad level changes – WTO-TRIPs, Hatch Waxman Act in the US and the opening of the Indian economy since 1991. Furthermore, we also asked firms to take their views on the above three and give us a sense of other happenings as they are surfacing in the industry. In the next section, we give a quick preview on linkages between Global and Indian pharmaceuticals, summarize the evolution of the sector’s R & D capabilities, highlight our pre-trip preparation and conclude with summary of our findings from the field trip.

India & the World in the Modern Pharmaceutical Industry

At this point it might be worthwhile to look at the global pharmaceutical industry and link its recent developments to the evolution of the Indian pharmaceutical industry. A quick look indicates that the industry is being guided by the following five forces as charted out in Figure 6 below. Global pharmaceutical pipelines are witnessing shrinkage as healthcare budgets in developed nations are rising spelling the need for careful pricing of new drug products coming out of the industry. This is resulting in industry consolidation, and a shift toward generic medicines to address the innovation-access debate, this beyond search by firms to look at biologicals as the next wave of advancement for new drug products. Amidst all of this, globalization has ushered in new destinations from where drug products are entering the developed world, a combination of that and firm necessity to speeden up innovation resulting in regulators like USFDA tightening the screws on allowing new drug products to the market. Overall though, a bleak prediction on new medicines and few innovative products at late stage of clinical development (See Figure 7) hint at a particularly tough time going ahead for global
pharmaceutical industry. Pipeline constraints have also meant that Big Pharma has increasingly been using product life cycle management tools to launch newer versions of older products. However this strategy has come with only a medium term view, not a long term panacea, with the industry accepting a new paradigm where it will have to focus on a volume strategy through generic sales, not banking on high-value events less so in the coming years.

FIGURE 6: GLOBAL PHARMA’S 5 FORCES

FIGURE 7: PREDICTION OF NEW MEDICINES FOR NEXT DECADE

Source: Author’s analysis in conversation with industry experts

Source: Ensemble Data Search, Jan 2006 from Zydus Cadila
<table>
<thead>
<tr>
<th>Firm Name</th>
<th>Sales &amp; % of exports (‘00 $ mn)</th>
<th>Firm Size</th>
<th>Sales per employee (2008 $ mn)</th>
<th>Location</th>
<th>Firm Founding Year</th>
<th>Foreign Equity Holding (Promoters/FIs/NRIs/et c)</th>
<th>Interviewees</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glenmark Pharma</td>
<td>498.9, 35%</td>
<td>4000+</td>
<td>0.12</td>
<td>a. Mumbai. b. R &amp; D centers in c. India &amp; EU. d. Global generics business.</td>
<td>1977</td>
<td>28.7%</td>
<td>Achin Gupta, Vice President, Corporate Strategy &amp; Sreenivas Narayanan, Vice President, Projects</td>
</tr>
<tr>
<td>Sun Pharma</td>
<td>867.5, 54.8%</td>
<td>8000+</td>
<td>0.11</td>
<td>a. Mumbai, India. b. Through acquisitions in US. c. R &amp; D in separate subsidiary, Germany, India.</td>
<td>1983</td>
<td>22%</td>
<td>Mr Dilip Shanghavi, Chairman &amp; Managing Director</td>
</tr>
<tr>
<td>Novartis India</td>
<td>153.5, 0.03%</td>
<td>2700</td>
<td>0.06</td>
<td>Corporate Office in Mumbai, India. 1947 with Sandoz Products entering India.</td>
<td>1947</td>
<td>53%</td>
<td>Mr Ranjit Shahani, Vice Chairman and Managing Director</td>
</tr>
<tr>
<td>Encure Pharmaceuticals</td>
<td>100, NA</td>
<td>NA</td>
<td>NA</td>
<td>Pune, India &amp; US subsidiary.</td>
<td>1901</td>
<td>Privately Held</td>
<td>Mr Kumaranathan Dhamrajgir, Chairman</td>
</tr>
<tr>
<td>USV Ltd.</td>
<td>200, 34%</td>
<td>2400+</td>
<td>0.07</td>
<td>Corporate Office in Mumbai-India. US subsidiary for generics business.</td>
<td>1961</td>
<td>Privately Held</td>
<td>Mr Prashant Tewari, Managing Director &amp; 4-member top management team.</td>
</tr>
<tr>
<td>Suven Labs</td>
<td>25, 72%</td>
<td>400</td>
<td>0.063</td>
<td>Hyderabad India</td>
<td>1989</td>
<td>NA</td>
<td>Mr Veenuk Sooth, Vice Chairman &amp; CEO</td>
</tr>
<tr>
<td>GVK Biosciences</td>
<td>17.3, NA</td>
<td>1500+</td>
<td>0.011</td>
<td>Hyderabad, India &amp; Generics and other business globally.</td>
<td>2001</td>
<td>Privately held by GVK Group</td>
<td>Dr J &amp; Gupta, Head of Biology SBU and Collaborative Research Initiatives of GVK</td>
</tr>
<tr>
<td>Dr Reddy’s</td>
<td>1750, 84%</td>
<td>9000+</td>
<td>0.138</td>
<td>Hyderabad, India &amp; Generics and other business globally.</td>
<td>1984</td>
<td>46.1%</td>
<td>Mr Raghul Chidambram, Advisor to Dr Reddy’s</td>
</tr>
<tr>
<td>Aurigena Technologies</td>
<td>3.8, NA</td>
<td>300+</td>
<td>0.012</td>
<td>a. Bangalore, India. b. Malaysia and US R &amp; D centers.</td>
<td>2002</td>
<td>100% subsidiary of Dr Reddy’s.</td>
<td>Mr CSN Murthy, CEO</td>
</tr>
<tr>
<td>Helvios Therapeutics</td>
<td>23, 1.4%</td>
<td>400+</td>
<td>0.05</td>
<td>a. Bangalore &amp; Pune-India. b. US R &amp; D facility.</td>
<td>2004</td>
<td>Owned by The Tata Group</td>
<td>Dr Reddy’s &amp; Dr Reddy’s, CEO &amp; Managing Director</td>
</tr>
<tr>
<td>Avestagen</td>
<td>2.5, 4+</td>
<td>400+</td>
<td>0.006</td>
<td>Bangalore-India</td>
<td>1998</td>
<td>Privately held with interests of NCs and PE.</td>
<td>Top Management Team.</td>
</tr>
<tr>
<td>Ranbaxy Laboratories</td>
<td>1600, 81%</td>
<td>11000+</td>
<td>0.15</td>
<td>Gurgaon, India.</td>
<td>1961</td>
<td>Acquired in 2008 by Daiichi Sankyo, Japan</td>
<td>Dr Tarun Patel, Head of Pharmacological Research, Dr. Vijay Bavle, Sr. Vice President, Urug Development</td>
</tr>
<tr>
<td>Jubilant Organosys</td>
<td>600, 77%</td>
<td>6000+</td>
<td>0.1</td>
<td>Moida-India &amp; R &amp; D centers in Canada, US</td>
<td>1978</td>
<td>32%</td>
<td>Mr Shyam Bhartia, Chairman and MD. Dr JN Khanna, Executive Director - Science &amp; Technology</td>
</tr>
<tr>
<td>Zydus Cadilla (listed as Cadilla Healthcare)</td>
<td>577, 37%</td>
<td>9000+</td>
<td>0.064</td>
<td>Corporate Office in Ahmedabad, India, located throughout India and abroad through major acquisitions.</td>
<td>1952</td>
<td>5%</td>
<td>Mr Jay Kotchhar, Head of Business Development</td>
</tr>
</tbody>
</table>

Source: Pharmaprojects, CMIE Database, Firm Annual Reports & Website, USPTO, Project Team Discussion and this applied to all tables.
For several reasons, the above discussion on Global Pharmaceuticals is important to understand, especially in context with the evolution of the Indian pharmaceutical industry. First, it is clear now that the global debate on *innovation versus access* needs a slingshot for new medicines done at low R & D costs. The Indian pharmaceutical industry offers just such a low cost destination for Global Pharma to locate its R & D – especially with India acceding to stronger patent norms since 2005. The flip side of doing so however is that, Big Pharma will now have to take decisions to *sleep with the enemy*, choosing offshore partners to conduct their R&D who at the same time will offer generic alternatives for Western firm’s products going off-patent. One can witness this with Indian firms collaborating with Western Pharma, offering R & D capabilities on one hand but on the other, also selling generic medicines in Western markets. Viewed from the perspective of the Indian pharmaceutical sector the timing seems just about appropriate at least ex-ante; the new business environment, of stronger domestic IPR, shrinking global pharmaceutical pipelines and an open Indian economy, offer them just the right incentives to upgrade and shift their capabilities. This raises a key question - could Indian firms offer in the coming decade low-cost affordable new medicines to Western pharmaceutical market? And amidst all this, what will then be the role of generic markets, and complementary capabilities developed over the period 1970-2000 in Indian firms? This is a tricky balancing act and if initial indications are to believed, Indian firms are walking the tight rope in their own unique manner balancing innovation and imitation. This is apparent in the industry’s life cycle since 1990 as charted out in Figure 8.

**FIGURE 8: TRANSITIONS IN INDIAN PHARMACEUTICAL CAPABILITIES**

![Graph showing transitions in Indian pharmaceutical capabilities](source: Zydus Cadila)
An industry which since 1990 was only making chemical copies of Western drugs and subsequently entering Western markets with generic products can be seen investing in NCE research between 1995 and 2005. 2005 onwards firms are carving out their own niches as R & D collaborators, independent NCE researchers, while maintaining their business lines in generics sales for Western markets.

For obvious reasons, this has not been an universal trend, the modern firms in the industry are leading the pack more than others, and anecdotal as much as the project team’s documentation of this clear segregation of the industry is already apparent. One can thus see a pyramidal settling of firm types in the industry (See Figure 9). At the bottom are firms who are content with supplying Active Pharmaceutical Ingredients to Global Pharmaceuticals, followed up by firms who are working on selling vanilla generics. Further up on the pyramid one can also witness existence of firms simply contracting/collaborating research services out for Western pharmaceuticals, besides pursuing their own drug discovery agenda with technology intensive drugs, patent challenges, NCE and NBE pipelines. It is worth pointing out here that first, our field trip sample attempts to talk all of these representative firm types. Secondly, one should also note that a single firm like say a Zydus Cadila (as also Glenmark, Sun Pharmaceuticals, Ranbaxy and Dr Reddy’s among others) can be witnessed to pursuing a bit of all possible firm strategies – selling imitative products (generics), contracting/collaborating on R & D with Western partners, and pursuing their own independent agenda of drug discovery over and above everything else. In strategy terms, this might be a unique blend of product market and technological market capabilities in emerging economy firms that might warrant further investigation.

FIGURE 9: INDIAN PHARMA ACROSS THE VALUE CHAIN

Source: Zydus Cadila
This is just the right point where one should now take a detour on understanding the modern Indian pharmaceutical industry’s capabilities in technological market and drug discovery research. This is a key question especially, when one places this in context with the global pharmaceutical industry’s desperate need for an innovation home run. Furthermore, an understanding of this aspect will also throw light on the evolution of emerging economy firms with complementary capabilities to the global technological frontier. The key driver clearly in Indian pharma R & D capabilities is costs – as suggested by all our survey discussants. While the Western world has been taking on an average 8 years and $800 mn to $ 1 billion to develop a NCE, (Di Masi et.al 2003 and see Figure 10 for Stages in The Drug Discovery Process), Indian industry experts argue that they can traverse the entire R & D value chain in something between 3-5 years at costs ranging between $200-$300 mn for each new NDA. Boston Consultancy Group has in a recent report also outlined specific capabilities in Indian pharmaceutical firms highlighting weaknesses and areas of future development (see Figure 11 Indian Pharma R & D capabilities along the value chain). Our broad takeaway related to the sector’s R & D capabilities are documented in the section charting out our findings in what follows.

**Firm Cases: Sample Selection & Broad Issues**

Our overall goal, given the discussion above was to understand firm capabilities and in this section we document our pre-trip preparation. We undertook arrangements for setting up face-to-face interviews with the pharmaceutical industry’s managers between Dec 13th and Dec 25th of 2008. Mr. D G Shah of the Indian Pharmaceutical Alliance, a premier industry body was extremely helpful to us in arranging the interviews. We wrote directly to the CEO of each firm and coordinated with the CEO’s office to set up 2-3 hourly interview slots with their top management including their R & D managers. A brief portrait of the sample and respondents are given in Table 7 above. Our aim was to get a stronger understanding of some of the following questions.

a. Was stronger IP really an incentive for the more technologically progressive Indian firm (and also others) to ramp its R & D efforts and investments? Could drug discovery have been undertaken by the modern firms as a natural progression (from the previous weak IP regime enabled complementary capabilities) while being agnostic to TRIPs? Did the changes in patent laws that underwent several amendments from the original 1970 version in 1999, 2002, and 2005 influence firm strategy?
FIGURE 10: THE DRUG DISCOVERY PROCESS TODAY

FIGURE 11: INDIAN PHARMA’S R & D CAPABILITIES

Source: Project Team’s Discussion with Zydus Cadila, in Ahmedabad, India
b. What kind of an impact did the Indian economic reforms since 1991 have on the Indian pharmaceutical firm’s (and the industry’s) strategic direction?

c. While stronger IP was officially approved to be in place since 2005 as per WTO-TRIPs, India has taken an inordinately long time to get its act going in terms of setting up its patent laws and administration. Might it then be true that this delay in getting its act right in establishing the nation’s IP laws, is in fact harming MNC entry in setting up R & D centers within the country?

d. How is the industry sub-segmenting out in the face of the new IP regime and global pharmaceutical changes? Do we see more acquisitions/mergers/exits? How are the firms generating cash if they are at all interested in doing drug discovery?

e. Are some firms able to better exploit the new business environment to fit in to the global pharmaceutical innovation value chain? What are the prospects of witnessing the first Indian blockbuster drug and the first Indian big pharmaceutical firm going forward? Finally, what is the role of the Hatch-Waxman in the US and generic market opportunities amidst all these changes in the industry’s capabilities?

**Summary of Findings**

Our discussion from here on documents the findings based on the firm-case interviews. First, we take a broad look at how entrepreneurial orientation has guided firm strategy and its R & D capabilities. Next, we document the overall response that we gauged from our field-trip participants on the broad response of their particular firm (and if possible of the industry) to WTO-TRIPs, the 1991 opening of the Indian economy and the Hatch-Waxman Act of 1984 opening US generic markets. Our discussions also generated some interesting hypotheses, some of which we believe could be tested in an econometric setting with future acquired data. We document these in a chart and note the discussion on each of these hypotheses at the firm level in a table in the appendix. We also include in the appendix a table on ‘interesting anecdotes’ from our conversations.

*Entrepreneurship & Firm Strategy*

Our 14 firms had very different entrepreneurial antecedents and our meeting with these firms clearly indicated that firm-strategy to a large extent in these firms were a legacy of
entrepreneurial orientation. The spectrum had a wide distribution and details are documented in Table 3 of the Appendix. In Mumbai for example, our first interviewed firm Glenmark had a dynamic CEO, Mr Glenn Saldanha (son of the original founder) with past US degrees and exposure to Western pharma. Mr Saldanha’s vision was clearly visible in the firm’s strategy, he having guided Glenmark out of a pre-1995 history of selling domestic formulations into being a NCE research driven firm with a separate generics entity. At the other end of the spectrum was Mr Dilip Shanghvi, CEO of Sun Pharmaceuticals who started his firm as a seller of APIs on cycles in Kolkata, India but today has guided Sun Pharma to being one of the most aggressive generic entrants in the US market. Mr Shanghvi clearly gave us a sense that he rather be conservative than have high hopes on becoming an innovative behemoth in global pharmaceuticals. Accordingly, Sun Pharma has also spun off its R & D into a subsidiary to de-risk investor expectations and R & D results from firm performance. At USV Limited, again in Mumbai, we met an entrepreneurial couple, Mr and Mrs. Prashant Tewari, both return migrants to India after an US education, who took up the family business from their previous generation ever since return. The Tewaris surprisingly gave us an impression of being far more conservative than what one would expect them to be, given their exposures to international settings. USV has been focusing strongly on its marketing strength to open up the bottom of the pyramid markets within India. Our travel from Mumbai to Hyderabad set us up with Mr Venkat Jasti at Suven Labs, a contract research firm. Mr Jasti, who came back from US again after a long stint as a pharmacist in the State of New York, seemed pretty clear about where he wants to take his firm, focusing on the markets for innovation in global pharmaceuticals citing Eli Lilly as a strong partner for its contract and collaborative research. We could not meet Dr Anji Reddy founder of Dr Reddy’s (DRL) but instead we got a strong sense that DRL was a scientifically driven firm having been one among the earliest in the industry to have taken to a scientific drug discovery approach. Moving over to Bangalore, we met Dr Rashmi Barbhaiya, an ex-scientist with a big Western pharmaceutical firm, who left his job in the US after close to two decades, came back and started Advinus with funding from the Tata Group. At Bangalore again, we met Aurigene and Avesthagen, two more scientific contract research firms\footnote{We have been using the term CROs for firms like these, standing for Contract Research Organizations, or CRAMS, standing for Contract Research and Manufacturing Services. CROs or CRAMs firms in Indian biopharmaceuticals in various quantities and quality essentially engage in doing contract or collaborative R & D work for their Western partners.}, the latter having an interesting
story of scientist-entrepreneurship with its CEO Dr Billoo Morawalla Patel setting up the firm in the labs of the National Center of Biological Sciences during her research career. In sum, the entire spectrum was indicative clearly of differing firm directions conditional on the entrepreneur’s assessment of new opportunities in line with the classical Schumpeterian world.

WTO-TRIPs, Indian Economic Reforms and Hatch-Waxman Act & US Generic Markets

One key motivation for our field trip was to understand the extent of firm-level impact of WTO-TRIPs, the opening of the Indian economy with the 1991 and onwards reforms process and the role of the Hatch-Waxman Act; this apart from getting an aggregated sense of these three exogenous shocks on the industry’s future strategic direction. Again, we received a wide distribution of responses, details of which in terms of the anecdotal discussion is noted in Table 4 of the appendix. In brief, WTO-TRIPs and its implementation in India seemed to have not played the most influential role as we thought it would have. Sure, signs of a stronger domestic IP environment gave courage to firms like Glenmark to embark on NCE research, but ala Grossman and Lai, they seemed to be well aware that should they succeed in drug discovery, more than domestic patenting what might matter are the markets for new products in Western markets. Others like Sun Pharma, Dr. Reddy’s, and Ranbaxy dead panned that with or without TRIPs the firm would have invested in drug discovery – and infact they did. Mr Dilip Shanghvi, Sun Pharma’s CEO was infact provocative in stating that ‘I often think about this, if without TRIPs my business model would have been the same’ – perhaps indicating that while WTO-TRIPs did play an overall role in improving India’s business environment image to the world (Ranbaxy and GVK managers noted this too), firms were not sure about how to interpret it for their own strategic direction. Some other firms infact used the new IP scenario to their advantage though indirectly, stating that they would do non-infringing research and thereby being able to win over Western clients for collaborative or contract research. We did get a sense of this in our interviews with Jubilant, Aurigene and Suven Labs. Finally, Zydus Cadila’s Jay Kothari was of the view that more than TRIPs, it was the shrinking pipeline and reduced R & D productivity of Big Pharma that was impacting the sector’s prospects as an outsourcing destination for R & D. This infact could be an issue for future research where we might want to tease out the impact of stronger IP and Big Pharma’s shrinking global pipelines on the incentives to innovate in Indian pharmaceuticals.
In terms of the role of Indian Economic Reforms started in 1991, the view was unanimous. Firms confirmed our previous economic intuition that indeed, a rationalized currency regime and easy access to foreign exchange, and more generally opening of the economy, aided firms to think big and use economic decision making to exploit opportunities in the global markets. This came about not only by increasing the competitiveness of pharmaceutical products from India, but also with increased Outward and Inward Foreign Direct Investment, and easier access to capital equipment that helped firms to increase their productivity.\(^\text{13}\) Finally, apart from Suven, GVK Bio, Aurigene and Advinus (pure contract/collaborative R & D entities), all our firm respondents responded by saying that they treated the growing generics opportunity in the US markets with the Hatch-Waxman Act to be of utmost importance. Some like Ranbaxy asserted that learning to surmount USFDA regulations have taken time, though since late 2003 onwards, this has in fact been overcome by most first time and subsequent entrants. Further, they wanted to also look at the world generic market opportunities in EU and Latin America. Finally, generics cash seems to be playing a key role in firm NCE research – at places like Ranbaxy and Zydus Cadila they are terming it as a *bridging strategy* - to use generic cash for funding NCE research, while (and this

\(^{13}\) In a related piece of research, we show econometrically, how firms are engaging in ex-ante investments in capital equipments before entering export markets, the scale of investments being more pronounced for entry into advanced markets like in US than in less advanced ones.
is not exclusive of employing a bridging strategy) at places like Dr Reddy’s and Sun Pharma, generics research is being viewed to be exclusive and non-intrusive from drug discovery – the result, spinning out of subsidiaries focusing on pure drug discovery.

**Conclusion**

This chapter documents shifts in policies across four distinct periods in the evolution of the modern Indian pharmaceutical industry. A *Pre-history period* marked initial forays of domestic entrepreneurs in the industry before India’s independence. A *MNC period* till around 1970s marked the predominance of multinationals in post-Independence India; this after the country had adopted product patents and therefore accorded market power to global pharmaceutical firms with monopolies in globally held drug patents. An *Intervention period* marked governmental intervention and re-aligning of the industrial policy regime, bringing alongside a growth of domestic firms in the industry. Finally, a *Liberalization period* has been well and truly underway for the industry (as well as the overall Indian economy) since the early 1990s. This has come with an overhauling of protectionist policies that kept domestic firms at bay from the forces of the global market economy. Our attempt in documenting shifts in institutions and the policies during these four periods is interwoven with their impact over the industry’s evolution. In the concluding section of this chapter we report our learnings from firm case studies, covered as part of a field trip to India in December 2008. The case studies of 14 Indian firms form the basis of our subsequent econometric investigations in Chapter 2. A key outcome of the trip was a far better understanding of 4 generation of bio-pharmaceutical firms in India: firms who were the early leaders in drug discovery during the early 1990s, firms who got into serious R & D towards the late 1990s and more so during the 2000s, firms who have remained focused on generics business lines and are focusing on exploiting their *complementary (and perhaps imitative) capabilities* in global pharmaceutical markets and finally firms who are making a business out of selling purely innovation to Western drug firms, taking advantage not only of a global need for low cost R & D destinations but even domestic business environment that has changed in the last few years in India. Our project team intends to carry forward this stream of research to understand the sector’s development. This we hope will have larger implications for one to get a firmer grip on the role of IP in the creation of incentives to innovate for R & D intensive industries of emerging economies.
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1 Introduction

Can a shift to strong intellectual property rights induce higher levels of inventive activity in developing countries? This question has acquired increased salience in recent years as developing country governments, international agencies, and economists have all struggled to understand the impact of the worldwide movement to stronger IPR on developing countries. The existing evidence on this question appears to be inconclusive at best.¹ Perhaps because of the lack of strong dispositive evidence, IPR continues to be a flashpoint of disagreement in international trade negotiations.

The debate on these issues is especially intense when it comes to the question of product patent protection for pharmaceuticals. The provision

¹Maskus (2000) provides a masterful overview of the critical issues. See also Fink and Maskus (2004) for a focused discussion of the role of intellectual property rights in the economic development process. Lerner (2002) presents evidence based on a very long, comprehensive set of patent reforms. The literature is quite extensive, and we make no attempt at a comprehensive review.
in the TRIPs agreement requiring such protection was one of the most hotly contested provisions of the agreement, and opposition to its inclusion and enforcement remains widespread. Developing country representatives claimed during the debate over TRIPs – and continue to claim, more than a decade after its ratification – that stronger patent protection for pharmaceuticals in developing countries would have no positive effect on innovation or technological upgrading in the local industries; the only effect would be to raise prices and reduce access to medicines. This skepticism has received powerful empirical backing from recent research. Qian (2007) provides persuasive evidence that the general effect of stronger pharmaceutical patent protection on local innovation is indistinguishable from zero; only in relatively advanced countries can one find any evidence of a positive effect.

The Indian pharmaceutical industry provides a particularly interesting context in which to explore these questions. From the early 1970s through 2005, India’s pharmaceutical industry operated under a legal regime that nearly nullified patent protection for pharmaceutical products. Indian firms were effectively free to sell imitations of patented Western medicines without sanction in their own country (and in other countries that did not enforce product patents for pharmaceuticals). This business model was gravely threatened by the ratification of the TRIPs Agreement in the mid-1990s.

Indian industry leaders and their advocates in the Indian government asserted that the creation of pharmaceutical product patents in India would force up prices for essential medicines without generating any positive benefit in the form of increased FDI and innovation or through multinationals shifting R&D to India. These concerns led Indian government officials to sharply criticize TRIPs. Several recent academic papers have echoed these concerns, using theory and/or empirics to forecast the potential welfare losses affecting current and future consumers, especially in countries like India, through the higher drug prices a stronger patent regime might bring. These papers include Chaudhuri, Goldberg, and Jia (2006), McCalman (2001), and Cockburn and Lanjouw (2001). A common feature of these papers is that they completely ignore or heavily discount the possibility stronger patents might
actually induce increases in R&D in developing countries. However, theoretical work such as Grossman and Lai (2004) emphasizes the reality that, in economic terms, the Indian pharmaceutical market is a fairly small one. Accession of a small market such as India to the strong patent bloc should have relatively limited impact on the incentives for pharmaceutical firms to conduct R&D – the large markets were already protected by strong patent laws.\(^2\) Recent empirical research, such as Qian (2007), tends to strengthen pessimism regarding the likelihood that stronger patents in pharmaceuticals would induce more R&D in India. Qian only finds evidence of an increase in R&D in countries that are relatively rich, possess a well-developed innovative capacity, and have a high degree of "economic freedom" as measured by the Fraser Institute’s economic freedom index. At the time it ratified TRIPs, India was a poor country with limited evident innovative capability. In terms of "economic freedom," a variable emphasized in Qian (2007), India scored below the mean – roughly at the same level as Namibia and below such countries as Zambia, Guyana, and Paraguay.\(^3\)

Despite these concerns, we have found evidence of a striking increase in the R&D intensity of Indian pharmaceutical firms since the ratification of TRIPs. In a companion paper, Arora, Branstetter, and Chatterjee (2008) – hereafter ABC – find that absolute R&D expenditure, R&D intensity, and measures of research output have all increased substantially since India ratified the agreement. Furthermore, the stock market valuation of Indian firms’ investment in R&D has also increased sharply. More detailed investigation of the data suggests a concentration of the increase in innovative activity in a small group of local firms with especially well developed research capabilities; this also appears to be the same group of firms in which the rising stock market valuation of R&D investment is concentrated. Press accounts, industry analysts, and the statements of Indian pharmaceutical executives all seem to point to a development once widely viewed as improbable – the

\(^2\)This point has been well understood for some time and was part of the basis for opposition to the TRIPs agreement. See Maskus (2000).

\(^3\)The Fraser Institute’s economic freedom index is available on the internet. We examined India’s ranking in the year its ratification of TRIPs went into effect.
The emergence of a domestic, research-driven pharmaceutical industry. The timing of this shift is so strongly coincident with important changes in India’s patent regime that it is hard not to view the shift to stronger patents as having played a causal role in this transition.

This sets up the central puzzle that this paper attempts to resolve. The logic behind the theoretical argument that patent reform in a small market should have little impact on incentives to do R&D seems hard to refute. Yet, this apparently irrefutable argument is directly contradicted by some inescapable facts. How shall we reconcile the two? We do so by employing a mixture of theory, empirical analysis, and process of elimination.

In theory, TRIPs could push Indian firms into innovation by foreclosing the traditional option of simply imitating Western firms’ inventions in the Indian market and in other markets with weak patent protection for pharmaceuticals. Under the old patent regime, Indian firms may have voluntarily foregone potential profits earned through sales of innovative products because of the high investment costs required and the limited technical capabilities of the Indian firms. Later in the paper, we sketch out a preliminary model in which this ceases to be an equilibrium if the "protected home market" adopts stronger patents. In essence, firms are forced to adopt a more research-intensive strategy because the former business model is no longer viable. The modelling logic portrays the new style of innovation protected by patent reform and the previous product development activities of the Indian firms as strategic substitutes in the sense of Milgrom and Roberts (1990). We find some empirical support for this story. It is clear that some Indian firms have gone to considerable effort to develop their own new patented products, and the top firms now have products in clinical trials. Nevertheless, these efforts have yet to yield a single new product that is a major commercial success. The efforts of the Indian firms have cast their technical limitations into sharp relief. Statistically, we find little evidence that the rise in R&D output or the market valuation of R&D inputs is primarily driven by these efforts toward "independent innovation." This may be the future of the Indian industry – or at least its top firms – but it is not the dominant
theme of the industry’s recent past.

In theory, TRIPs could push firms into R&D collaboration with Western firms rather than into a strategy of independent drug development. Stronger patent laws could make it relatively more attractive for Indian firms with limited technical capability to eschew imitation and specialize in particular stages of the production process that play to their strengths in process engineering, low-cost manufacturing, and basic chemistry. Elsewhere in the paper, we sketch out a (very) preliminary model that has this implication. Public statements by industry leaders in both India and the U.S. bear witness to the strong interest in both countries in the potential benefits of collaboration, and we do find in the data a sharp growth in alliances and collaborations between Western pharmaceutical and biotechnology concerns and their Indian counterparts. Wadwha et al. (2008) has claimed that Indian firms are now playing a key role in an increasingly globalized innovation value chain within the pharmaceutical industry. Unfortunately, these bold assertions do not bear up well under close scrutiny of the available data. A careful inspection of the data from on strategic alliances between Indian and foreign pharmaceutical companies show that only a small number of these alliances focus substantively on real R&D collaboration. Furthermore, this trend has been quite recent, and only a small fraction of the R&D output of the leading firms can be reliably ascribed to the fruits of international R&D collaboration. We also find limited evidence that the established pharmaceutical and biotechnology firms in the West have begun to outsource significant amounts of R&D to Indian subsidiaries or partners. This is another story that is likely to figure prominently in the future of the Indian industry, but it can only explain part of the industry’s recent past.

Our analysis in this paper emphasizes a different explanation. A detailed analysis of the content of Indian pharmaceutical firms’ innovative activities over the last ten years reveals that relatively little of it has been focused on the kind of new product innovation that one might have expected fun-

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4 This paper, funded by the Kauffman Foundation, generated extensive comment in the business press.
fundamental patent reform to encourage and reward. Instead, R&D efforts have remained (largely) focused on process innovations, manufacturing improvements, and refinements of existing products pioneered elsewhere. The principal mechanisms by which Indian firms have appropriated the returns to their expanding R&D investments have been sales of generic products, exports of bulk drugs and active ingredients, contract manufacturing rather than new drug development or R&D services to Western firms. India’s domestic patent reform played a role in the expansion of this activity, but other reforms and external market developments coincident in time with key steps of the patent reform process were also quite important. These other developments had the combined effect of opening up to Indian firms a foreign market for "TRIPs-legal" imitations – the generics market – that had not been sufficiently attractive before the mid-1990s. Exploiting the Western market for generics and related products required investments in process innovation and technological upgrading that were costly for Indian firms but well within the range of their technical capabilities.

The plan for the rest of the paper is as follows. Section 2 provides a brief overview of the recent history of the Indian pharmaceutical industry. Section 3 reprises the main empirical findings of Arora, Branstetter, and Chatterjee (2008), and sets out the "puzzle" of industry transformation in further detail. Section 4 presents evidence documenting the degree to which Indian pharmaceutical R&D efforts have focused on process, rather than product innovation. This section also describes the role that regulatory and market developments other than TRIPs may have played in the growth of R&D activities in the Indian pharmaceutical industry. Section 5 examines the (limited) extent of fundamental product innovation in the Indian pharmaceutical industry to date, and offers up a sketch of a model by which TRIPs and related Indian patent reforms could have contributed to growing product innovation. Section 6 examines the growth of R&D collaboration between the Indian pharmaceutical industry and foreign producers. Section 7 concludes.
2 The Evolution of India’s Pharmaceutical Industry

India began its history as an independent nation with relatively strong intellectual property rights for pharmaceutical products. India adopted the British Patents and Design Act of 1911 after independence in 1947 and kept this law in place until 1972. Under this statute, firms could patent all the processes by which a given drug could be manufactured, they could obtain product patents, and patents lasted for 14 years. This relatively strong patent regime allowed multinational companies to translate their research strength into high market shares. Foreign drug companies dominated the Indian drug industry throughout the period during which this law was in effect, collectively holding a 68% market share in 1970. It was widely believed, at least in India, that the strong IPR regime effectively prevented the development of an indigenous drug industry.\(^5\)

In response to these concerns, the Government of India enacted a fundamentally different law, the Indian Patent Act of 1970, which was implemented in 1972. This law shortened the life of a patent to 5-7 years and allowed a manufacturer to patent only one method of production for a drug. Other producers were free to produce the same product, so long as they used a different production process. This dramatically weakened patent protection – in many cases, it effectively nullified it – and the market position of the multinational firms. Indian firms could now legally imitate newly introduced drugs without sanction in their own country, so long as they did not use patented processes. By 1980, the market share of the multinationals had fallen to 50%, and it would continue to fall over the next two decades as these new, weaker patent laws remained in place.\(^6\) Indian firms that had been founded prior to the Patent Act of 1970 grew, and large numbers of new firms entered the market over time.

\(^5\)See Chaudhuri (2005) for a comprehensive history of the intellectual property rights regime for drugs in India. Many of the key facts presented in this section are drawn from this source.

\(^6\)Chaudhuri (2005) emphasizes this point.
Indian pharmaceutical production grew rapidly after the implementation of the new patent act, as is shown in Table 1. The table divides production into bulk drugs (the raw materials used in pharmaceuticals) and formulations (mixtures of substances ready for human consumption). Both categories grew substantially. Given the weak patent regime, little effort was devoted to drug discovery, but the manufacturing capabilities, reverse engineering skills, and imitative capacity of domestic firms became steadily more advanced. Indian firms were able to produce and sell drugs initially invented in the West within only a few years of their introduction into major markets. Low costs of production increasingly provided Indian firms with a competitive edge outside India, particularly in product categories or markets in which patents were not an issue. By 1988-89, India had become a net exporter of pharmaceutical products, exporting more than 75% of its bulk drug production and about 25% of its production of formulations.

Early formulations exports tended to be concentrated in developing countries with weak patent laws. India’s price controls limited profit margins in the domestic market, so Indian firms began to look for opportunities elsewhere. A limited devaluation of the rupee in the 1980s arguably reinforced India’s competitiveness in these poorer markets, although it also raised the prices Indian firms paid for raw materials. One of the most significant reforms in terms of the industry’s future came in 1984, with the passage of the Hatch-Waxman Act in the United States. This widened the market for generic competitors to off-patent branded medicines, and India’s Ranbaxy had the foresight to pursue this opportunity early on, but it took years before Indian firms would realize significant success in the U.S. generics market. In 1991, India succumbed to a balance of payments crisis that required it to seek financial assistance from the IMF, which forced a thorough trade liberalization and further devaluation of the rupee. This coincided with a delicensing of the domestic industry. A liberalization of international financial transactions, completed by the mid-1990s, made it much easier for Indian firms to invest abroad and vice versa. Indian firms continued to refine their manufacturing capabilities in the 1990s.
Meanwhile, the Indian intellectual property regime for pharmaceuticals was about to undergo fundamental change. In 1986, the Uruguay Round of international trade negotiations was launched. It would drag on for nearly a decade. One of the most divisive issues in these negotiations was the demand of the developed countries for developing countries like India to substantially strengthen their patent laws by ratifying the Trade Related Intellectual Property Rights (TRIPs) Agreement that would eventually become part of the WTO charter. Western countries insisted that India adopt strong patent protection for pharmaceutical products, a demand that appeared to pose a grave threat to the Indian pharmaceutical industry. Product patents would protect a chemical entity, not a manufacturing process. All conceivable manufacturing processes that produced a chemically identical substance would be effectively covered by such a patent regime, making the kind of reverse engineering practiced by Indian firms illegal. Indian industry leaders and their advocates in government asserted that the creation of effective patent protection for pharmaceutical products in India would force up prices for essential medicines without generating any positive benefit in the form of increased R&D and innovation.\(^7\) Despite strong Indian objections, however, a TRIPs Agreement incorporating relatively strong patents for pharmaceuticals survived the negotiating process. If India wanted to be a part of the newly created World Trade Organization, it would have to ratify the TRIPs Agreement along with the other components of the WTO Charter. Reluctantly, the Indian government did so, signing the TRIPs treaty in late 1994.

When the Indian government took this step, it effectively committed itself to a path of reform that would eventually produce a patent statute consistent with the standards outlined in the new TRIPs Agreement. However, the treaty allowed developing country member states a number of years in which to come into full compliance with the treaty. India stretched out its patent reform process for more than a decade, and the domestic debate that raged

\(^7\)Opposition to stronger patents was not universal within the Indian pharmaceutical industry. Bhandari (2005) claims the leadership of Ranbaxy took a more positive view of stronger patent rights.
within India over exactly how to honor its WTO obligations complicated the reform process in some ways. Table 2 provides a summary of the key steps in the reform process.

This evolution of the patent regime suggests that the years since 1990 can be divided into three parts. In the years 1990-1994, there was considerable uncertainty regarding the outcome of the Uruguay Round negotiating process. Only by 1994 was it clear that the Indian government would sign the TRIPs Agreement. We therefore consider this to be a period in which knowledgeable industry observers and the stock market would discount the probability of a substantial change in the Indian IPR regime for pharmaceuticals.

That changed significantly in the period from 1995 through 1999. The Indian government began accepting and processing applications for product patents and exclusive marketing rights. However, national legislation was required to provide a legal basis for these product patent applications. While a patent amendment was introduced in 1995, it was not fully enacted for another 10 years. Disputes continued, both within India and between India and its trading partners, regarding the exact contents and timing of this legislation. Patent reform was now inevitable, but the exact nature of that reform was still not completely clear to market participants. This suggests a different sort of discount factor being applied by the market. Indian patent law was amended in 1999, but this amendment fell short of India’s obligations under TRIPs.

At the end of the 1990s, India requested and was granted an extension by the WTO for additional time to complete its institutional reform process. The WTO gave India until Jan. 1, 2005 to complete the process. We believe that, in this final period, the "end game" was increasingly evident to all market participants and observers. This view is supported by conversations with industry practitioners and a reading of the contemporary business press. The final amendment legally authorizing product patents was passed just before the deadline, and came into force in 2005.

If our reading of the policy reform process is correct, then we should be
able to identify discrete shifts in market behavior corresponding to the three subperiods outlined above. Working with a panel of 315 Indian pharmaceutical firms from 1990 to 2005, ABC found evidence of a shift in behavior that parallels changes in India’s pharmaceutical patent regime. This are discussed in the next section.

3 The Transformation of India’s Pharmaceutical Industry after TRIPs

The raw data on R&D spending and inventive output in the Indian pharmaceutical industry suggest there was significant change as the IPR reforms were phased in. Table 3 and Figure 1 illustrate the rise in R&D intensity within the Indian pharmaceutical industry. One sees a surge that is roughly coincident with the ratification of TRIPs and an even more striking increase as the implementation of a product patent law approaches. This latter movement reflects both an increase in absolute levels of R&D spending and a decline in sales by less R&D-intensive firms in the industry.

Given the movements in R&D spending, it is not surprising that one also sees a substantial increase in R&D outputs. Table 4 lists illustrates rapid growth in U.S. PTO patent grants, grants of pharmaceutical product patents by the Indian patent office, and applications to the FDA for the market offering of generic drugs as measured by ANDAs (abbreviated new drug applications). At a later point in the paper, we will discuss the degree to which the introduction of generics into the U.S. market requires innovative effort. For now, we stress that these different indicators all affirm the same story.

Table 5 illustrates the central result of ABC, showing what is obtained when one uses stock market data on the 315 publicly traded pharmaceutical companies to estimate the stock market’s valuation of R&D spending. Following a long line of empirical research inaugurated by Zvi Griliches (1981), ABC calculate the ratio of the market value of the firm to the replacement
cost of its tangible assets and regress this on a measure of the ratio of intangible assets (R&D spending) to tangible assets. The specification is

$$\ln\left(\frac{V_{it}}{A_{it}}\right) = \ln q_{it} + \beta_t \left(\frac{R_{it}}{A_{it}}\right) + \epsilon_{it}$$

Sales and firm effects are included in the regression. In order to allow for a change in the market valuation of R&D spending, ABC estimate separate coefficients on the knowledge stock to tangible asset ratio for the periods 1990-1994, 1995-1999, and 2000-2005. As Table 5 indicates, the point estimates of these valuations increase dramatically over time, and the increase is clearly concentrated in firms that ex ante, had superior technical capabilities. ABC measure "technical capabilities" in three different ways – possession of a recognized R&D or product development center ("modern firms"), recognition by stock market analysts as being a technologically progressive firm ("analyst firms"), or having a production facility inspected and approved by the U.S. FDA. Regardless of the measure used to identify them, the technologically progressive subset of firms shows a rise in market valuation of R&D that is of greater magnitude and is statistically significant at conventional levels. ABC demonstrate that these results are robust to the imputation of missing R&D data, the use of various different rates of depreciation for R&D expenditure, and to various other changes in specification.

This shift stands in stark contrast to the typical effect tightening pharmaceutical patent laws has had in poor developing countries, especially on the indigenous firms that developed under weak patent systems. Qian’s (2007) comprehensive study of the strengthening of pharmaceutical patent laws cites and builds on a long series of papers which show, at best, no positive effect and, at worst, a seriously negative effect on the domestic indigenous industry after reform. Qian’s results suggest that only relatively wealthy countries with highly developed institutions stand much of a chance of benefitting from these patent law changes. At the time of its patent reform, India was not wealthy and its institutional quality was not terribly high. India would seem to be an unlikely candidate to realize large gains in indigenous research.

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\(^8\)ABC present a derivation of this equation, cite numerous related studies, and report the results of several robustness checks.
inputs and outputs after the passage of a stronger patent law.

4 The Post-TRIPs Innovation Surge in the Indian Pharmaceuticals Industry: Did TRIPs Really Matter?

4.1 India’s Invention Boom: Process Innovation, not Product Innovation

We begin our investigation of the post-TRIPs innovation surge with a close inspection of the innovative outputs it has produced. To the extent that Indian firms are creating useful inventions, they will have an incentive to patent them in the U.S., and these data are easily accessed by the researcher. By mid-2008, Indian assignees had been granted about 620 U.S. patents. The majority of these can be linked to the listed Indian pharmaceutical companies in our data set, and Figure 2 depicts the growth over time in these patents. The post-TRIPs surge in patenting is clear.

However, this rising tide of patents and R&D has yet to yield a single new product that has yielded major commercial success. Table 6 provides data culled from a variety of sources on the development of NCEs (new chemical entities) by Indian firms. Only one compound – Dr. Reddy’s Bagliatazone, coded as DRF-2593, is close to a commercial launch, and that particular compound has been developed through an outlicensing agreement with Denmark’s Rheoscience. Eight Indian firms have new products in various stages of the clinical trials process, but the numbers are quite modest. Leading Indian firms have had some success licensing manufacturing processes or drug delivery systems to Western firms, but the creation of new drugs – the kind of innovation for which domestic patent reform strengthened legal protection

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9 We thank Matt Higgins of Georgia Tech for steering us to PharmaProjects data on Indian drug firms’ drug development efforts.
the most – has yet to be successfully accomplished. This meager record of fundamental product innovation raises the question of exactly what the stock market is valuing – how could rational investors place such a dramatically rising premium on investments that have yielded so little, at least so far?

One reason may be because very little of India’s post-TRIPs innovation surge has focused on product innovation, per se. A complete reading of the patent abstracts and claims for a sample of these patents suggests that the vast majority of these patents describe process innovations. This impression is confirmed when we seek to broadly categorize inventions into product and process inventions based on keyword searches of the text of the patent documents. Even an extremely expansive, generous definition of "product patent" yields relatively small numbers. This is evident in both Figure 2, which tabulates flows of patent grants by grant year, and Figure 3, which depict trends in cumulative patent stocks.

A significant fraction of the process inventions can be directly linked to existing compounds the Indian firms are currently selling in Western markets. Business press accounts have emphasized that the most financially successful Indian incumbents have derived an important fraction of their global revenues from sales of generic products in Western markets. We do not (yet) possess data that break down our sample firms’ sales by product, but we can use publicly available data from the FDA Orange Book to identify Indian firms that have been granted approval to sell generic products in the U.S. market, which is the most important single generics market by a considerable margin. The publicly traded Indian firms in our sample had been granted approval for 143 Abbreviated New Drug Applications (ANDAs) by 2005, when our stock market data end. This marked the beginning of a surge in ANDA applications and approvals – by mid-2008, Indian firms had been granted more than 400 ANDAs. For the firms in this particular generics market, it seems that the majority of their inventive output can be linked to their generic product offerings. 12 Indian firms have both approved ANDAs and U.S. patents. For these firms, more than 52% of their U.S. patents describe processes or modifications related to the active ingredient contained in their
ANDAs. If we restrict our purview to process inventions, the fraction rises to about 60%.

While the number of Indian firms with approved ANDAs remains limited as of the end of our sample period, a much larger group have received FDA approval for the manufacture of particular compounds and active ingredients for the U.S. market. Ongoing research is attempting to link process inventions to the compounds for which FDA inspectors have granted approval. We anticipate computerized text searches will plausibly link a large fraction of Indian drug patents to these compounds.

4.2 Does the Market Value Product Innovation?

It is possible that the number of product innovations could be small, yet still account for a very large fraction of Indian firms’ total R&D investment and the stock market’s valuation of that investment. To formally test this hypothesis, we re-ran the baseline regressions in ABC, inserting stocks of product patents, divided by assets, as an alternative measure of knowledge capital. If the market is placing disproportionate value on that fraction of R&D that is connected to product innovation, then this additional regressor should be positive and statistically significant. It is not. Table 7 summarizes the results of various specifications suggested by this line of reasoning. The regression results suggest that there is no premium attached to product innovation, even in the broad way we have measured it. The regression coefficient is statistically indistinguishable from zero.

A related specification employs data generated by the Indian patent reform itself. Upon ratification of the TRIPs agreement, the Indian patent authority began accepting applications for pharmaceutical products that would be eligible for protection under a TRIPs-consistent patent regime. We can track, by firm and year, the number of Indian patent applications generated by Indian and foreign firms. In principle, a patent stock constructed from these data offers the most direct possible measure of invention that is directly
impacted by the patent regime change. Yet, as we see in Table 7, patent stocks do not function well as a proxy for intangible assets. In a market value equation, Indian patent stocks are not statistically insignificant. Further analysis (not shown) revealed no trend of a rising valuation of Indian patent stocks over time. That is, even as the legal underpinnings for protection of these particular inventions were strengthened, the market failed to react.

The implication of this seems clear: the rising valuation of R&D spending is not closely tied to the kind of fundamental product innovation directly targeted by India’s pharmaceutical patent reforms. Instead, it is much more driven by the incremental, process-oriented invention Indian firms had engaged in before TRIPs, and for which India’s pre-TRIPs patent regime offered at least some degree of protection. More confirmation of this comes from the results of an additional specification (not shown), in which we separate our sample into Indian firms with ANDAs and the rest. The tendency for the market valuation of R&D spending to rise over time is no longer statistically significant in the non-ANDA sample, but it remains statistically significant – despite the small sample size – in the ANDA subsample.

4.3 The Evolution of Indian Invention: Firm Capabilities and Market Opportunities

That Indian firms would make only limited progress in fundamental product innovation is a reasonable outcome, given their constraints. India is not well endowed with many critical scientific and technical skills required for drug discovery research. At the front end, there is a serious shortage of well trained molecular biologists and molecular geneticists, and limited capability for high throughput screening and combinatorial chemistry. At the back end, relatively few organizations have a strong clinical research capability. Indian scientific strengths are in the middle stages: It is well endowed with organic and medicinal chemists. Moreover, there are a number of well established
and very large firms in America and Europe (and perhaps also Japan) that are already in the market, frequently allied with smaller startups to get technology and and the compounds to be developed. Thus, patent protection should not be expected to increase NCE R&D significantly in India.

Viewed at the firm level, there are additional reasons why one would not expect to see Indian pharmaceutical firms investing much in NCE research. The most important reason is that change is difficult. Firms accustomed to imitating existing products could evolve towards discovering new ones, but this is fraught with difficulties. The first is the organizational challenge of blending reverse engineering research with true discovery.

"What you need is innovative chemistry, which is not the same as reverse engineering. So in fact we do not prefer the people in discovery chemistry who have the experience of reverse engineering. If the scientist has done some non-infringing work or he has some some original work then we will take him... For innovative R&D, you need to form a forum in a way that there is interaction between different departments, whereas reverse engineering is an individual job... Drug discovery is a completely team effort so you have to have chemists talking to biologists, biologists talking to the kinetist, kinetist and biologist talking to (the) analytical fellow. .. So you need to form a forum and structure where these will actually come together...

(Glenmark executive, cited in Kale.)

The second, and perhaps more formidable, difficulty is that drug discovery (and development) is very expensive and very risky. Even if managers were willing to take the plunge, shareholders would (correctly) be loath to risk a profitable franchise, namely the production of pharmaceutical intermediates and, more recently, generics.

These difficulties manifest themselves in a number of ways. First, existing firms have moved only slowly into NCE research. 10Those that have, have

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10Ranbaxy and DRL were the pioneers, investing in R&D starting in the late 1980s. Drug discovery R&D came later, in the 1990s. Many of the firms that began R&D later hired away R&D managers from Ranbaxy and DRL. In addition, some R&D labs were
tended to separate their NCE research into separate organizations. This ameliorates the organizational challenges of combining businesses with very different risk-reward profiles, and correspondingly different models for recruiting and compensating skilled employees. It also insulates investors, allowing private equity investors the possibility of investing in NCE research, with its much bigger upside gains. This separation also facilitates the tapping of the scientific talent pool overseas. Dr Reddy’s Labs (DRL) and Sun Pharmaceuticals have adopted this route, and Ranbaxy was reportedly planning to do. DRL’s drug discovery organization is called Aurigene. Unlike most Indian efforts, it uses a structural approach (rational drug design) to drug discovery.\(^{11}\) Similarly, Sun has set up a drug discovery unit, SPARC, which is itself publicly listed. A more recent report indicates that more firms are planning to follow suit by hiving off their drug discovery efforts in a separate organization.\(^{12}\) However, none of the efforts have succeeded as yet, although a number of compounds are in various stages of clinical trials, underscoring the wisdom of separating drug discovery from the main business.

These difficulties also imply that new firms, not burdened with having to change an existing organization and without a profitable business to protect, are more likely to be the ones investing in NCE research. A rough and ready way to illustrate this point is to look at the share of “product” patents filed at the US PTO by unlisted Indian firms in their total pharmaceutical patents. This share has steadily risen between 2000 and 2007, from about 29% to over 50%. The corresponding share for listed firms (which are typically larger and older) has slipped from about 35% to below 20%. This is a crude test in a number of ways. Our measure of product patents is rough, and some publicly

\(11\) DRL has also formed Perlecan Pharma, whose business model is to in-license molecules developed by DRL. Since clinical development is the financially most demanding, the inference is that the separation is to manage risk rather than organizational diseconomies of scope.

listed firms are of recent vintage. Nonetheless, the data are consistent with the anecdotal accounts. For instance, GVK Bio was set up by the ex-CEO of Ranbaxy, whose business model is to in-license compounds from overseas firms, and develop them through the phase II clinicals and then outlicense back to established pharmaceutical firm.\textsuperscript{13} In some cases, this could also be provided as a contracted service.

Advinus, a part of the Tata group, is another start-up focused on drug discovery, and also offers drug development services to Western pharmaceutical firms. Its drug discovery efforts are targeted to small molecules (i.e., not large proteins). It has entered into a joint venture with Merck in metabolic deseases, with Merck owning the right to in-license compounds in late stage clinicals. Avasthagen, founded in 1998, focuses on biotechnology. One of its division develops the generic version of large molecule (biotech) compounds, but has also launched drug discovery programs and programs in agrobiology.

It should also be emphasized that much of drug discovery research in Indian firms has tended to be “analogue” research. Working with validated targets or with compounds whose activity is well understood, firms can search for molecules that are more effective or have fewer side effects. In other words, these are not the “first in class” compounds, which target the disease in a new way. Kale (2005) provides a good example. Sanyo had discovered a molecule that sensitizes the body to the action of insulin. DRL scientists developed two other molecules in the same class that had better properties and licensed those to Novo Nordisk.

But NCE research is not the only type of “genuine” or “creative” technical activity available. Firms can innovate by improving an existing drug, such as a more desirable dosage form. This was the case when Ranbaxy developed a “once a day” dosage form for an important antibiotic, ciprofloxacin, which was licensed to the original innovator, Bayer, for $65 million in 1999. Firms can innovate by developing better ways to deliver the drug, such as through

\textsuperscript{13}As Ranbaxy’s head of R&D noted in 2003 (cited in BusinessWorld, cited in Kale, PhD thesis) there are a number of drugs with a potential market size of $100 - $200 million, too small for the major pharmaceutical firms but large enough for the Indian firms.
a skin patch or through an inhaler. Firms can also develop cheaper ways to produce an existing drug, using new intermediates. Such process innovation may also accompany new dosages or drug delivery systems. Finally, even plain reverse engineering is seldom so. The established pharmaceutical firms surround their products with a bevy of patents, some of which remain in force even after the principal patent expires. A firm that seeks to launch a generic version of the now off-patent drug must be skilled enough to avoid tripping up on the cluster of unexpired patents. In many cases, this may require developing new processes to avoid using patent protected intermediates. These types of innovative activity draw more directly on the capabilities that Indian firms developed during the time when pharmaceutical products did not enjoy patent protection.

What was happening was a more innovative way of producing the drug; if you would look at what Pfizer did, what DRL did and what Ranbaxy did for various products. Example, Prozak which is Fluoxetine used to be sold in particular dosages and strength. DRL not only developed the new process to make Fluoxetine but also they developed new dosage form and therefore got exclusivity in the US. ..."  


Moreover, many of these innovative activities naturally lead to collaborative alliances with Western firms. As Ranbaxy’s then CEO put it, “We moved through a maze of over 70 process patents around Cefaclor (commercialized by Eli Lilly) to produce a non-infringing version of the molecule” (cited in the Company Annual Report, 1993). This led to a joint venture with Lilly to produce this improved version of Cefaclor!

4.4
4.5 Could TRIPs Have Driven a Surge In Process Innovation?

The previous section argues that the accumulated skills and labor endowments of Indian firms made a major transition to product innovation costly, risky, and therefore unlikely. Given these constraints, the direction of R&D effort over the last ten years seems to make sense. But can we explain its scale and the degree to which this scale has expanded over time? We began the paper by noting that the increase in R&D spending and patenting appears to be broadly coincident in time with the domestic patent reforms mandated by TRIPs. However, the incidence of these reforms was greatest for product innovations, where the Indian R&D response has been relatively modest. Is the association between patent reform and the innovation surge purely coincidental? If not, then how could the two be logically connected?

Part of the answer could lie in the implications of TRIPs-mandated patent reforms for process innovations. While the incidence of these reforms was surely greatest for product innovations, they also measurably strengthened protection for process innovations. In theory, the pre-TRIPs Indian patent statute protected process patents, but drug producers were only allowed to patent a single process per drug, and the length of patent protection was limited to 5-7 years. India’s patent amendments lengthened patent protection considerably (to 20 years from the filing date), and allowed for the patenting of multiple processes related to the same drug. In principle, this could broaden the scope of process patent protection as well as the length, since trivial modifications of existing processes could be anticipated and patented by the innovator. But these additional protections for process innovations would only apply in the Indian market. That brings us back to the Grossman-Lai point: the Indian market was and is still too small to constitute a meaningful source of demand pull for innovation. The results of Table 7 are instructive here. The market does not appear to place much weight on Indian patents taken out under the new law, which applies to both product and process innovations. These considerations would appear to constitute, at best, a weak link between TRIPs and the innovation surge.
The real impact of TRIPs almost certainly came about through a very different mechanism: by foreclosing the opportunity for Indian firms to continue to grow through simple imitation of Western products in weak patent markets. Contemporary press accounts suggest a broad realization throughout the industry that TRIPs meant the eventual obsolescence of the historical business model. Since the 1970s, India and much of the developing world had been a preserve in which Indian firms were reasonably free to infringe on Western patents. That preserve was going to shrink rapidly, forcing Indian firms to pursue other business models. This effect can be modeled in a number of ways and, in the next section, we present a sketch of one such model. The broader point, though, which goes beyond the particulars of our theoretical specification is this: to the extent that TRIPs really mattered, it mattered not as a carrot but as a stick.

When we look for the carrot, it becomes clear that factors other than TRIPs mattered, and some of these other factors were broadly coincident in time with TRIPs-mandated patent reforms. Among the most important of these has to be the evolution of the market for generic drugs in Western countries, especially the United States. An extensive literature has described how the Hatch-Waxman Act of 1984 dramatically widened this market in the United States by reducing the regulatory hurdle firms faced when introducing products to compete with off-patent drugs.\footnote{See Morton (2002).} It was no longer necessary to go through an expensive and lengthy clinical trials process with the rival compound; it was sufficient to prove bio-equivalence. This dramatically lowered the market entry hurdle facing firms with limited drug development capability; in effect, the fixed costs of product development dropped sharply. The high prices prevailing in the U.S. market for patented drugs created strong market incentives to substitute to lower-priced generics when the latter became available. The Act allowed this low regulatory hurdle apply to products that competed with patented drugs, so long as the producer could certify both bioequivalence and non-infringement of the patent(s) still in force. Generic drugs introduced through this feature of the Act (so-called
paragraph four certifications) could face a legal challenge from the patent holder, raising the costs of introduction and increasing the uncertainty of future revenue flows, so the Act provided a benefit to compensate such producers for the additional risk: a half-year of market exclusivity is granted to successful paragraph four entrants. The generic producer competes with the patent-protected product but is itself protected from additional generic competition for 180 days.

Drug producers in the West quickly realized the significance of this reform, and the FDA was flooded with so-called applications for new drug approvals (ANDAs). Access to this market was temporarily interrupted by a scandal at the FDA in the late 1980s in which officials were found to have taken bribes in order to certify generic products. The adoption of more stringent controls over the certification process dramatically slowed the rate of generic approvals and created a backlog of applications which only began to clear in the early 1990s. Generally high drug prices in the U.S. created demand for generic products, so the size of this market steadily expanded. The market also grew in Europe, but its growth was limited by the fragmented nature of the European pharmaceutical industry in general, the absence of a central European authority or a common set of standards and procedures for the certification of generic products, and the fact that European drug price controls kept prices for branded medicines – even those with patent protection – at relatively low levels, indirectly suppressing the market for an alternative product. Over the last 10 years, European generics markets have reached significant size. In the mid-2000s, the generics market began to expand globally as a series of blockbuster drugs lost patent protection in the major Western markets.

As we have already indicated, a large fraction of Indian patent output can be linked to the generic products Indian firms sell in the U.S. market. The owners of the patents for successful drugs have a strong incentive to patent processes and other ancillary aspects of their inventions in order to prolong their period of monopoly rents.\textsuperscript{15} So, successful entry into the generics

\textsuperscript{15}This is extensively discussed and convincingly documented by Graham and Higgins
market can require strong process engineering skills and considerable R&D investment. This is even more true for paragraph IV product introductions, where the original patent holders have an incentive to resort to patent infringement litigation. The business press notes that many of the major milestones in the financial growth of leading Indian firms like Ranbaxy and Dr. Reddy’s were linked to successes in the U.S. generics market, including successful paragraph IV certifications. Part of the sharp increase in Indian R&D intensity observed in Figure 1 is surely related to the explosion of Indian ANDAs filed in the last 3-4 years.\textsuperscript{16}

But while Indian pursuit of the generics market is widely acknowledged today, the initial response of Indian producers to the Hatch-Waxman Act was relatively muted. Why is it that Indian firms appear to have vastly intensified their pursuit of this market after TRIPs? It is plausible that it could have taken some time for the significance of this new market to be realized by all leading firms. The FDA’s generics scandal and the resulting backlog of applications also may have played a role. But it is also true that, in the 1980s, the attractiveness of foreign markets was limited by a significantly overvalued currency and a restrictive trade and FDI regime.

That changed sharply with India’s fundamental trade and FDI reforms in the early 1990s. These reforms have been extensively described in Panagariya (2005, 2006) and are the subject of a large literature in their own right. For our purposes, it is sufficient to note the following facts. In 1991, India suffered a major balance of payments crisis and was forced to seek financial assistance from the IMF. The IMF required a substantial liberalization of India’s trade and FDI regime, which was phased in over the course of the 1990s. The rupee depreciated substantially, losing about two-thirds of its value vis-a-vis the U.S. dollar. This dramatically raised the rupee value of overseas sales. The trade, FDI, and foreign exchange restrictions limiting the ability of Indian firms to access overseas markets were substantially

\textsuperscript{16}See Graham and Higgins (2007). We thank Matt Higgins for further discussions on these issues.
reduced by the mid-1990s, allowing Indian firms to purchase marketing organizations and FDA-approved manufacturing facilities that already existed in their major target markets. These liberalizations impacted not only the generics producers but also firms that exported bulk drugs or were willing to engage in contract manufacturing (often on behalf of cost-sensitive generic producers based in more advanced countries). The collapse of the rupee left India-based manufacturers with a strong cost advantage in the major Western markets.

This helps resolve the second dimension of the Grossman-Lai paradox. Domestic patent reform intensified protection, but in a market that was too small to induce much additional R&D spending. The patent policies protected fundamental product innovation in the Western markets did not change, but the fundamental attractiveness of those Western markets for Indian producers did change in the early 1990s, thanks to devaluation and trade/FDI reform. Meanwhile, the generics market – which Indian firms could access even without significant new drug development capability – grew steadily over time, as did the interest of foreign producers in outsourcing drug manufacturing. TRIPs may have supplied a stick, but there was also a carrot, and the carrot came through the confluence of India’s opening to trade and the Western countries opening to generics and related products.

5 The Growth of Product Innovation in India: A Role for TRIPs?

5.1 Product Innovation in India: Limited, but Growing

In the previous section, we have characterized the innovation surge of India’s pharmaceutical industry has having been largely focused on processes rather than new products. As we suggested, that requires a reconsideration of the role played by TRIPs in promoting the large increase in numbers of
R&D dollars (or rupees) and numbers of patents generated since TRIPs ratification. We also that Indian efforts to produce truly new drugs have had limited success to date. But it is also true that Indian firms, including the most financially successful, are making nontrivial investments in new drug development, in spite of the costs and the risks. The aggregate size of these investments is increasing over time. And the Indian industry has seen a more recent wave of new entrants whose business models are much more tied to new drug development – or at least particular phases of the drug development process – than has been the case for the established incumbents. While we want to avoid the mistake of ascribing too much importance to this phenomenon, it still calls for an explanation.

Why are Indian firms increasingly investing in product innovation after TRIPs? Efforts to tie even this relatively small component of India’s innovation surge to domestic patent reform in the conventional way founder on two inconvenient facts. First, the Indian market is too small to matter. Second, it is abundantly clear that the product development efforts in India are not principally focused on tropical diseases or India-specific maladies; instead, they are focused on drugs with markets in the Western world. Yet, the timing of this increase in investment and the statements of the investing firms themselves suggest a strong link to patent reform, especially its most recent stages. And we cannot appeal to alternative driving forces, as we did in the previous section. The gap in time between fundamental trade/FDI reform and the growth in product innovation efforts is too great for there to be a plausible strong link between the two. The evolution of the generics market is even less relevant.

So we have been forced back to the Grossman-Lai paradox. Our efforts to resolve this paradox bring us back to the role of TRIPs as a stick rather than a carrot. This was a point we made in the previous section, but did not develop in terms of a formal model. In this section, we introduce a model of domestic IPR reform as a "stick." To put this in more professorial language, one way to reconcile theory and fact is to consider the possibility that Indian firms were not pulled into innovative activity by the lure of a
newly protected domestic market; rather, they were pushed into innovation by the foreclosure of a domestic haven for imitative activity. This loss of the opportunity for imitation increased the payoff to research. In other words, imitation and research must be strategic substitutes (Milgrom and Roberts, 1990). This strategic substitutability could arise directly from the cost function, due to budget constraints or limited managerial resources. However, we consider another form of substitutability below, arising from demand. We do not intend to provide here a complete theoretical exposition – the following analysis presents a sketch model that illustrates how strategic substitution could arise for a deliberately simplified example.

5.2 The Model

Suppose there are two firms: $h$ and $f$, where $f$ is the foreign firm and $h$ the home firm. Firm $h$’s production options are a function of its investment choices, of which it has four. It can invest in: (a) imitation of good $x$; (b) innovation which leads to a new/differentiated good $y$; (c) both innovation and imitation; or (d) neither innovation nor imitation. Imitation requires a fixed investment $F_m$ and it is successful with probability $1 - k$ whereas innovation requires fixed investment $F_n$ and it succeeds with probability $\alpha$. In what follows, we will consider two different proxies for the degree of IPR enforcement: (a) the fixed cost of imitation $F_m$ and (b) the likelihood that imitation is detected by local authorities and therefore fails, which is captured by the parameter $k$.

The timing of decisions is as follows. First firm $h$ makes its investment decision. Next, firms compete in prices in the product market. Firm $j$’s profit in good $i$ is denoted by $\pi_i(n_x, n_y)$ where $i = x, y$; $j = h, f$; and $n_i$ denotes the number of competing firms that have the ability to produce good $i$. When only firm $j$ produces good $i$, its profit in good $i$ is written as $\pi_i^j(1)$ and when its the sole producer of both goods, its profit over both goods is given by $\pi_{xy}^j(1)$ where we must have $\pi_{xy}^j(1) > \pi_i^j(1)$. We assume that the local firm has a sufficient cost advantage over the foreign firm in producing good $x$. 

27
such that post imitation it can limit price the foreign firm out of the market while charging its optimal monopoly price. This implies that if the home firm invests in imitation its profit equals \( \pi^h_x(2, 0) = \pi^h_x(1, 0) \) whereas if it invests in both imitation and innovation, it becomes a multi-product monopolist and collects \( \pi^h_x(2, 1) + \pi^h_y(2, 1) = \pi^h_y(1) \) in the product market.

Now consider firm \( h \)'s investment decisions. If firm \( h \) invests in neither activity, its profits equal zero. If it invests only in innovation, it collects

\[
v_I \equiv \alpha \pi^h_y(1, 1) + (1 - \alpha) F_n - F_n = \alpha \pi^h_y(1, 1) - F_n 
\]

whereas if it invests only in imitation, its payoff equals

\[
v_M(k) \equiv (1 - k) \pi^h_x(1, 0) + k F_m - F_m
\]

If firm \( h \) invests in both imitation and innovation, its payoff is given by

\[
v_{IM}(k) \equiv -F_m - F_n + \alpha(1-k)[\pi^h_y(1)] + \alpha k \pi^h_y(1, 1) + (1-k)(1-\alpha) \pi^h_x(1, 0) + k(1-\alpha) F_m
\]

To simplify calculations, suppose \( \alpha = 1 \). Using \( \alpha = 1 \), equations (1) through (3), firm \( h \)'s profit maximizing investment strategy can be illustrated graphically. However, to do so we first need to describe when each investment option is profitable as well as when it is profit maximizing. First note from (1) that innovation is profitable as a stand alone activity iff \( F_n < F^*_n \equiv \pi^h_y(1, 1) \) and that imitation alone is profitable iff \( F_m < F^*_m \) where \( F^*_m \equiv (1-k)\pi^h_x(1, 0) \). Finally, investing in both activities is profitable iff

\[
v_{IM}(k) > 0 \iff F_m + F_n < \pi^h_y(1, 1) + (1-k) [\pi^h_y(1) - \pi^h_y(1, 1)] \quad (L_B)
\]

In the \((F_m, F_n)\) space, \( F^*_m \) is a vertical line; \( F^*_n \) a horizontal one; while line \( L_B \) is downward sloping. Note also that the horizontal intercept of line \( L_B \) exceeds \( F^*_m \) because \( k \pi^h_y(1, 1) + (1-k) [\pi^h_y(1) - \pi^h_x(1, 0)] > 0 \). Similarly, the vertical intercept of line \( L_B \) exceeds \( F^*_n \) because \( (1-k) [\pi^h_y(1) - \pi^h_y(1, 1)] > 0 \).

Note further that innovation is more profitable than imitation iff

\[
v_I > v_M(k) \iff \pi^h_y(1, 1) - F_n - [(1-k)\pi^h_x(1, 0) - F_m] > 0
\]
which is the same as

\[ F_n < F_m + \pi_y^h(1, 1) - (1 - k)\pi_x^h(1, 0) \quad (L_{IM}) \]

When inequality \( L_{IM} \) binds, it can be plotted as an upward sloping line in the \((F_m, F_n)\) space with a vertical intercept of \(\pi_y^h(1, 1) - (1 - k)\pi_x^h(1, 0)\) and slope equal to 1. Note that since \((1 - k)\pi_x^h(1, 0) > 0\), the vertical intercept of line \(L_{IM}\) is below \(F_n^*\). Finally, note also that the point \((F_m^*, F_n^*)\) lies on line \(L_{IM}\).

Furthermore, investing in both activities dominates investing in imitation alone iff

\[ v_{IM}(k) > v_M(k) \Leftrightarrow -F_m - F_n + (1 - k)\pi_{xy}^h(1) + k\pi_y^h(1, 1) > (1 - k)\pi_x^h(1, 0) - F_m \]

which is the same as

\[
F_n < F'_n \equiv (1 - k)\pi_{xy}^h(1) + k\pi_y^h(1, 1) - (1 - k)\pi_x^h(1, 0) \quad (L_{BM})
\]

\[
= k\pi_y^h(1, 1) + (1 - k)[\pi_{xy}^h(1) - \pi_x^h(1, 0)] \quad (4)
\]

Similarly, investing in both activities dominates investing in innovation alone, iff

\[ v_{IM}(k) > v_I \Leftrightarrow -F_m - F_n + (1 - k)\pi_{xy}^h(1) + k\pi_y^h(1, 1) > \pi_y^h(1, 1) - F_n \]

which is the same as

\[ F_m < F'_m \equiv (1 - k)[\pi_{xy}^h(1) - \pi_y^h(1, 1)] \quad (L_{BI}) \]

where \(F'_m < F_m^*\). It is easy to establish the following: (i) lines \(L_B\) and \(L_{BI}\) intersect at \((F'_m, F'n)\); (ii) lines \(L_B\) and \(L_{BM}\) intersect at \((F_m^*, F'_n)\); and (iii) \(L_{IM}\) and \(L_{BI}\) intersect at \((F'_m, F''n)\).

The simple investment model described above can be made more concrete by assuming that the representative consumer’s utility is a function of the consumption of the two differentiated goods \((x, y)\) and a numeraire good \(m\) and is given by

\[ u(q_x, q_y, m) = a(q_x + q_y) - \frac{(q_x^2 + q_y^2)}{2} - sq_xq_y + m, \quad 0 \leq s \leq 1 \quad (5) \]
where $q_i$ is the total consumption of good $i$ and $p_i$ its price, $i = x, y$. Utility maximization gives rise to the following demand system

$$p_x = a - q_x - sq_y$$ and $$p_y = a - sq_x - q_y$$

(6)

The parameter $s$ represents the degree of substitutability between $x$ and $y$: the goods are perfectly homogeneous if $s = 1$ and completely differentiated when $s = 0$. Note that an increase in the degree of product differentiation (a decline in $s$) shifts the demand curves for both firms outward.

If firm $h$ invests only in imitation, good $y$ is not invented, and both firms compete in the market for good $x$. Due to its cost advantage over the foreign firm, post imitation, the home firm monopolizes the market for $x$ and chooses $p^h_x$ to maximize

$$\max_{p^h_x}(a - p^h_x)p^h_x$$

Solving this problem yields

$$p^h_x(1) = a/2$$ and $$\pi^h_x(1, 0) = \frac{a^2}{4}$$

If the home firm invests in only innovation and succeeds, then firms produce differentiated goods: the home firm produces $y$ and the foreign firm $x$. At the product market stage, firm $j$ chooses its price $p^j$ to solve

$$\max_{p^j} \frac{p^j(-p^j + a(1 - s) + sp^{-j})}{1 - s^2}$$

Standard calculations show that the equilibrium price of each firm and the associated profits levels are given by

$$p^j(1, 1) = \frac{a(1 - s)}{2 - s}$$ and $$\pi^j(1, 1) = \frac{a^2(1 - s)}{(s + 1)(2 - s)^2}$$

Finally, if the home firm invests in both activities and succeeds, it becomes a multi-product monopolist and solves

$$\max_{p^h_x, p^h_y} \left[ \frac{p^h_x(-p^h_x + a(1 - s) + sp^h_y)}{1 - s^2} \right] p^h_x + \left[ \frac{p^h_y(-p^h_y + a(1 - s) + sp^h_x)}{1 - s^2} \right] p^h_y$$
which gives

\[ p^h_x(1) = p^h_y(1) = \frac{a}{2} \]

and

\[ \pi^h_x(1) = \pi^h_y(1) = \frac{a^2}{4(s + 1)} \]

so that \( \pi^f_{xy}(1) = \frac{a^2}{2(s + 1)} \).

Given these relationships between the different investment options and the profitability of each option, we are now ready to describe how the strengthening of IPR protection. Suppose first that stronger IPR enforcement makes it more difficult for the home firm to imitate the foreign firm, i.e., the cost of imitation \( F_n \) increases. How does this increase alter the investment choices of the home firm?

\section*{5.3 Empirical Implications and Discussion}

Suppose IPR protection is quite weak initially so that imitation is rather cheap (i.e. we are to the left of line \( L_{BI} \)). In this region, the home firm always finds it profitable to imitate good \( x \). Whether or not it also finds innovation profitable depends on the magnitude of \( F_n \). When \( F_n \) is low (i.e. less than \( F^*_n \)), the home firm undertakes both activities, as indicated by the pair \((I, M)\) in Figure 4. But if \( F_n \) exceeds \( F^*_n \), it undertakes only imitation to the left of line \( L_{BI} \), which is indicated by \( M \) in Figure 1. Prior to India’s patent reforms, imitation of foreign pharmaceuticals was fully legal so that Indian firms did not really face any significant costs of imitation. Furthermore, during the early phase of its development, the industry was somewhat limited in terms of its innovative capacity and likely faced intermediate (or maybe even high) costs of innovation so that it invested only in imitating foreign products. By making imitation illegal and therefore subject to high costs (that would result from being prosecuted for example) Indian IPR reforms had the potential to substantially encourage local innovation by moving local firms from an \( M \) region to an \( I \) region in Figure 4. Note, however, that if local innovative capacity is rather limited (i.e. when \( F_n > F^*_n \)), a sufficient strengthening of
IPR reform would shut down local imitation (a profitable activity) without leading to any local innovation – i.e., the home firm could move from a region where it invests only in imitation to a region where it invests neither in imitation nor innovation (to the right of $L_M$ and above $L_I$). Critics of TRIPS would contend – and did contend – that the real world situation is much closer to latter scenario than it is to the former.

Fortunately for many Indian firms, the real world situation did not turn out to be that grim. Some Indian firms have managed to develop the capabilities for production innovation and are investing accordingly. That is the real world phenomenon that may most directly reflect this model. And a model like this could help explain a link between TRIPs and the rising degree of product development in India. In this particular theoretical specification, the strategic substitution between imitation and innovation comes through the demand side. Substitution could also arise through the cost function, due to internal resource constraints. We intend to explore this alternative possibility in ongoing research.

This kind of model may also shed some additional light on the claims of the previous section. In effect, the global market for generics (and the related market for bulks and APIs) represents an intermediate place in the product space between pure innovation and pure imitation. Our existing model lacks such an intermediate step, but the language of the model helps us envision what role such an intermediate step could and possibly did play. The fixed costs of entering this intermediate market declined before TRIPs, because of relaxed regulatory hurdles. The profitability of entering this intermediate space expanded thanks to rupee devaluation and trade/FDI reform that was broadly coincident with TRIPs. And this intermediate market grew substantially just as TRIPs or the prospect of TRIPs was endangering the traditional business model. Indian firms did not all have to progress quickly from pure imitation to drastic innovation. There was an intermediate step to which they could move first.

And this may help explain why indigenous Indian producers have fared better as a group than indigenous producers in other countries where patents
were weak prior to some reform event. Not only did Indian producers have
a relatively long transition period, but they were well set up to profitably
serve this intermediate market. Countries like Taiwan and South Korea
had reasonably advanced domestic engineering capacity, but both countries
instituted stronger patents before the generics market had fully emerged,
and their post patent reform currency appreciations and wage growth limited
their competitiveness as commodity manufacturers.

6 Increasing Indo-Foreign R&D Collaboration
in Pharmaceuticals: A Role for TRIPs?

6.1 Indo-Foreign R&D Collaboration: Limited, but
Growing

Just as Section 4 downplayed the importance of product innovation, it also
downplayed the importance of R&D collaborations between Western and In-
dian firms in which Indian and Western firms cooperate to develop drugs. At
this point in the paper, though, we wish to focus on precisely this phenom-
enon. A number of commentators in the business press have suggested that
few Indian firms will compete directly with the likes of Merck and Pfizer. A
larger number of Indian firms will focus their "inventive" activity on tasks
that are, broadly speaking, complementary to the strengths of the Western
giants. In this view, Indian firms will specialize in particular components
of the drug development process that reflect India’s comparative advantage
– contract research (especially in the labor-intensive parts of the research
process), clinical trials, contract manufacturing under license, or outlicens-
ing of promising compounds to Western firms for further development and
marketing. Under this hypothesis, a large component of Indian R&D ac-
tivity will take eventually place explicitly within formal collaborations with
Western firms, or it will be undertaken with an eye toward selling what
amounts to an intermediate input to Western firms. In the analysis below, we sketch out a model that illustrates how a strengthening of the local IPR regime could "push" firms out of imitation and into collaboration.

6.2 The Model

Innovation in the pharmaceutical industry has a substantial development component that arises from the need to conduct clinical trials etc. Since such development is distinct from basic research and indeed can be carried out in an entirely separate location, it is useful to consider how local IPR enforcement matters when innovation is a two stage process that comprises of basic research \( (R) \) and drug development \( (D) \). Of course, such vertical separation creates the possibility that the foreign firm may wish to delegate the development part (i.e. the \( D \)) of its R&D for a new drug to the local firm so that the innovation activities of the local firm are complementary to the research conducted by the foreign firm. Whether or not such a vertical arrangement of R&D can arise depends upon a variety of factors but the crucial consideration for our purposes is the role played by the local IPR regime. Our basic idea is that whether such a collaborative arrangement is acceptable to the local firm will depend upon the profitability of other options available to it – in particular, on the profitability of pursuing a go-it-alone option under which it imitates the foreign firm’s technology and develops the drug on its own.

In most discussions of the pharmaceutical industry, "development" refers to clinical trials and related activities. In our usage, "development" is meant to refer more broadly to various stages of the R&D process in which an Indian firm could possess (or attain) a comparative advantage. The text of the paper has cited numerous examples. It need not be closely connected to clinical trials and, in fact, to date, the development of clinical trials in India has perhaps lagged expectations.

To capture the trade-offs involved, consider the following simple game and restrict attention to the market for the new drug (call it \( y \)). At the first
stage, the foreign decides whether or not to outsource development of the new drug to the local firm (we assume that the basic research $R$ for the drug has already been done by the foreign firm and that the investment in such research is sunk). If the local firm agrees to undertake $D$ on a collaborative basis, it incurs the fixed cost $\theta F_d$, where the parameter $\theta$ measures the degree to which knowledge transfer from the foreign firm lowers the development cost for the local firm. In addition, collaboration eliminates the need for imitation on the part of the local firm since results of the basic research are provided by the foreign firm. As will become clear, this illustrative model is most reasonable when viewed in the context of a drug targeted at the developing country market. We fully acknowledge that most R&D collaborations have tended to focus on drugs with substantial Western markets, and we plan to incorporate in future work theoretical specifications that will be more natural in that setting.

Under collaboration, post drug development, the local firm becomes the sole producer of the drug and the two firms split the total profit: the home firm gets $v_D(k)$ where $v_D(k) \equiv \pi_h^h(1)/2 - \theta F_d$. If, however, the home firm rejects the foreign firm’s offer it then has two options: invest in both imitation and drug development (both of which are necessary to bring the drug to market) or invest in neither activity. Since the home firm’s cost advantage is assumed to be large enough for it to be able to limit price the foreign firm out of the market while charging its optimal monopoly price, post imitation the foreign firm’s payoff equals zero while that of the local firm equals $v_{MD}(k) \equiv (1-k)\pi_g^h(1) - F_m - F_d$. Also, suppose that if IPR enforcement is completely lax (i.e. $k = 0$), the local firm finds imitation and development profitable – i.e. $v_{MD}(0) > 0$.

Since imitation drives the foreign firm out of the market, it also leads the foreign firm to not develop the drug itself. If, however, the home firm undertakes neither imitation or development, the foreign firm finds it profitable to undertake development and collects $v_f^D \equiv \pi_f^h(1) - \theta F_d > 0$.

At the first stage of the game, the foreign firm chooses whether or not to collaborate with the local firm. This choice clearly depends upon whether or
not imitation is profitable. Suppose that it is: i.e. \( v_{MD}(k) > 0 \). Then, the foreign firm prefers to collaborate with the home firm – local imitation and development would occur if it chooses not to collaborate and its profit would then equal zero. By engaging the local firm in a collaborative arrangement, the foreign firm can deter imitation. The issue is whether or not the local firm finds it profitable to undertake drug development under a collaborative arrangement with the foreign firm. The home firm prefers collaboration to going solo iff

\[
v_D(k) > v_{MD}(k) \iff \frac{\pi^h_y(1)}{2} - \theta F_d > (1 - k)\pi^h_y(1) - F_m - F_d
\]

which is the same as

\[
\frac{\pi^h_y(1)}{2}(2k - 1) + F_m + (1 - \theta)F_d > 0
\]

It is clear from above that if \( k \geq 1/2 \) (i.e. IPR enforcement is strong), then the home firm prefers to undertake drug development under a collaborative arrangement to imitation and development on its own. However, if \( k \) is small enough (i.e. IPR enforcement is sufficiently weak), then the local firm may not be willing to give up imitation and undertake drug development. For example, when \( k \simeq 0, \theta \simeq 1, \) and \( F_m \leq F_d \) the above inequality necessarily fails since \( v_{MD}(0) > 0 \). This suggests that prior to IPR reform in India, one reason we did not see much outsourcing of drug development to local Indian firms is because these firms found imitation to be much too lucrative to be willing to enter into partnerships with foreign firms under which they would agree to undertake development and forego the opportunity to imitate. Thus, the binding constraint may not have been that the foreign firms were reluctant to collaborate but rather that the Indian firms were not interested in doing so. By shutting down the profitable imitation channel (i.e. by lowering \( k \)), the patent reform in India indirectly nudged Indian firms to agree to conduct drug development on a collaborative basis.

When local imitation and development is not profitable, i.e., when \( v_{MD}(k) < 0 \), the foreign firm may still prefer to outsource drug development due to the
local firm’s cost advantage and this happens iff

$$\frac{\pi^h_y(1) - F_d}{2} > \pi^f_y(1) - F_d \Leftrightarrow \pi^h_y(1) + F_d > 2\pi^f_y(1)$$

i.e. development costs and/or the home firm’s cost advantage is sufficiently large.

### 6.3 The Evidence

Having outlined a theoretical rationale for an impact of IPR reform on collaboration, we can then seek to assess the extent to which this channel of influence is operative in the Indian pharmaceutical industry. The popular press has emphasized this channel quite strongly and, at first glance, it seems to have a certain plausibility. Major Western pharmaceutical companies, including Merck, Eli Lilly, Bristol Myers Squibb, Wyeth, and Pfizer have all entered into well-publicized research collaborations with Indian firms. Relatively new entrants into the Indian pharmaceutical industry, such as Glenmark Pharmaceuticals, have explicitly based an important component of their business strategy on research collaborations with foreign partners. The industry trade press has pointed to a small number of prominent out-licensing deals between Indian and foreign firms that could be a leading indicator of future developments. India’s seemingly abundant supply of low-cost scientific and engineering talent would seem to offer exactly the kind of environment in which some degree of R&D outsourcing would make sense.

However, these recent developments need to be placed in appropriate perspective. Using the SDC-Thomson database on strategic alliances, it is possible to track alliance activity between Indian pharmaceutical firms and their foreign counterparts in a fairly comprehensive fashion. Figure 5 provides cumulative counts of these alliances since 1990 and Figure 6 depicts a "flow" measure of these alliances, year by year. Close inspection of the content of these alliances, however, reveals that only a small fraction have involved any meaningful degree of R&D collaboration with Western pharmaceutical or biotechnology firms. Most of these alliances have come in the
most recent years. The number of deals explicitly involving the licensing of technology has been small.

Still, there appears to be a clear trend break in the data that is correlated with the final steps of patent reform. There is something here, and it appears to be growing over time. Alternative data sources on international alliances, such as the MERIT database and Recombinant Capital indicated similar trends to those depicted in the SDC-Thomson data.

Might the outcomes of R&D collaboration emerge in other ways? In principle, Western pharmaceutical firms could be exploiting India's favorable human capital resource endowments by conducting "D" type research in their Indian subsidiaries or through joint ventures in which the patented output is assigned to the Western partner rather than the Indian firm conducting research. However, a careful review of the data do not support these hypotheses. With a few exceptions, multinational firms have neither spent significant sums on R&D in India nor have they generated more than a trivial number of patents assigned to the Indian subsidiary. We also found surprisingly few drug patents developed by inventor teams that include an Indian member and a member in a Western country. This latter finding stands in sharp contrast to observed trends in technical fields related in information technology and related fields. Western IT manufacturers like LSI, Intel, and IBM have set up substantial R&D operations in India which are generating literally hundreds of patents through the efforts of international teams. This trend is depicted in Figure 7, and Figure 8 provides a ranking of foreign firms in terms of the numbers of patents assigned to them which include Indian-based scientists and engineers. In IT, the numbers of patents involved are large enough to substantively affect the trends in India’s total U.S. patent count, and the sharp acceleration is clearly visible in the data despite the fact that the patent regimes for IT hardware in India have not changed significantly over the past 15 years and despite the fact that few Indian IT hardware manufacturers have yet acquired much of an international market share or an international reputation. Set against these trends, the numbers of Indian co-invented patents being generated in the pharmaceu-
tical and biotechnology industries appear to be quite small. Still, there is a detectable uptick that is coincident with the most recent stages of patent reform.

7 Conclusion

Can a shift to strong intellectual property rights induce higher levels of inventive effort in developing countries? The conventional wisdom in economics has come to regard this proposition with skepticism. Theoretical contributions, most recently that of Grossman and Lai (2005), and a long line of empirical contributions have laid out sound theoretical arguments and empirical evidence suggesting that this is unlikely to be true in general. Qian’s (2007) work focuses on pharmaceuticals and suggests especially strong grounds for skepticism there.

The recent experience of the Indian pharmaceutical industry seems to challenge this received wisdom. As documented in ABC (2008), the industry has experienced a profound shift since India ratified the TRIPs Agreement in late 1994. Measures of R&D input and inventive output have grown sharply, in ways that seem to be driven by important developments in India’s IPR reform process. The stock market’s valuation of R&D investment by firms has grown significantly, at least among the top 50 or so Indian producers. Is the conventional analysis wrong?

Yes and no. Our analysis points to two dimensions along which the conventional analysis may be incomplete. First, if imitation and innovation are strategic substitutes, then a domestic policy change could, in principle, push firms to a greater level of research intensity by foreclosing the imitation option. Second, if R&D collaboration between established producers and potential new entrants is possible, then a domestic policy change could have a similar, related effect, by pushing domestic firms into partnerships that would have not been incentive compatible so long as the imitation option were open. Our empirical analysis provides some evidence for both kinds of
developments in the Indian pharmaceutical industry, and we fully endorse the strong possibility that these two dimensions could become more important over time. Indigenous industry analysts and public statements by industry executives suggest this will be the case.

However, a deeper and more comprehensive examination of the Indian pharmaceutical industry’s innovation surge to date points to important causes other than TRIPs and the patent reform process TRIPs ratification triggered. The 1984 Hatch-Waxman Act opened up a market for legal imitations in the world’s largest economy. The opening of the Indian economy in the early 1990s reinforced the attractiveness of this external market and similar markets for generics opening up in Western Europe and industrial East Asia, while enhancing the global competitiveness of Indian producers. In a sense, TRIPs provided the stick – the imperative for Indian pharmaceutical firms to seek alternative market opportunities. The generics market (and the related API/bulk drugs market) provided the carrot – a new market opportunity that required some investment to profitably access, but one for which Indian firms arguably had a comparative advantage even in the mid-1990s. India’s long transition period to the new regime – a decade of reform – may have also played an important role, providing indigenous firms with continued access to a protected domestic market while they invested in the capability to sell abroad. Over the course of the 1990s and early 2000s, Indian firms were able to upgrade their manufacturing and process R&D capability to the point where they could succeed in a generics market that grew rapidly as a series of blockbuster drugs went off patent. We have presented in this paper substantial evidence linking the largest pieces of the expansion of R&D input and output to process innovations focused on existing drugs rather efforts to develop new drugs or to engage in collaborative R&D with Western pharmaceutical firms. The market’s rising valuation of R&D expenditure is largely unrelated to product development.

These considerations suggest important reasons why the Indian drug industry was able to grow and develop even as other indigenous industries in developing countries adopting stronger patent rights were unable to weather
the changes in their markets. To some extent, Indian firms were simply in the right place at the right time. Other developing countries, such as Taiwan, South Korea, and Mexico, were forced to adopt strong patents before the generics market had fully opened up, and they were not given the lengthy transition period India managed to negotiate. Other potential producers, such as Brazil and Argentina, were handicapped by uncompetitive exchange rates and domestic macroeconomic turmoil that undermined their efforts to explore foreign markets.

These considerations also reinforce the difficulties developing countries face in trying to shift from imitation and incremental invention to more substantive product development. These barriers to upgrading may be especially significant in the pharmaceutical industry, but they surely exist to varying degrees across the product space. Is our version of the Indian industrial development story generalizable? Is it true that most developing country industries that have successfully weathered the imposition of strong IPR have done so by identifying an industry submarket in which largely incremental, process-oriented R&D was sufficient to secure a defensible global market position. One wonders if parallels can possibly be drawn between the Indian pharmaceutical industry and the Korean semiconductor industry. Further investigation of this possibility is the focus of ongoing research.

Finally, the indigenous trade press, analysts reports, and the public statements of leading Indian drug CEOs all suggest that the reliance on generics is viewed as a winning strategy in the short run, but not necessarily in the longer run. Rising salaries and an appreciating currency are slowly eroding Indian cost advantages. Producers elsewhere in the developing world are seeking to serve the generics market, increasing competition. Western pharmaceutical companies are increasingly seeking to create their own generics divisions to exploit post-patent market opportunities. Will indigenous drug development or foreign collaboration displace generics as the primary driver of innovative activity in the longer run? We look forward to tracking the ongoing development of this interesting story over the next few years.
8 Note on Data Sources

Patent Data. U.S. patent data were downloaded from the U.S. PTO website in early July 2008. "Drug" patents were defined as patents in the IPC classes associated with organic chemistry, organic macromolecular compounds, biochemistry (including genetic engineering and fermentation), and medical or veterinary science. Some Indian drug patents were assigned to their U.S. subsidiaries; where possible, care was taken to "re-assign" these to the Indian parent. In some cases, these data were supplemented by the use of the U.S. PTO Cassis CD-ROM (December 2006 version). "Product innovation" patents were defined as those that made explicit references to compounds or compositions in the patent title, and were identified through keyword searches. Patents that listed inventor addresses both inside India and outside its borders were marked as "international coinvention" patents. In some figures, we use counts of patents in this category as an indicator of research collaboration between Indian scientists/engineers and foreign sources of drug development expertise. Data on Indian patents were taken from the EKSAWA database described in Arora et al. (2008) and Chatterjee (2008).

ANDA Data. Data on the abbreviated new drug applications (ANDAs) of Indian firms were taken from the on-line FDA Orange Book registry maintained on the FDA website. Patents were matched to ANDAs by undertaking a keyword search of the patent abstract and claims. Patents were linked when explicit reference of the ANDA active ingredient was made in the abstract or claims of the patent.

Stock Market/Financial Data. Our primary dataset comes from the Prowess database of the Centre for Monitoring of Indian Economy, which gives a ready-made industry classification of the firms. The Prowess database is similar to Compustat database for U.S. companies providing information that incorporated companies are required to disclose in their annual reports. Our study is conducted on a panel of 315 drugs and pharmaceutical firms (National Industrial Classification 2423) from 1990 to 2005. For these firms, the dataset also provides us annual data from 1990 to 2005, on market
capitalization of the firms at the Bombay Stock Exchange (BSE). This gives us the market value of the common stock of a firm; we also collect data on preferred stock for these firms. To capture the debt component of a firm’s market value, we collect data on borrowings and current liabilities; all of this comes from the CMIE dataset. We also collect data on the total assets of firms as a measure of the tangible component in a firm’s valuation. Our firm data also includes information on ownership groups, R & D expenditures, exports, sales, profits and age of the firm as measured from their year of incorporation. We validate our firm financial data from annual reports of firms and from the electronic data source, EDIFAR, of the Securities and Exchange Board of India, Government of India. Measures of knowledge assets were constructed using the R & D expenditure reported by firms in their books. We use annual reportage on both the capital and current account of firms and treat the additive combination as the total R & D expenditure of the firms. R&D stocks were created with depreciation rates of 15%.

Alliance Data. Data on Indo-Foreign strategic alliances were obtained from the SDC-Thomson Strategic Alliances Database. We restricted our coverage to alliances that involved Indian firms and foreign firms; alliances involving only Indian or only non-Indian firms were deleted. We also deleted alliances that did not focus on pharmaceutical products. Alliances were categorized as being R&D or product development alliances based on the textual description of alliance goals recorded in the SDC database. Trends in these data were cross-checked against those evident in the MERIT database on technology transactions and data on strategic alliances involving Indian pharmaceutical/biotech firms found in the Recombinant Capital database.

References


Table 1 Production of Bulk Drugs and Formulations

<table>
<thead>
<tr>
<th>Year</th>
<th>Bulk</th>
<th>Formulations</th>
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</thead>
<tbody>
<tr>
<td>1974-75</td>
<td>900</td>
<td>4000</td>
</tr>
<tr>
<td>1979-80</td>
<td>2260</td>
<td>11500</td>
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<tr>
<td>1984-85</td>
<td>3650</td>
<td>18270</td>
</tr>
<tr>
<td>1989-90</td>
<td>6400</td>
<td>34200</td>
</tr>
<tr>
<td>1994-95</td>
<td>15180</td>
<td>79350</td>
</tr>
<tr>
<td>1999-2000</td>
<td>37770</td>
<td>158600</td>
</tr>
<tr>
<td>2003-2004</td>
<td>77790</td>
<td>276920</td>
</tr>
</tbody>
</table>


Figures in Indian Rupees million – at current prices.
<table>
<thead>
<tr>
<th>Year</th>
<th>IPR events in India</th>
<th>Implications</th>
</tr>
</thead>
</table>
| From Pre’72 to Post ’72 | British Patents and Design Act, 1911 - Patents Act 1970                          | • Pre 1972: A product and process patent regime; Life of drug patents 14 years; One could patent all processes for drug manufacturing.  
• Post 1972: Product patent regime abolished, patent only a method or a process, Life reduced to 5 – 7 years, for a particular drug only one method or process patentable. |
| 1994-1995            | Signing of the WTO TRIPs treaty by India as a result of the 1986-1994 Uruguay Round of negotiations | • Dec 31st, 1994: The Patents (Amendment) Ordinance allowing filing and handling of product patent applications for pharmaceutical and agricultural chemical products, as well as the granting of exclusive marketing rights, EMRs on those products. The Ordinance became effective on January 1, 1995.  
• The Patents Amendment Bill 1995 was introduced. |
| 1996-1997            | Transition period                                                                  | • Indian Patent office keeps receiving product patent applications.  
• Meanwhile disputes with US and EU at WTO related to violation of product patents.  
• WTO asks India to complete institutional reform on new IPR laws by April 1999. |
| 1998 – 2001          | India signs and ratifies Paris convention and PCT                                  | • Indian patent law partially amended in 1999  
• WTO reviews the TRIPs terms and grants an extension to India beyond 2000 but before January 1st 2005 – the new deadline to implement product patents. |
| May 2002             | Patent Amendment Act Promulgated                                                    | • Terms of all patents in force on this day including process patents are extended to 20 years from the grant date.                      |
| 2002-2003            | Period of change, interest groups fight granting of EMRs by IPO, City High Courts put up stay orders. | • Examples of disputes: Rejection of EMR for GSK’s Rosiglitazone and Hoffman La Roche’s HIV drug Squinavir, based on patent application having been filed before 1995. Natco Pharma gets a stay order from Chennai High Court on EMR for Novartis’s cancer drug Glivec – the Indian generic producers getting a safe cushion against government enforcement. |
| Dec 2004 – 1st of Jan’ 2005 | Amendments to Patents Act | • Product patent regime in place. |

### Table 3 R&D Intensity

<table>
<thead>
<tr>
<th>R &amp; D</th>
<th>Year</th>
<th>R &amp; D/Sales (%)</th>
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<tbody>
<tr>
<td>9</td>
<td>1990</td>
<td>0.23</td>
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<tr>
<td>162</td>
<td>1995</td>
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</tr>
<tr>
<td>419</td>
<td>2000</td>
<td>1.80</td>
</tr>
<tr>
<td>553</td>
<td>2001</td>
<td>2.22</td>
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<tr>
<td>832</td>
<td>2002</td>
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<tr>
<td>1,059</td>
<td>2003</td>
<td>3.12</td>
</tr>
<tr>
<td>1,568</td>
<td>2004</td>
<td>4.19</td>
</tr>
<tr>
<td>2,171</td>
<td>2005</td>
<td>8.51</td>
</tr>
</tbody>
</table>

R&D expenditures are given in 10 million INR.

### Table 4 Rising Measures of Innovative Output

<table>
<thead>
<tr>
<th>Year</th>
<th>US Patent Counts</th>
<th>Indian Patent Counts</th>
<th>ANDAs</th>
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</thead>
<tbody>
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<td>1990</td>
<td>6</td>
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<td>0</td>
<td>0</td>
<td>4</td>
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<td>1992</td>
<td>2</td>
<td>0</td>
<td>2</td>
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<tr>
<td>1993</td>
<td>2</td>
<td>0</td>
<td>2</td>
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<tr>
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<td>2005</td>
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<td>2006</td>
<td>45</td>
<td>552</td>
<td>50</td>
</tr>
<tr>
<td>2007</td>
<td>63</td>
<td>689</td>
<td>72</td>
</tr>
</tbody>
</table>
Table 5 Period trends in $\beta$ - in industry subsets and overall sample

<table>
<thead>
<tr>
<th>Pooled OLS</th>
<th>Entire Industry</th>
<th>Only Modern Firms</th>
<th>Analyst Firms</th>
<th>FDA Firms</th>
<th>Other Firms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990-1994</td>
<td>1.360</td>
<td>0.182</td>
<td>-1.673</td>
<td>-3.830</td>
<td>2.048</td>
</tr>
<tr>
<td></td>
<td>(0.95)</td>
<td>(0.12)</td>
<td>(0.84)</td>
<td>(1.38)</td>
<td>(0.96)</td>
</tr>
<tr>
<td>1995-1999</td>
<td>1.990</td>
<td>2.074</td>
<td>2.704</td>
<td>2.681</td>
<td>1.765</td>
</tr>
<tr>
<td></td>
<td>(3.19)**</td>
<td>(2.95)**</td>
<td>(2.62)**</td>
<td>(1.62)</td>
<td>(2.21)*</td>
</tr>
<tr>
<td>2000-2005</td>
<td>2.569</td>
<td>3.301</td>
<td>4.567</td>
<td>5.103</td>
<td>1.706</td>
</tr>
<tr>
<td></td>
<td>(6.41)**</td>
<td>(6.94)**</td>
<td>(6.02)**</td>
<td>(5.55)**</td>
<td>(3.58)**</td>
</tr>
<tr>
<td>Log of sales</td>
<td>0.010</td>
<td>0.163</td>
<td>0.231</td>
<td>0.158</td>
<td>-0.005</td>
</tr>
<tr>
<td></td>
<td>(0.95)</td>
<td>(9.16)**</td>
<td>(5.68)**</td>
<td>(3.80)**</td>
<td>(0.42)</td>
</tr>
<tr>
<td>Industry Q</td>
<td>0.219</td>
<td>0.274</td>
<td>0.239</td>
<td>0.208</td>
<td>0.212</td>
</tr>
<tr>
<td></td>
<td>(4.95)**</td>
<td>(5.50)**</td>
<td>(2.75)**</td>
<td>(2.22)*</td>
<td>(3.93)**</td>
</tr>
<tr>
<td>Constant</td>
<td>-0.254</td>
<td>-0.711</td>
<td>-0.932</td>
<td>-0.739</td>
<td>-0.235</td>
</tr>
<tr>
<td></td>
<td>(4.03)**</td>
<td>(8.65)**</td>
<td>(5.12)**</td>
<td>(4.05)**</td>
<td>(3.10)**</td>
</tr>
<tr>
<td>P-value of Wald Tests of Equality</td>
<td>0.5047</td>
<td>0.0390</td>
<td>0.0061</td>
<td>0.0041</td>
<td>0.9861</td>
</tr>
<tr>
<td>Observations</td>
<td>2686</td>
<td>1330</td>
<td>426</td>
<td>399</td>
<td>2236</td>
</tr>
<tr>
<td>Number of Firms</td>
<td>315</td>
<td>143</td>
<td>41</td>
<td>42</td>
<td>268</td>
</tr>
<tr>
<td>R Squared</td>
<td>0.11</td>
<td>0.25</td>
<td>0.41</td>
<td>0.37</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Regressions Using Imputed R&D Data

| 1990-1994  | 1.210           | 0.048            | -1.738        | -4.822    | 1.884       |
|            | (0.94)          | (0.03)           | (0.91)        | (1.79)    | (1.08)      |
| 1995-1999  | 1.764           | 1.704            | 1.999         | 1.351     | 1.707       |
|            | (2.96)**        | (2.57)*          | (1.95)        | (0.88)    | (2.26)*     |
| 2000-2005  | 2.249           | 2.899            | 3.90          | 4.634     | 1.575       |
|            | (5.95)**        | (6.36)**         | (5.33)**      | (5.03)**  | (3.49)**    |
| Log of sales | 0.010           | 0.165            | 0.239         | 0.160     | -0.005      |
|            | (0.98)          | (9.23)**         | (5.82)**      | (3.80)**  | (0.42)      |
| Industry Q | 0.218           | 0.273            | 0.237         | 0.215     | 0.210       |
|            | (4.89)**        | (5.45)**         | (2.69)**      | (2.27)*   | (3.87)**    |
| Constant   | -0.253          | -0.715           | -0.959        | -0.746    | -0.233      |
|            | (4.01)**        | (8.66)**         | (5.20)**      | (4.05)**  | (3.07)**    |
| P-value of Wald Tests of Equality | 0.5677 | 0.0368 | 0.0087 | 0.0009 | 0.9742 |
| Observations | 2686           | 1330             | 426           | 399       | 2236       |
| Number of Firms | 315         | 143              | 41            | 42        | 268        |
| R Squared  | 0.11            | 0.25             | 0.40          | 0.37      | 0.09       |

(T-stats given in parentheses)
Table 6 Indian Pharmaceutical Product Development, 2005-6

<table>
<thead>
<tr>
<th>Output</th>
<th>Outlicensing Products</th>
<th>Preclinical Development</th>
<th>Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. Reddy’s</td>
<td>DRF 4158 to NovoNordisk</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DRF 2725 to NovoNordisk</td>
<td></td>
<td>Phase I (1)</td>
</tr>
<tr>
<td></td>
<td>DR 4158 to NovoNordisk</td>
<td></td>
<td>Phase II (3)</td>
</tr>
<tr>
<td></td>
<td>DRF 2593 to Rheoscience</td>
<td></td>
<td>Phase III(1)</td>
</tr>
<tr>
<td></td>
<td>DRF 1042 to Clin Tech</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glenmark</td>
<td></td>
<td></td>
<td>Phase I (1)</td>
</tr>
<tr>
<td>Lupin</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Nicholas</td>
<td></td>
<td>1</td>
<td>Phase I (2)</td>
</tr>
<tr>
<td>Piramal</td>
<td></td>
<td></td>
<td>Phase II (1)</td>
</tr>
<tr>
<td>Panacea Biotech</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Ranbaxy</td>
<td>RBx 2258 benign prostatic hyperplasia molecule to Scharwz Pharma – later abandoned;</td>
<td>2</td>
<td>Phase I (1)</td>
</tr>
<tr>
<td></td>
<td>RBx 10558 to Pharmaceutical Product Development (CRO)</td>
<td></td>
<td>Phase II (1)</td>
</tr>
<tr>
<td>Torrent</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Wockhart</td>
<td></td>
<td>2</td>
<td>Phase I (1)</td>
</tr>
</tbody>
</table>

Table lists numbers of products under development, by originating firm, in various stages of the development process. Calculations based on PharmaProjects Data, Company Web Sites, and Athreye et al. (2008)

Table 7 Market Valuation of Indian Product Innovation

<table>
<thead>
<tr>
<th>Knowledge Capital Measure</th>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
<th>(4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R&amp;D</td>
<td>1.78</td>
<td></td>
<td>2.14</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(5.38)***</td>
<td></td>
<td>(5.73)***</td>
<td></td>
</tr>
<tr>
<td>U.S. Product Patents</td>
<td></td>
<td>5.12</td>
<td>1.43</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1.51)</td>
<td>(0.42)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indian Patents</td>
<td></td>
<td></td>
<td></td>
<td>-.1531</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(-0.26)</td>
</tr>
<tr>
<td>Sales</td>
<td>.005</td>
<td>.011</td>
<td>.010</td>
<td>.011</td>
</tr>
<tr>
<td></td>
<td>(.045)</td>
<td>(1.07)</td>
<td>(.96)</td>
<td>(1.10)</td>
</tr>
<tr>
<td>Obs</td>
<td>2,686</td>
<td>2,686</td>
<td>2,686</td>
<td>2,686</td>
</tr>
<tr>
<td>R-Squared</td>
<td>.1049</td>
<td>.0980</td>
<td>.1104</td>
<td>.0972</td>
</tr>
</tbody>
</table>

Table presents results of a regression of the market value to assets ratio on the ratio of knowledge capital to tangible assets. Sales, time effects, and firm fixed effects are incorporated in the regression. Patent stocks are cumulated from patent flows, then divided by tangible assets. T-statistics are given in parentheses.
Figure 1 R&D Intensity in Indian Pharmaceuticals

![R&D Intensity in Indian Pharmaceuticals Graph]

Figure 2 Patent Trends for Listed Indian Pharmaceutical Companies, 1990-2006

![Patent Trends Graph]
Figure 3  Cumulative Patent Trends for Listed Indian Pharmaceutical Companies, 1990-2006
Figure 4  Optimal Investment Choices
Figure 5  Cumulative Indo-Foreign Strategic Alliances in Pharmaceuticals

Cumulative Alliance Activity by Indian Pharmaceutical Firms, 1990-2008

Figure 6  Indo-Foreign Strategic Alliances in Pharmaceuticals by Year

The Strategic Alliances of Indian Pharmaceutical Firms, 1990-2008
Figure 7  Multinational Patenting using Indian Inventors

U.S. Patents Granted to Multinationals Employing Inventors in India, 1990-2006

Figure 8  Top Foreign Patenting Enterprises in India

Top Foreign Patenting Enterprises in India
Cumulative U.S. Patent Grants through 2006

Source: Author's calculations using USPTO Cassis CD-ROM, December 2006
Chapter 3:

Generic competition, consumer surplus, and revenue erosion in the US pharmaceutical industry
Abstract

This chapter proposes to estimate consumer surplus generated with generic competition in the US pharmaceutical industry. In parallel, we also want to quantify the extent of revenue erosion for brand name pharmaceutical firms in many key products. These key drug products have seen aggressive generic entry here in the United States, especially during the last 5 years. Our access to detailed, comprehensive, and commercial data sources allows us to quantify the impact of this increase in competitive intensity on consumers, established pharmaceutical producers, and incumbents. Thanks to proprietary data we will have access to monthly price and revenue data at the product level for all pharmaceutical producers selling in all major markets over the period 1997-2007. The data also links products to highly disaggregated therapeutic areas and to the producing firm. In principle, these data allow for sophisticated demand-side modeling of consumer choice in a differentiated market for pharmaceutical products (Scott Morton, 1999; Stern, 1996; Cleanthous, 2002). Our analysis exploits provisions under what is now a 25-year old Federal Act in the US (Drug Price Competition and Patent Term Restoration Act, known more commonly as the Hatch-Waxman Act’ 1984). We aim at extending our analysis across different classes of generics producers, different therapeutic areas, and time.
Generic competition, consumer surplus, and revenue erosion in the US pharmaceutical industry

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July 2009 Very Preliminary Draft,

Heinz College, Carnegie Mellon University

Advisory Committee

Lee Branstetter, Carnegie Mellon

Matthew Higgins, Georgia Institute of Technology

Serguey Braguinsky, Carnegie Mellon

Introduction

The global pharmaceutical industry is undergoing a profound transformation. An apparent decline in the productivity of pharmaceutical R&D undertaken by established Western manufacturers has led to a substantial slowdown in the number of new patent-protected “blockbuster” drugs hitting the market (Cockburn, 2006; Higgins and Rodriguez, 2006). Meanwhile, new sources of competition have diminished profits from existing drugs. As drug patents expire at the end of market exclusivity established producers meet increasingly intense competition from generics manufacturers. Often, generics manufacturers are not even waiting for patent expiration. Instead, they are pursuing a well-known feature of the Hatch-Waxman Act that allows would-be generic competitors to introduce competing products at the end of data exclusivity while the original patents are still in force. Many of these generics companies are based overseas, where low factor costs and favorable movements in exchange rates allow them to achieve a marginal cost of production that established manufacturers in the West cannot match. This has also worked to intensify competition and the speed with which the profits of established firms are eroding.

Our access to detailed, comprehensive, commercial data sources allows us to quantify the impact of this increase in competitive intensity on consumers, established pharmaceutical producers, and incumbents.
Thanks to proprietary data, we will have access to monthly price and revenue data at the product level for all pharmaceutical producers selling in all major markets over the period 1997-2007. The data also links products to highly disaggregated therapeutic areas and to the producing firm. In principle, these data allow for sophisticated demand-side modeling of consumer choice in a differentiated market for pharmaceutical products (Scott Morton, 1999; Stern, 1996; Cleanthous, 2002). Under plausible assumptions, the change in consumer surplus obtained from shifts to generics products can be quantified. Our data are sufficiently rich that we can not only estimate total consumer surplus gains arising from generic entry but also calculate the distribution of this impact across different classes of generics producers, different therapeutic areas, and time.

The wealth of detailed data at our disposal enables us to examine how subtle changes in the circumstances surrounding generic entry could impact consumer and producer surplus in the key U.S. market. Of particular interest are the legal maneuverings that have surrounded Paragraph IV challenges to profitable drugs (Berndt, Mortimer, and Parece, 2007). Legal scholars, antitrust experts, and academics familiar with the industrial organization of the pharmaceutical industry have all expressed concern about the anticompetitive effects of licensing deals and other legal agreements between branded and generic firms which tend to restrict the entry of real generic competitors to established products (Bulow, 2004). Similar concerns have been voiced about the ability of established pharmaceutical firms to defend in court the validity of questionable patents, prolong patent protection, or prove infringement when the legal basis for such inference has appeared to be weak (Graham and Higgins, 2008). By undertaking detailed structural analyses of consumer and producer surplus changes resulting from actual and deferred entry by Paragraph IV challengers, we could obtain high-quality estimates of potential consumer and producer loss that could inform the policy debate in this area.

We also intend to examine the impact of this surge in generic entry on producer surplus – of the entrants and of the branded producers they compete against. Of particular interest in this part of the study will be the rise of an increasingly important set of generic firms (TEVA and Israeli firm and some 12 Indian firms are key players) whose emergence has already been documented in Arora, Branstetter, and Chatterjee (2007, 2008). Trade, FDI, and currency reforms in the early-to-mid 1990s coincided with a pronounced real depreciation of the rupee that positioned Indian firms to compete effectively in the American generics market. At the same time, the ratification by the Indian government of the TRIPs agreement signaled an eventual shift toward stronger patent protection for pharmaceuticals and the limits of a business strategy based on unauthorized duplication of Western products. The combination
of the foreign market carrot and the stronger IPR stick appears to have had a dramatic effect on the Indian industry. In response to these changes, a new wave of entrepreneurs entered the industry and existing firms shifted their strategies. Successful penetration of the Western generics market required an upgrading of manufacturing capabilities and significant investments in process R&D. Use of the IMS data at the product level should allow us to produce much more accurate measures of the return to these investments than have yet been possible. However, we expect to find that the impact of these firms on consumer surplus in their target markets is likely to be orders of magnitude larger than the producer surplus they have extracted through successful generic entry.

As the intensity of generic competition rose in the 2000s, established pharmaceutical firms began to question the sustainability of large-scale commitments to risky R&D programs across a broad spectrum of therapeutic areas and disease targets. Is there any evidence that the generics onslaught is actually leading to a significant reduction in big pharma R&D spending? The final segment of our project will assess the hypothesis that generic competition has shifted the direction and level of big pharma R&D investment in ways that may call into question the future availability of high-impact new drugs. Our highly detailed data allow us to construct a detailed picture of the revenue erosion being experienced by established producers across therapeutic classes, regional markets, and time as generic entry increased. Can this be statistically associated in the data with changes in firm-level R&D spending and the volume and distribution across fields of patent applications? Could the balance between access and innovation be shifting too far in one direction?

**Background on Estimation of Pharmaceutical Demand**

The literature on estimation of pharmaceutical demand has built on the Almost Ideal Demand System proposed by Deaton and Muellbauer (1980b). Subsequently, scholars have introduced two levels in identifying markets and estimating pharmaceutical demand. This has particularly helped in an approach where one starts with a particular *therapeutic area* as a market and then looks within that market, for molecules, that are held by originator firms (or pioneer firms) and generic firms. For example, Stern in his 1996 NBER working paper uses the tree below to use the 2 level nested logit models. This results in maximizing the value $V$ in the jth product for patient $I$, with a value function as given below. In the specification below, $X$ is the vector of product characteristics, $p$ denotes the price, and $\mu$ is a consumer specific deviate, and $\xi$ is unobserved product characteristics not observable to the econometrician.
Using Cardell (1993), one can then parameterize \( \mu \) using a joint distribution to relax the assumption of independence across products and allowing for richer substitutions. If product is a pioneer molecule facing competition even in the same market from fellow pioneers or other generic firms, the specification breaks up the \( \mu \) in terms of shocks at the molecule level first, and then at the generic level. Further algebra yields the estimation framework:

\[
\max_{j \in \{0, J\}} V_j = X_j \beta + \alpha p_j + \xi_j + \mu_j = \delta_j + \mu_j
\]

where \( \delta_j \) indicates pioneer molecule and the notation if G for generic molecule. \( s_j \), \( s_{G,M} \), \( s_{P,M} \) and \( s_M \) denote the total market shares of product \( j \), the generic cluster in Molecule M, the pioneer version of Molecule M, and Molecule M, respectively. In a nutshell, an ordering, starting from therapeutic market, going into molecules, and for each molecule noting the presence of pioneer and generic firms enable
them to regress market shares on price data of the jth product. This approach is useful given the large number of subsequent papers that has adopted the methodology (Ellison et.al 1997, Cleanthous 2002, Dutta 2006, Chaudhuri et.al 2007).

**Theory of Pharmaceutical Demand – Using a Berry Levinsohn Pakes (BLP) 1995 Approach**

An alternative approach is to use the literature on estimation of demand using the characteristics space approach. In such a setting, we can write the utility function of a utility-maximizing consumer i (i = 1…I) in a given time period t (t=1…T) who faces various alternatives (these are the various subclasses in accordance with the therapeutic areas) in each therapeutic area, along with the option of not purchasing any of the drugs, the outside option where j=0. This utility is \( u(x_{jt}, x_{jt}', \epsilon_{jt}, \epsilon_{jt}; \theta_d) \) -- the general conditional indirect utility function and this is a function of \( v \), individual consumer characteristics, drug characteristics \( (x_{jt}, \epsilon_{jt}, p_{jt}) \), where \( x_{jt} \) and \( \epsilon_{jt} \) are observed and unobserved drug characteristics, \( p \) is the drug price and \( \theta_d \) is the vector of demand parameters to be estimated.

Following BLP (1995), Petrin (2002) and Cleanthous (2002) we can write the utility function as:

\[
\begin{align*}
\hat{u}_{ijt}(v_{jt}, x_{jt}, \epsilon_{jt}, p_{jt}; \theta_d) &= \delta_{jt}(v_{jt}, x_{jt}, \epsilon_{jt}, p_{jt}; \theta_d) + \mu_{ijt}(v_{jt}, x_{jt}, \epsilon_{jt}, p_{jt}; \theta_d) + \epsilon_{ijt} \\
\end{align*}
\]

(1)

The utility level has three components. First, \( \delta_{jt} \) is the mean utility level and is a drug-specific term common to all consumers; \( \mu_{ijt} \) captures the heterogeneity in consumer preferences for observed (by the econometrician) drug characteristics. \( \epsilon_{ijt} \), is a random utility component across drugs and consumers and is assumed to be independent and identically distributed across both drugs and consumers. The last two terms denotes deviation from the mean utility level for each consumer i and is a measure of the idiosyncratic valuation of drug j’s characteristics. Each consumer purchases one unit of the drug that provides her with the highest utility. Given \( x_{jt}, \epsilon_{jt} \) the observable and unobservable drug characteristics along with \( p \), the price, consumer i chooses one unit of drug j rather than one unit of drug k (both in the same therapeutic area) if:
\[ u_{ijt}(\Theta_d) > u_{ikt}(\Theta_d) \text{ where } k \neq j \quad (2) \]

The next step is in estimating/calculating the market shares. Let’s assume a consumer population consuming drug j, where \( \varepsilon_j \) will then be the drug market share. A set of observable characteristics will induce this choice of the drug j, let’s say that this set is \( A_j(\Theta) = \{ \mu_j, \sigma_j, \varepsilon_j \} \). If we now define a joint distribution \( F(\mu, \sigma) \) for consumer characteristics with density \( f(\mu, \sigma) \), then \( \varepsilon_j \), the market share for drug j, is the probability that \( \mu_j \), the heterogeneous consumer preference based on observed drug characteristics falls within \( A_j(\Theta) \), or:

\[ \varepsilon_j(v_i, p_i, p_{ij}, \Theta_d) = \int_{A_j(\Theta)} f(\mu, \sigma) \, d\mu \quad (3) \]

At every time period t, each consumer i maximizes her level of utility as follows:

\[ \max (u_{ijt}) = \delta_{jt} + \mu_{ijt} + \varepsilon_{ijt} \quad (4) \]

where mean utility level \( \delta_{jt} = \alpha p_j + x_j^t \beta + \varepsilon_{jt} \) following Berry 1994.

Here, \( \beta \) is the marginal utilities of the drug’s observed characteristics and the \( \alpha \) is the marginal utility associated with price. Unobserved characteristic is identical for all patients (or consumers as you want to term them). Price coefficient varies across consumer in the full random coefficients model, \( \varepsilon_j \) captures elements of vertical product differentiation by therapeutic area – and we need to apply this model to all our therapeutic areas. The assumption of the error term being Type 1 extreme value results in the system of equations 1 through 3 translating to a logit and more specifically a multinomial logit specification. The above is also closely related to Trajtenberg’s model in his seminal 1989 paper where he specifies the following:

The demand share:

\[ \pi_{jt} = \frac{\exp V_i}{\sum \exp V_j} \]

The deterministic portion of the conditional indirect utility function \( V_i \) is critical:

\[ V_i = z_i^t \beta + z_i^t Gz_i + \alpha p_i \quad \& \quad p_i^- = p_i - p(z_i) \]
Trajtenberg 1989 uses the above setup to first estimate the price function and compute the residuals; these residuals are then entered in the demand fraction expression with suitable substitution of the functional form of the indirect utility function \( V \) and multinomial logits are applied to estimate the coefficients. In his case he does a test for IIA and finds that head and body scanners are uncorrelated – however in our case, we might find correlations between our various nests (suggested nest for each therapeutic area being branded versus generics). We intend to for those cases, conduct NML1 to NML2, NML3 (if we break up into further nests) etc following Berry 94, Mcfadden 78, Cardell 97. Cleanthous 02 shows that for NML2 the overall market share for drug \( j \), broken down into nests of type-molecule-brands is:

\[
\begin{align*}
\varepsilon \left( \delta_j, \rho_c, \rho_{m_c} \right) &= \varepsilon_{j/m_c} \left( \delta_j, \rho_c, \rho_{m_c} \right) \cdot \varepsilon_{m/c} \left( \delta_j, \rho_c, \rho_{m_c} \right) \cdot \varepsilon _{j/c} \left( \delta_j, \rho_c, \rho_{m_c} \right) \\
&= e^{\delta_j / (1 - \gamma)} \cdot D^{-\rho_{m_c}}_m \cdot D^{-\rho_c} \cdot D^{-1}.
\end{align*}
\]

Where, \( \gamma = [1 - (1 - \rho_{m_c})(1 - \rho_c)] \in [0, 1] \), \( \rho \) is the correlation at the molecule or type level depending on the subscript, \( D_s \) represent overall market shares at each nest level \( c \) or \( m \) or overall when there is no subscript. The share of the outside good option is chosen as \( I/D \) and this leads Cleanthous into an analytic form for estimation of the type:

\[
\ln \left( s_j \right) - \ln \left( s_0 \right) = \delta_j + \rho_{m_c} \ln \left( \varepsilon_{m/c} \right) + \gamma \ln \left( \varepsilon _{j/m_c} \right),
\]

One can then estimate the multinomial logit coefficients (with IV too since there is endogeneity here of price and unobserved characteristics) on the imposed functional form of \( V_s \) and then use that with the \( z \) vector, the observed characteristics vector and price to compute year-by-year welfare. The difference in these year-by-year values gives one a sense of the upper bound of welfare increase. Following previous literature, the expression for the welfare in our case of drug \( j \) is thus:

\[
W_{jt} = \int_{i=1}^{n_s} \frac{1}{\alpha_i} \int_{q_j}^{\infty} \varepsilon_{ijt} \left( q_j \mid q_k = p_k \forall k < j, q_k = \infty \forall k > j \right) dq_j dF(\alpha_i, \sigma_{\alpha})
\]

Nesting at the generic level too apart from the type-molecule nest, will help us get the expression for the NML1 to NML3 shares.
Industry Background & Other Issues

*Overview of Hatch-Waxman Act*’ 1984 and the Paragraph Four Feature

At this juncture, it would be necessary to understand the para IV process. A paper (Gaming of Pharmaceutical Patents, Bulow 2004) gives a nice preview in this context. I point specifically to a diagram (see below) in this paper, which should allow us to understand the timing issues with respect to para IV applications. In accordance with the Federal Food, Drug, and Cosmetic Act, a brand-name company seeking to market a new drug product must first obtain FDA approval by filing a New Drug Application (NDA). Included in this filing is information that is expensive and time consuming to create (such as clinical studies) relating to the safety and effectiveness of the product. Literature has found that on an average, 1.3 years passed between patent grant and the beginning of clinical trials, that clinical trials took an additional 3.8 years, and that FDA review took an additional 2.6 years, leaving a little over 9 years left after approval on the old 17 year patent system (Laurie 1989).

**Paragraph IV Certifications**

![Diagram of Paragraph IV Certification](source: Bulow 2003)
The Hatch-Waxman Act of 1984 increased patent and exclusivity protection for brands while making pre-patent and post-patent entry easier for generics. Manufacturers are allowed to extend one patent for each new chemical entity, with extensions usually on a drug’s chemical compound (a product patent) but sometimes on the use of a drug. Extensions must be applied for within 60 days of FDA approval of the marketing of the drug and may be for up to half the time the drug spent in clinical trials plus all the time it spent in FDA review, subject to a maximum extension of five years and a maximum effective life of 14 years. Furthermore, the Act provides that the FDA not accept a generic application to produce a new chemical entity for a minimum of five years, benefiting drugs with no or very short patent protection. Since approval of such an application averages over 30 months, effective exclusivity is even longer. Finally, manufacturers can use NDAs or supplemental NDAs to obtain additional years of market exclusivity (as opposed to patent extension) for new dosage forms, a new use, or for marketing a drug over the counter, provided the NDA requires additional clinical testing.

On a different note, Hatch-Waxman facilitates generic entry. When an NDA is filed, the brand-name company provides the FDA with information regarding patents that cover the product that is the subject of the NDA. Upon approval of the NDA, the FDA lists the patents in an agency publication commonly known as the “Orange Book.” Hatch-Waxman allows a generic firm to file an Abbreviated New Drug Approval (ANDA), which means that it only has to show that its product is bioequivalent to a referenced NDA’s brand name product and also that the generic product has the same active ingredient, dosage form and strength, and proposed labeling as the brand-name product. The Act also made clear that generics may use the patent drug to develop their ANDA even before patent expiration. Allowing for ANDA filings has tremendously expanded the availability of generic pharmaceuticals. According to the CBO (1998) the usual period between patent expiration and generic entry has fallen from 3 to 4 years to frequently 1 to 3 months, the generic share of prescription drug volume rose from 19 percent in 1984 to 47 percent in 1996, and the percentage of top-selling drugs facing generic competition increased from 36 percent in 1983 to nearly 100 percent in 1998.

An ANDA must contain a certification regarding each patent listed in the Orange Book covering a referenced NDA. One of four such certifications is made:

- “Paragraph I Certification” – certifying that patent information has not been filed in connection with an NDA. The FDA may approve immediately an ANDA making this certification.
• “Paragraph II Certification” – certifying that a patent covering an NDA has expired. Again, the FDA may approve immediately an ANDA making this certification.

• “Paragraph III Certification” – certifying that ANDA approval is sought after a listed patent expires. The FDA may approve the ANDA only after such patent expiration.

• “Paragraph IV Certification” – certifying that a listed patent is either invalid or will not be infringed by the generic drug for which the ANDA applicant seeks approval.

Paragraph IV ANDAs imply two additional provisions of the Hatch-Waxman Act, both of which relate to the FDA’s approval of an ANDA. First is the automatic “30-month stay” protection afforded to brand-name companies. As part of a Paragraph IV certification, an ANDA filer must provide to the patent holder and NDA filer (which is often, but not always, the same company) a notice of the Paragraph IV certification as well as a detailed statement of the factual and legal bases for the ANDA filer’s assertion that a patent is invalid or not infringed by the ANDA filer’s generic product. Once the ANDA filer has provided such notice, a patent holder must file an infringement suit within 45 days to take advantage of the statutory stay provision. If a suit is not filed within 45 days, the FDA can approve the ANDA as soon as the regulatory requirements are fulfilled. Filing a patent infringement suit within 45 days, however, stays FDA approval of the ANDA until the earliest of: (1) the date the patent expires, (2) a court determination of non-infringement or patent invalidity by a court in the patent litigation, or (3) 30 months after a patent holder was notified of the Paragraph IV certification. Second is the provision that gives rise to a 180-day exclusivity right. This right is extended to the first company to file a Paragraph IV ANDA. Once such an ANDA filer receives this right, the FDA may not approve any other ANDA for the same drug product until six months after (1) the ANDA filer with the right first markets its product or (2) a court decision declaring the patent at issue invalid or not infringed, whichever is sooner.

One remarkable consequence of this rule is that if a first filer has not triggered its exclusivity period, say because it resolved its litigation with the brand by agreeing not to enter the market for several years, the brand could foreclose entry by later filers, even if they clearly did not infringe on its patents, simply by not filing (and losing) an infringement suit. As noted in the discussion above, the paragraph four feature facilitated by the Hatch-Waxman Act results in various trigger dates in the game between incumbent patent-holder brand name firm and the generic entrant. We would want to start our work keeping these trigger dates on our mind while estimating consumer welfare.
Stepping back, it is well documented that the US pharmaceutical industry has been a high-risk high-reward research based industry since the 1940s. This has resulted in a spiraling price of new drugs, costs of R & D being transferred directly to the consumer. Since 1984 however, legislation created an industry sub-sector that offers low-risk low-reward alternatives, the legislation aimed towards increasing access to consumers for medicines. Americans in the past two decades have thus significantly latched on to this, buying generic versions of branded originator drugs coming off-patent. As documented above, the Drug Price Restoration and Competition Act (Hatch – Waxman Act’ 1984) also offers 6-month exclusivity to a generic maker through an instrument called the paragraph IV filing (Higgins and Graham 2008, Graham and Higgins 2007, Berndt et.al 2005). Generics entry at large and more specifically using the paragraph IV route has generated consumer welfare; our project aims to estimate precisely that using firm-product-month level data from 1997 to 2007. That said, scholars and industry experts increasingly agree that the entry of generics (Hughes, Moore and Snyder 2002) is also impacting new drug development reducing future consumer welfare from innovation by originator firms. Our estimates on consumer welfare with generic entry will also reconcile increased consumer welfare with this impact on originator innovation from generic entry. Our work will also have firm-level, industry-level and policy implications on the way research and development is being carried out in today’s pharmaceutical industry. To conclude, our work should lead us into answering the following key research question:

- How much consumer welfare was generated in US pharmaceutical markets between 2003 and 2007 with generic entry (with and without paragraph IV challenges)? How does this welfare estimate balance out with loss of future consumer welfare from reduced new drug innovation by incumbent originator firms? Can we observe substantial revenue erosion across key drug products for incumbent originator firms, that over time and therapeutic area markets?

Initial Descriptive Statistics

Paragraph Four Data

A look at initial descriptive statistics at our dataset points to the following. First, drug products facing Para-IV certification have been on the rise as shown in Figure below. Several key shifts occurred in the policy concerning Para-IV filings between 1998 and 2003. The year 1998 saw two famous court cases between brand name and generic makers changing the interpretation of 180-day exclusivity. Since then, 180-day exclusivity as granted by the FDA started including generics, whose Para-IV certifications the
NDA holder did not subsequently challenge. Before that a successful defense in court was necessary for getting 180-day exclusivity. From 2000, FDA started allowing generics to enter market and start their 180-day marketing exclusivity following the first favorable court decision, irrespective of the ruling entered by the 'court that enters final judgment'. And from 2003, 180-day exclusivity was granted to multiple applicants if they filed Para-IV certifications on the same day. No wonder, that while between 1984 and 1989 Para-IV ANDAs were only 2% of all submitted ANDAs, this percentage went up to 12% between 1990-1997 with a more generic encouraging policy environment and reached some 20% between 1998 and 2000 (Berndt et.al 2007).

![Drugs Facing first Para-IV certification](image)

How do increasing Para-IV certifications translate into pipelines for generic firms? In an industry analysis by the Thomson Reuters Group, TEVA, a Israeli generics firm ranks as the most prolific Para-IV filer – with some 124 products being challenged by them (See Figure Below). Our data shows that Para-IV certifications in all involved interactions between 474 firms, both the branded firms as well as their generics challenger, with some 11 Indian firms being in the dataset. Further, IMS Sales data shows that TEVA had presence in at least 150+ molecules in our entire dataset of 200+ molecules with Para-IV challenges. We also document the data exclusivity end date, the market exclusivity end date and first-filer, first-entrant and subsequent-entrant names for our initial sub-sample of few drug products investigated. The details on this are given in the table in the following page.
Table on Exclusivity End Dates and Entry Dates of First and Subsequent Entrants

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Product Name</th>
<th>Data Exclusivity End Date</th>
<th>Market Exclusivity End Date</th>
<th>First Entry Date</th>
<th>First Filer</th>
<th>First Entrant</th>
<th>Any Indian</th>
<th>Subsequent Entry Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinapril</td>
<td>Accupril</td>
<td>Q41996</td>
<td>Q12007</td>
<td>Q22004</td>
<td>Teva</td>
<td>Actavis</td>
<td>Yes-Subsequent</td>
<td>Q42004</td>
</tr>
<tr>
<td>RAMIPRIL</td>
<td>Altace</td>
<td>Q11996</td>
<td>Q12005</td>
<td>Q42007</td>
<td>Cobalt Labs</td>
<td>Cobalt Labs</td>
<td>Yes-Subsequent</td>
<td>Q12008</td>
</tr>
<tr>
<td>ZIDOVUDINE</td>
<td>Retrovir</td>
<td>Q31992</td>
<td>Q32005</td>
<td>Q32005</td>
<td>Barr Laboratories</td>
<td>Many</td>
<td>Yes-First Entrant</td>
<td>Q12008</td>
</tr>
<tr>
<td>PAROXETINE</td>
<td>Paxil</td>
<td>Q41997</td>
<td>Q42006</td>
<td>Q32003</td>
<td>Geneva</td>
<td>Apotex &amp; Par Pharm</td>
<td>Yes-Subsequent</td>
<td>Q42003</td>
</tr>
<tr>
<td>CARBOPLATIN</td>
<td>Paraplatin</td>
<td>Q11994</td>
<td>Q22004</td>
<td>Q22004</td>
<td>TEVA</td>
<td>TEVA</td>
<td>None</td>
<td>Q32004</td>
</tr>
<tr>
<td>ZALEPLON</td>
<td>Sonata</td>
<td>Q32004</td>
<td>Q22008</td>
<td>Q22008</td>
<td>TEVA</td>
<td>TEVA</td>
<td>Yes-Subsequent</td>
<td>Q32008</td>
</tr>
<tr>
<td>ROPINROLE</td>
<td>Requip</td>
<td>Q32002</td>
<td>Q42007</td>
<td>Q22008</td>
<td>TEVA</td>
<td>TEVA</td>
<td>Yes-Subsequent</td>
<td>Q32008</td>
</tr>
</tbody>
</table>
**IMS Sales Data on Para-IV Molecules**

Our other key data comes from sales of molecules and drug products from IMS. We have some 300000+ molecule-brand-firm-quarter-year sales figures, ranging from 2nd quarter of 1997 to 4th quarter of 2008. Total number of molecules with Para-IV triggered entry was some 106+ out of total 350+ molecules in our dataset. Mean sales in last quarter of 2008 was some $2.18 million in constant 2000 US dollars. Out of our entire molecule level information, some 70+ were first-launch molecules, with average dosages forms per brand being some 2.1. The molecule level information translated to sales in total 196+ ATC4 level markets – which we intend to use to calculate shares of molecule-brand at the quarterly level for each generic or branded firm. ATC or Anatomical Therapeutic Chemical Classification System is used as the standard to classify drug markets. At the 4 digit level, we have information on some 489 ATC markets. Further descriptive statistics on ATC4 markets are outlined in the box in the subsequent page.

**ATC4 MARKET SUMMARY STATISTICS**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Market Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>C10A1</td>
<td>STATINS (HMG-COA RED)</td>
<td>$2.69 bn</td>
</tr>
<tr>
<td>N5A1</td>
<td>ATYPICAL ANTIPSYCHOTICS</td>
<td>$1.78 bn</td>
</tr>
<tr>
<td>N6A4</td>
<td>SSRI ANTIDEPRESSANTS</td>
<td>$1.56 bn</td>
</tr>
<tr>
<td>N3A0</td>
<td>ANTI-EPILEPTICS</td>
<td>$1.48 bn</td>
</tr>
<tr>
<td>B3C0</td>
<td>ERYTHROPOIETIN PRODUCTS</td>
<td>$1.44 bn</td>
</tr>
<tr>
<td>N2A0</td>
<td>NARCOTIC ANALGESICS</td>
<td>$1.11 bn</td>
</tr>
<tr>
<td>C8A0</td>
<td>CALCIUM ANTAGONIST PLAIN</td>
<td>$0.98 bn</td>
</tr>
<tr>
<td>R6A0</td>
<td>ANTIHISTAMINES SYSTEMIC</td>
<td>$0.82 bn</td>
</tr>
<tr>
<td>L4A0</td>
<td>IMMUNOSUPPRESSIVE AGENTS</td>
<td>$0.74 bn</td>
</tr>
</tbody>
</table>

Source: IMS Midas, paragraphfour.com, FDA data

**Initial Price/Revenue Investigation**

In line with our goal of estimating consumer surplus, we identified 9 drug products and conducted some initial investigation on them. We can document (see Figure below) an average revenue erosion of some 40 to 50% for our initial sub-sample of drug-molecules. On an average we also observed some 13 subsequent entrants after the first entrant in this sub-sample of drug products investigated.
The average discount factor offered by the first-generic entrant was some 52% in our sub-sample. We also observed, that the originator firm, increased its prices after generic entry, in line with what the literature has documented earlier (Ellison et.al 1997). One could also in this sub-sample investigation witness a further price drop offered by subsequent generic entrants from the price levels of the first-generic entrant hinting towards increasing of competition once the generic floodgates are opened for a drug product.
PRICES OF ORIGINATORS, FIRST ENTRANT & SUBSEQUENT ENTRANTS, BEFORE AND AFTER ENTRY

Implications & Ongoing Work

Our descriptive statistics are encouraging in the sense that we can observe in our initial investigations substantial revenue erosions of brand name products, with first and subsequent generic entry. Having said that, identifying the first-entrant and subsequent entrant needs to be done with care on a molecule-by-molecule basis for all our 200+ molecules, before we can apply our multinomial nested logit or BLP type estimation techniques and the shares equation to our dataset.

We are however confident that when completed, our research will have several implications. First, the estimation of consumer welfare generated by generic entry and that facilitated by the paragraph IV route should provide clues on the extent of impact by therapeutic areas (within group and outside group substitution), North-South competition and market size of originator molecule etc. This should be of interest to scholars and industry stakeholders. Second, our work should urge an immediate revisiting of the innovation-access debate here in the United States. Results could hint at a necessity to adopt a dynamic exclusivity policy environment or even design exclusivity auctions product-by-product once originator patent expires in branded pharmaceutical products, this especially given pending Congressional resolutions in the area of biologics. Third, a North-South framework would allow us to explore the impact of WTO-TRIPs on firm capabilities of R & D intensive sectors like pharmaceuticals of the New South. This work would also throw light on past research on the economics of R & D in the pharmaceutical industry that documents the role of scale and scope spillovers at the firm-level. We also want to throw light on the fact that certain therapeutic markets are more prone to paragraph-IV facilitated generic entry and this could result in originator firms shifting in and out of sub-markets. We
expect it to further throw up findings that will hint at reasons behind increasing drug discovery costs and shrinking pipelines of Northern incumbent originator firms – this beyond looking at evolving business and drug discovery models in Northern pharmaceutical industries at the technological frontier.

As of now, following is a detailed step by step documentation of our ongoing work. We have identified 300 odd paragraph four cases by drug trade name and therapeutic area, along with other available information on firm-level information, exclusivity and patenting from USFDA and USPTO. We used the above dataset to merge into our IMS data on sales of drugs retrieved through searches at the molecule level, each molecule (and its associated trade name) being the one targeted in a paragraph four challenge. To also reconcile social returns with private returns, we are in the process of merging the above into firm-financial information using COMPUSTAT. We would like to finally complete our data work by merging the entire dataset with firm pipeline information from IMS R & D Focus, NBER Patent Dataset and Recombinant Capital dataset on pharmaceutical firm alliances to use for various firm-molecule-year or quarter level controls in our estimations. Our next step would be to clearly outline our theory and estimate our nested multinomial logit coefficients that will give us a sense of the welfare expression. Robustness checks will be carried out using alternative approaches of product-space approaches, compensating variation, and introducing variation in the analysis.
References


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http://www.cbo.gov/showdoc.cfm?index=655&sequence=0&from=0#anchor


