An Investigation of Alliances Between Western Life-Science Therapeutic and Indian Firms

By: Patrick Brian McGarvey

B.S., Molecular Biophysics and Biochemistry

Yale University, 2001

Submitted to the
MIT Sloan School of Management & Harvard-MIT Division of Health Science and Technology in Partial Fulfillment of the Requirements for the Degree of:

Master of Science in Management & Master of Science in Health Science and Technology

At the

Massachusetts Institute of Technology

September 2008

Signature of the author.....
.....
MIT Sloan School of Management
Harvard - MIT Division of Health Science and Technology

Certified by.....
.....
Fiona Murray, Ph.D., ~~Assistant~~ Associate Professor
Thesis Supervisor, MIT Sloan School of Management

Certified by.....
.....
Martha Gray, Ph.D., Co-Director
Thesis Supervisor, Harvard – MIT Division of Health Science and Technology

Accepted by.....
.....
Martha Gray, Ph.D., Co-Director
Thesis Supervisor, Harvard – MIT Division of Health Science and Technology

Acknowledgements

I would like to thank Frank Douglas, Charles Cooney, Yasheng Huang and Antoinette Schoar for their comments and input during early discussions of the topic of this paper. Fiona Murray for her continued support and guidance through the execution of this paper and Martha Gray for her support and comments. Amanda Jenkins, Adrian Bignami, Jason Robins, and Hampus Hillerstrom for their *esprit de corps* in completing the BEP requirements and the thesis.

Table of Contents

Abstract

Large pharmaceutical companies (Multinational Pharmaceutical Companies or MPCs) have struggled in recent years with the rapidly accelerating costs of drug-discovery research and development. These costs continue to rise while resulting in fewer drug leads. Several industries have realized significant cost savings by outsourcing operations to countries with low-cost labor like India and China. Several factors have traditionally kept MPCs from moving high value, patent-sensitive discovery operations to India despite these drastically lower labor costs. However recent improvements in the Indian patent system in response to WTO compliance have stimulated an increase in both domestic investment in innovative research and in deal making within the life science industry. Nonetheless, there are few systematic analyses of the quantity of deal making between international and domestic Indian firms. Based on our analysis, we conclude that MPCs are establishing alliances at a greater rate than Biotechnology-based firms. In addition, we find that the improvements in patent law have created the structures necessary to stimulate innovation-based life science companies to establish relationships with Indian firms that put their most important types of intellectual property at risk.

Statement of Purpose

While the popular press highlights the opportunities to capture cost-based productivity advantages by performing high-value R&D in India and China, there are few to empirically analyze the quantity and nature of deal activity between multinationals and Indian firms, particularly in the pharmaceutical sector. In filling this gap, this thesis highlight two key questions:

1. What are the defining characteristics of the MPCs that are forming relationships with domestic Indian firms relative to the population of MPCs that we might consider to be "at risk" to establish such relationships?
2. To what degree has deal activity been affected by improvements in intellectual property laws and enforcement?
    a. Have the characteristics of firms engaging in R&D deals in India changed when we compared deals pre and post changes in IP law?
    b. In the same time period, have the types of deals changed and in what ways?

Background

Rationale for Research & Development Partnerships

The R&D challenges of the entire life science sector are well known. With some estimates for new drug development topping out at more than $1BB (DiMasi, 2002), and with the number of FDA approvals for new therapeutics flat to declining, both pharmaceutical and biotech companies face declining productivity. These problems are not limited to the major U.S.-based pharmaceutical firms: European firms including GlaxoSmithKline, AstraZeneca, and Novartis, all face similar challenges. Pharmaceutical companies are not alone in this struggle with larger biotechnology players like Genentech and Amgen also face mounting costs of drug development. Whether these firms can address the shortcomings in their R&D operations will directly affect the future viability of their firms and their industry.

Like many other technology-based fields, the life science sector (specifically in therapeutics) has historically been an area of intense deal making. The discrete nature of these deals has made it an area of study on the nature of contracting, deal structure, capital structure (Lerner & Merges, 1997; Lerner & Tsai, 2000), capital allocation decisions, and as a model for the dynamics of disruptive innovation (Pisano, 1990). There are myriad reasons for firms to enter into strategic alliances. Varadarajan (1995) cited the following motives underlying the entry of firms into strategic alliances: gaining access to new markets; accelerating the pace of entry into new markets; sharing of research and development, manufacturing, and/or marketing costs; broadening the product line/filling product line gaps; and learning new skills. Contracting has many advantages to internal activity including increased flexibility,

improved specialization, and lower overall costs. Drawbacks of contracting include poor alignment of incentives, quality shortcomings, and intellectual property concerns (Balla, et al., 2006).

It is when firms reach beyond their defined organizational boundaries do they enter the realm of contracting theory. The academic literature has many theoretical and empirical analyses on the corporate form and the constraints that determine the boundaries of the firm (Williamson, 1975). Contracting can be described generally as the process by which a firm obtains the capabilities of another firm on a time limited, activity-defined basis for a negotiated exchange of resources (including money, effort, property rights etc.). These analyses make clear that companies work inside a given set of resources, and it is the margin of these constraints that define the corporate form. While some of these resources can be acquired, it is often in the interests of corporate performance to access these assets through the contracting of activities (Teece 1986).

Firms must either acquire or license certain technological capabilities that they cannot invent themselves or that are patented by other firms. It has been found that firm cooperation leads to greater innovations, but innovations don't necessarily lead to cooperation (Shane, et al., 1994). In addition, Rosenkopf and Nerkar (2001) showed that exploration beyond the firm's technological and organizational boundaries leads to the greatest amount of innovation. Given the rigid constraints surrounding the products and processes of the therapeutics industry, even the smallest of life-sciences firms must consider alliances as part of their strategic vision.

As part of their strategy, firms are constantly weighing the benefits of the exploration of new ideas versus the exploitation of previously discovered ideas and the best ways of balancing the need for

efficiency with the need for new ideas. Exploration activities are illustrated with terms like research, innovation, risk-taking, variation, discovery, and search. Exploitation is described as refinement, choice, execution, and implementation (March, 1991). When faced with decisions on capital allocation, the decision can be reduced to a decision to either explore or exploit. Koza and Lewin (1998) further postulate that licensing and joint venturing options either have an exploitive or an explorative intent. A particular firm's history, strategic rationale, and organizational alignment all determine whether the firm will focus on exploration or exploitation in their alliances.

Research and development alliances can generally be considered to be exploratory as the goal is to create new opportunities for exploitation. Aghion and Tirole (1994) concluded that research should only be done in an integrated organization if all three of the following conditions are met:

(1) capital requirements are large and intellectual input is small (which is not the case in life science R&D)

(2) the marketing organization has negotiation power over the research unit subsequent to innovative insight (MPCs are constantly searching for new clinical drug leads)

(3) the marketing organization has large amounts of capita

MPC only meet the third requirement suggesting that therapeutic development should be performed in an organization separate from the marketing organization. The degree to which firms make decisions that correspond to these theory-based conclusions and the reasons for these shortfalls is an area of intense study in the academic literature.

While the Aghion and Tirole conclusions make sense for a generalized, idealized firm, the study failed to account for other effects which can limit the ability of firms to fully separate R&D from the

marketing organization. As firms face the classic make vs. buy decision, they must weigh the costs and benefits of building capabilities and performing the work themselves again the decision to partner to gain access to these capabilities. Pisano (1990) found that in the 1980s, firms were much more likely to internalize R&D capabilities due to the small-numbers bargaining problem, but hypothesized that this would be changing particularly for pharmaceutical companies whose key capabilities and most powerful assets lie in later-stage development, marketing, and sales relationships. Pisano further notes that "firms with a relatively high percentage of their sales in pharmaceuticals did not, historically, develop a higher proportion of their traditional pharmaceutical products through in-house R&D" indicating that at the time of the study, there was a growing need for pharmaceutical companies to initiate alliances to fill out their product portfolios. More recently, however, the need to access products has induced the industry to increase the rate of deal making and R&D collaboration.

In addition to the benefit of aiding in the creation of the organizational form that maximizes resource efficiency, alliances can increase the firm's ability to maximize shareholder value. Empirical evidence indicates that when managers are presented with multiple options for allocation of limited capital, that having more options improves the performance of their allocation decision. Guedj and Scharfstein (2004) show that single-product, publicly traded biotechnology firms have less efficient internal capital markets when compared to multi-product firms in deciding which clinical opportunities to pursue. Single product firms were more likely to pursue projects that ultimately failed while larger, multi-product firms saw improved outcomes from their clinical trials. Therapeutics companies are thus able to enhance shareholder value through increased capital allocation efficiency by entering into multiple R&D partnerships and increasing their number of investment opportunities.

Aghion, Dewatripont, and Rey (2002) show that when parties give away some control rights in their joint agreements, then both firms can increase the value of the collaboration. Specifically, both firms have an incentive to cooperate more fully in the joint effort, which can lead to further cooperation in the future. Thus contracts where both parties have the ability to assign rights subsequent to the initiation of the contracted activities are superior to fully articulated contracts because both parties have the ability to signal through their behavior their desire to continue in their arrangement. Furthermore, in the case of R&D much of the research that is undertaken leads to complex and unpredictable outcomes, thus making so called "complete contracts" more difficult to write.

There is significant theoretical and empirical evidence that pharmaceutical and biotech companies to enter into partnerships for R&D activities and in doing so create benefits for both participating parties. The next challenge is to define the institutional requirements that allow successful, mutually beneficial R&D collaborations. One of the most important institutions is consistent IP regime which includes not only the granting of patent rights over a wide range of ideas relevant to the sector (i.e. both drugs and the processes through which they are made) and a system allowing IP owners to prosecute those that infringe upon their property rights. Within developed economies, particularly in the area of life sciences where IP is strongly upheld through litigation, relatively robustly enforced and precise in its boundaries (relative to other arenas such as semiconductors) these two requirements are met. This creates a rich environment for collaboration between large, established pharmaceutical companies and smaller, innovation-based research and development firms (Gans and Stern 2000).

In their study of American industry, Levin, et al. (1987) found that pharmaceutical industry managers ranked both utility and process patents of higher importance than any other industry in the effectiveness

of patents in enabling the firm to appropriate value from innovations. This is because it is through patents that therapeutics firms realize a return on their R&D investment and resulting innovations. The absence of these protections makes the payouts from these efforts far less lucrative and the business case for the high-cost, high-risk R&D fails. The importance of IP is not limited to Life Science companies and plays a major role in stimulating innovations across many different industries. Arora and Ceccagnoli (2004) showed that the strength of the Intellectual Property regime determined the extent of partnering. They argue that the strength of Intellectual Property protections in developed countries explains the extensive degree of partnering in the life sciences when compared to the semiconductor industries where patent pools and acquisitions have been more common (until the recent developments clarifying modular designs that could be mapped to well identified and protected elements of IP, [Grindley and Teece, 1997].) Aurora and Ceccagnoli further conclude that the IP regime determines the limits of the firm thereby encouraging companies to enter into alliances to increase their access to new technology.

While it has been argued that India has the industrial capacity to perform IP-generating research through its strong installed capabilities in chemical manufacturing, medicinal chemistry, and engineering (Pore, Pu, Perekell, and Cooney, 2007) prior to the implementation of the WTO agreements MPCs shied away from collaborations with Indian-based research organizations (be they pharmaceutical or biotechnology firms, or contract research organizations). One of the main reasons typically given for this decision was that from 1970 until 1995 the Indian patent system did not recognize many of the patents that enabled Western companies to see such dramatic results from their R&D operations. The genesis of those circumstances is of historical importance and also informs the environment under which the recent changes are being implemented.

IP laws have a very strong influence on the structure of the industries operating under those regimes. Arora, Branstetter, and Chatterjee showed in their 2005 paper that with the changes in Indian Intellectual Property laws (outlined below), that private returns to the firms continue to rise, and those Indian firms that cross-file patents in the U.S. are appropriating higher returns from those patents than they did prior to strong IP laws. They further explore the South Korean IP regime that underwent similar changes to India's in the mid-1980s. They conclude that when stronger IP laws are implemented, firms that increase R&D investment and file for US patents see nonlinear increases in private returns, while firms that do not increase their investment in innovative activities do not realized these gains.

A (Brief) History of the Indian Patent Regime

India has experienced a dynamic patent regime through its history beginning with its colonization by the British Empire in the second half of the 19th century. In 1856 the first patent protection was passed into law thereby granting "exclusive privileges" to inventors for a period of 14 years. The Indian Patents and Design Act of 1911 replaced the 1856 statute and continued the Western-style protections. The 1911 act came under examination many times subsequent to India's secession from the British Empire in 1947, culminating in the Patent Act of 1970 that limited an invention to the "manufacture" of novel products. Section 2(1)j of the act defined an invention to be:

> "any new and useful—
>
> (i) art, process, method or manner of manufacture;
>
> (ii) machine, apparatus or other article;
>
> (iii) substance produced by manufacture." (Basheer, 2005)

This definition limited patents only to those processes culminating in either an article or substance. This clearly differs from the Western patent laws that allow patents on the "use" of novel substances, and the 1970 Act opened the door for domestic firms to engineer around U.S.-based method patents on the

manufacture of pharmaceutical products. Subsequent to passage of the 1970 law, most of the MPCs that had established operations in India either shuttered their operations or sold them to domestic firms.

With their inclusion in the establishment of the WTO in 1995, India was required to bring their Intellectual Property laws in to alignment with the Agreement on Trade-Related Aspects of Intellectual Property (TRIPS) under their characterization as a developing country. Failure to implement TRIPS compliant IP laws would result in trade penalties and aid losses inducing the Indian parliament to begin amending their statutes. The basic tenets of TRIPS include:

(a) Patent protection of 20 years from filing

(b) Protection be available in nearly all technology fields

(c) Rejection of patents due to moral questions is not allowed (Yalamanchili, 2007)

As a developing country, India was given 10 years to bring their Patent system into compliance with TRIPS. Beginning in 1999 (following an audit by the WTO in 1998), India passed an amendment that allowed applicants to establish a filing date for their patents, which allowed patents to be filed, but the review of these patents would be suspended until 2005 when the patent law would be TRIPS compliant.

An update passed in 2002 updated the definition of a patent to include "a new product or process involving an inventive step and capable of industrial application." Also added was a new definition of an "inventive step," which was defined to be "a feature that makes the invention not obvious to a person skilled in the art," (Yalamanchili, 2007). Several other changes were made in the 2002 Amendment to improve the process of prosecuting patent infringements, but these changes did not bring Indian law into full compliance with TRIPS.

In 2005, a final set of amendments was introduced that were intended to bring Indian code in line with the TRIPS standards. These included eliminating specific exceptions for pharmaceutical and medicinal product manufacturing patents, further expanding the definition of an inventive step, and further improvements on the assignment and ownership of patents once they had been filed (Yalamanchili, 2007).

The intent of the 2005 Amendment was to bring Indian fully in line with TRIPS, but specific details surrounding the definition of an "inventive step" remain ambiguous and will continue to be points of discussion between India and the WTO as to whether their IP regime is fully compliant with the TRIPS provisions. The reluctant transition of India's patent regime from 1995 to 2005 represents a unique opportunity to examine the role that these institutions play in Western company's appetite for entering India's market with their Research and Development operations.

India & the Life Science Industry

The Indian economy has grown at a torrid pace recently realizing real annual GDP growth of 8.9% from 2003-2007 and emerging internationally competitive information technology, pharmaceutical manufacturing, and business services industries. As western pharmaceutical companies have seen increasing R&D costs and the lower cost opportunities presented by Indian companies, multinationals have increased their interest in the region. Kumar (1996) noted that US firms prefer to locate their R&D activities in locations where there are large markets, technological resources, and infrastructure to support their activities. Given the large market and the well-established technology sector in India, MPCs are interested in India today primarily because they can realize significant R&D savings, smooth capacity bottlenecks in their internal operations, improve their access to human capital, and increase access to the Indian Pharmaceuticals market (Pore, et al 2007). Despite these opportunities, life science

firms have been timid relative to their compatriots in software, information technology, and business services in their pursuit of partners in India. The most commonly cited reasons for their reticence have included:

- Failure of Indian law to recognize Utility patents
- Restrictive investment laws limiting capital flows
- Limited infrastructure development constricting operational capabilities
- Convoluted role of property rights within the judicial system
- Laws limiting involvement of university faculty in independent enterprise

During the past decade, the Indian government has moved to address several of these shortcomings including bringing IP laws into TRIPS compliance, increasing the liberalization of the capital controls, and passing amendments that now allow for university faculty to work with private companies while maintaining their university affiliation. While these changes have increased the likelihood of involvement by the MPCs and other participants in the life-science industry, the changes have forced the domestic Indian pharmaceutical industry to also change. Rather than manufacturing and marketing Western-developed pharmaceutical products and selling them domestically and throughout the third-world or focusing on the generics businesses, Indian companies are increasingly realizing that they must develop in-house proprietary Research & Development operations and are evolving into innovation-based firms. This transition has been aided by the alliances that they have made with MPCs to improve access and learn the regulatory and marketing strategies utilized by the established pharmaceutical companies.

Current Approaches

Frew, et al (2007) attempted to outline the current state of domestic biotechnology focused firms through an interview-based study. Their study identified 22 innovation-based firms and conducted structured interviews with their senior management in an attempt to define the characteristics of those companies. Based on their interviews, they proffered suggestions as to what changes must be made in the Indian corporate structure in order to foster more entrepreneurship in Indian biotechnology companies. They conclude that the Indian Innovative Life-Sciences industry remains under developed due to lack of investment and managerial talent, but believe that the industry will continue to develop at an impressive pace.

Frew, et al., also inquired about the alliance activity of the 22 firms under study and were able to uncover several deals that remain out of the scope of this current study due to a lack of public disclosure. This lack of public announcement will continue to hinder the domestic firms as credibility for biotechnology firms is often established through their alliances. A lack of alliance is often interpreted as a lack of credibility and the link between valuations and public disclosures of alliances shows that the public markets recognize the value of these alliances in validating a company's capabilities.

The Boston Consulting Group (Bhala, et al, 2006) recommended that MPCs take a strategic approach to outsourcing their R&D to India and China focusing the work on the comparative advantage of each country in specific activities. The group concluded that India offers the quicker and more permanent payoff because of the service focus of the domestic Indian groups as well as the improved IP infrastructure. They further examine the capabilities of the country that have been developed through domestic competencies and training facilities and note that India has an established base in basic chemistry, data management, clinical trials, and emerging strengths in end-to-end chemistry and

preclinical studies. Their conclusion is that selective alliances will allow MPCs to leverage the opportunities in India.

When establishing a presence in India, companies can pursue four strategies: buying or building a wholly owned corporate enterprise, creating Joint Ventures to fulfill established goals, partnering through alliances, and contracting with local firms on a fee-for-service basis. Our analysis is particularly focused on the alliance building as it provides the greatest leverage for a life-sciences firm pursuing opportunities in India. As outlined above, partnering provides operational flexibility should the partner not meet expectations, allows the firm to establish a presence in the country without over-committing, gives the firm the opportunity to learn about local economics, methods of interaction, and business practice without exposing themselves to exploitation, gives the firm access to the capabilities that they seek at the economics they desire, and finally gives the firm a better understanding of the domestic landscape to inform future decision-making about the region.

Question 1: What are the defining characteristics of the MPCs that are forming relationships with domestic Indian firms?

Generalizations have been made about the types of organizations that are currently engaged with Indian firms, but no attempt has been made to fully categorize the types of MPCs that are entering into agreements. This analysis attempts to sample sufficient deals to allow for better understanding of the characteristics (Size, Financing, and Focus) of the Western firms that are engaging with Indian firms. It is also important to know the distribution of the deal making and whether the deal activity has been

spread across several different firms or whether it has been isolated to a few Western and Indian firms. This analysis will seek to shed light on those questions.

Question 2: How has deal activity been affected by TRIPS compliance?

There is evidence that TRIPS compliance has stimulated internal investment for domestic firms and that this has resulted in outsized returns for investors in these enterprises (Arora, Branstetter, and Chatterjee, 2005), but the degree to which TRIPS compliance has stimulated Western firms to engage more extensively with Indian firms has not been robustly characterized. TRIPS compliance has been fully in effect for three calendar years and there is sufficient data to allow for high-level characterizations of how the changes in Intellectual Property laws have influenced the overall level of deal activity. This analysis also provides the opportunity to examine whether the types of deals have changed as a result of the patent law modifications. From a macroeconomic perspective, the goal of TRIPS compliance is to stimulate global trade; the end being for India to take on more value-add goods production and service opportunities. The extensive amount of deal making that occurs in the Life Sciences industry makes it an ideal industry to study the effects that Intellectual Property reform can have on an industry. An analysis of the deal types should provide insight into whether this effect can be seen in India subsequent to its acceptance of WTO patenting and intellectual property standards.

Question 2a: Have the characteristics of the firms entering deals changed before and after TRIPS compliance?

In addition to investigating the overall level of deal activity, this analysis presents the opportunity to systematically describe the types of companies that are doing deals with Indian firms. Broad brushed attempts have been made in the past to characterize the nature of the firms, but these are generally based on anecdotal evidence rather than detailed analysis of the life science space. This analysis should inform whether TRIPS compliance is sufficient to stimulate innovative, cutting-edge life science firms to enter the Indian market, or whether more needs to be done by governments to stimulate deal activity.

Prior to the WTO agreement in 1995, MPCs would frequently enter into collaborations with domestic Indian firms primarily to facilitate entry into the market and secondarily as a step toward a better understanding of the domestic pharmaceutical market; these firms were rarely entering alliances for the true cost or capability advantages. The alliance would be consummated as a tradeoff in exchange for the opportunity to enter the domestic market. For example, emerging economy governments would often require an investment in capabilities prior to granting licenses to operate in the domestic economy, and these alliances were the result of these requirements. Subsequent to WTO compliance, an outstanding question is whether the types of firms entering alliances have changed and the implications on future deal activity.

Question 2b: Have the types of deals changed and in what ways?

In addition to affecting the types of firms that create alliances with domestic firms, TRIPS compliance would also have an affect on the types of deals that the firms enter. If India's goal is to increase the degree of innovative research and development work that is done inside the country, then it is even more important that the firms enter into greater collaborations where the domestic Indian firms gain the

knowledge and experience generating new ideas and patentable discoveries. Whether modifications in the IP laws to comply with TRIPS standards have stimulated these kinds of deals is examined.

Methods

The data for this analysis was culled the Recombinant Capital database (ReCap.com), a database that collects Alliance Information from various sources including SEC filings, company press releases, and news reports. Data on the deals with Indian companies was identified via two methods:

1. A search of Alliances listing "India" in the Alliance name
2. A search of the Press Releases in the Alliance database for the term "India".

In total close to 1000 alliances were culled from the database, but search 1 returned too narrow of a search (many relevant deals were missed) and Search 2 cast too wide of a net (many irrelevant deals were included). Consequently, Search 2 results were scanned for relevance to deals between MPCs and Indian firms. Both search results were further filtered to eliminate redundant deals and then merged into a single dataset. In total the dataset comprised 255 deals. Every company that appears in the data was researched to identify its defining characteristics for Size, Ownership, Focus, and Geography. Table 12 lists the categories into which each company was slotted.

To identify a firm as Multinational or Indian, a firm was identified as domestic Indian if the most senior parent was incorporated in India. Similarly, multinationals were identified as such if their largest shareholding parent company was registered in Western Europe, the United States, or Japan. Therefore, a deal between a wholly owned Indian subsidiary and a domestic Indian firm would be included, but a deal between a wholly owned foreign subsidiary of an Indian firm and a domestic Indian firm would not be included.

After the parties to each deal were characterized, each individual deal was categorized as to the intent of the MPC in their intent at initiation of the alliance to be exploring new ideas or exploiting old realities. This was based on the methodology of Rothaermel and Deeds (2004) in their characterization of biotechnology research initiatives. If the alliance was related to the development of the therapeutic product prior to an IND filing, then the alliance was classified as exploratory. If the alliance focused on manufacturing, distribution, or Phase I clinical trials or later, the alliance was classified as exploitive. For generics firms, so long as the product did not have an ANDA filed on the product, it was assumed that the purpose was explorative for that type of firms. Otherwise the alliance was considered to have the exploitive intent. To analyze the effect of the passing of the patent reforms in 2005, the deals were also grouped into pre-TRIPS deals (1994-2005) and post-TRIPS (2006-07). Deals undertaken in 2005 were included in the pre-TRIPS assessment because the types of deals that are under investigation take several months or even years to initiate, negotiate and finalize and the final TRIPS compliant legislation was not signed into law until April 2005 (Patent Act of 2005). This was four months after the target date set by the parliament and the law included last minute modifications contributing to significant uncertainty about what the new patent laws would actually look like (TRIPS compliance was mandated by January 1st, 2005).

The analysis comparing contract types prior to and after TRIPS compliance used the ReCap annotation of the deal type. The assumption made was that Joint Ventures and Collaborations are fundamentally different than Licenses. A license generally means a transfer of assets, while collaborations and joint ventures require active management by the participating firms. T-tests and Chi-square test were performed on the data to determine whether TRIPS had induced a statistically significant change in the

types of deals that were being initiated with Indian companies. The null hypothesis for these tests was that the proportion of deals having exploratory intent was the same before and after TRIPS, and that the proportion of deals that were licenses would be unchanged.

Limitations

This data is the result of a scan of a single database and all conclusions that result from it will have the same biases as the biases of the curators of the ReCap database. This would be a bias against identifying deals that are:

1. Not publicly disclosed for confidentiality reasons
2. Originate between small, relatively unknown firms
3. Have not sufficiently documented the nature of their agreements to assess their validity

A further limitation is the amount of information that can be determined from the public releases about the deals. While certain key words reveal significant information about the types of activities and structures, a limitation is the assumption that the interested parties are using a common language.

Results

The Dataset

The data was collected on October 1st, 2007, with and reviewed on January 5th, 2008 to fill in additional 2007 deals. The dataset likely under-represents the deals consummated in 2007 due to the lagging effects of database curation, and thus the results from 2007 are unlikely to be comprehensive. Nevertheless, the data under analysis contains the deal landscape beginning from 16-Feb-1994 through 27-Nov-2007. In all 255 alliances are represented with 75 Indian companies and 180 western companies.

Question 1: What are the defining characteristics of the MPCs that are forming relationships with domestic Indian firms?

The first step was to understand the characteristics of the firms forming alliances with India. The characteristics of the companies considered in the study are their size and focus. Table 1 shows the focus of the companies undertaking alliances with Indian companies and sheds some light on their relative deal activity.

Table 1: The number of deals having a western firm with a given focus, the number of firms having that focus that have participated in the deals, and an average of the number of deals that each firm has undertaken.

Focus of Western Firm	Total Deals	Total Firms	Mean Deals per Firm	Median Deals per Firm [Range]
Pharmaceuticals	86	56	1.536	1 [1-7]
Generics	57	35	1.629	1 [1-13]
Biotech	53	32	1.656	1 [1-11]
Lab Tools	25	24	1.042	1 [1-2]
Contract Research Organization (CRO)	16	14	1.143	1 [1-2]
Devices	11	9	1.222	1 [1-3]
Contract Manufacturing Organization (CMO)	7	7	1.000	1 [1-1]
Total	255	177	1.441	1 [1-13]

Pharmaceutical, generics and biotechnology firms are the companies demonstrating the most activity in the region. This is not surprising given the amount of capital that these companies have at their disposal, the cost pressures that they face in research and development, and the global reach of their operations. Given the manufacturing cost efficiencies that are possible for generics manufacturers, it is not surprising that they have been very active in their partnering with India. As Western generics companies fully exploit the cost efficiencies offered by Indian firms, whether the rate of deal making continues or not will need to be revisited. The past few years has seen significant increases in outward acquisitions by

Indian majors in their pursuit of global generics opportunities that allow them to expand their operations and increase their market presence in developed economies. In addition, several of the India-based majors like Ranbaxy are funding their innovation-based research and development with cash they earn through their generics divisions. The effect this will have on Western generics propensity to do deals with Indian companies remains to be seen, but it is likely that there aren't many opportunities remaining for pure supply arrangements given the economies of scale needed to fully realize the cost arbitrage when transportation of the finished goods is included in the realization of the savings.

The number of deals per company is also noteworthy as it further illuminates that a given generics company is entering more deals than is either a single pharmaceutical or biotechnology company, but the difference in the rates remains small.

The sizes of the multinational firms that are entering into alliances with Indian firms are shown in Table 2. Small firms (those with fewer than 1,000 employees) represent the bulk of the firms that are engaging with Indian firms, with Large (greater than 10,000 employees) firms followed by Medium sized groups.

Table 2: The number of deals having a western party with a given size, the number of firms having that size that have participated in the deals, and an average of the number of deals that each firm has undertaken.

Western Firm Size	Total Deals	Total Firms	Mean Deals per Firm	Median Deals per Firm [Range]
Large	74	35	2.114	1 [1-11]
Medium	58	37	1.568	1 [1-13]
Small	74	56	1.321	1 [1-4]
Total	255	177	1.441	1 [1-13]

Most interestingly, the large firms have a higher number of deals per firm, with smaller firms having only about one deal per firm. Small western firms represent over half of the firms that have done a deal with an Indian firm. The large number of deals for Large parties is ever more significant given that there are fewer firms falling into the Large subgroup in the Indian market.

While the majority of the deals in Multinational firms were by the pharmaceutical firms, the Indian firms were not led by the pharmaceutical sector. Table 3 lists the primary focus of the Indian firms that are entering into alliances with international firms.

Table 3: The number of deals having a Indian party with a given focus, the number of parties having that focus that have participated in the deals, and an average of the number of deals that each party has undertaken.

Focus of Indian Firm	Total Deals	Total Firms	Mean Deals per Firm	Median Deals per Firm [Range]
Generics	73	19	3.842	2 [1-31]
Pharmaceuticals	65	15	4.333	2 [1-16]
Contract Research Organization (CRO)	40	12	3.333	1 [1-21]
Contract Manufacturing Organization (CMO)	28	15	1.867	1 [1-7]
Biotech	25	8	3.125	2.5 [1-11]
Lab Tools	21	4	5.250	2.5 [1-15]
Devices	3	3	1.000	1 [1-1]
Total	255	76	3.355	1 [1-31]

Most striking is the large difference in the rates of deal participation between Indian and multinational firms. The rate is consistently twice and three times that of the multinationals entering into alliances. One reason this might be is that once a firm has entered into a single alliance, then it has the credibility and it is much easier for it to attract the interest of other multinationals. Additionally, there are fewer

globally focused firms inside of India, and it is likely that these firms attract the attention of multinationals with their more sophisticated operations, management, and scientific acumen.

Not surprisingly there are geographic differences between the sizes of the firms that participate in the deals. Table 4 lists the sizes of the Indian firms that have entered into alliances.

Table 4: The number of deals having a Indian Party with a given size, the number of parties having that size that have participated in the deals, and an average of the number of deals that each party has undertaken.

Size of Indian Firms	Total Deals	Total Firms	Mean Deals per Firm	Median Deals per Firm [Range]
Large	54	7	7.714	4 [1-31]
Medium	143	38	3.763	2 [1-21]
Small	58	31	1.871	1 [1-15]
Total	255	76	3.355	1 [1-31]

The number of deals undertaken by medium size firms is most likely due to the smaller size of most of the Indian firms. Their lack of a global presence, innovation-based Research & Development, and capital-intensity of the their industrial base, limits the size of the companies in India. In addition, many of these firms are using alliances to expand their market presence (in the domestic market as well as in the global market). Also of note is the intensity with which the large firms are partnering. Much of this is driven by Ranbaxy's 31 deals (details in Table 6), which leave 23 deals for the other 6 firms putting the large firm's deal intensity in line with the Medium firms (3.40 deals/firm).

After establishing the characteristics of the firms entering the alliances, the next step was to examine the most active firms from both groups, as to their size and focus. Table 5 shows the most active MPCs

participating in alliances with India, which contain some, but not all of the largest pharmaceutical majors.

Table 5: The most active Western companies in deal making with India [Note that Gilead's 11 deals were initiated under the threat of the Indian courts of nullifying their patents].

Western Party Name	Number of Deals with Indian Firms	Size	Primary Product Focus
Akorn	13	Medium	Biotech
Gilead	11	Large	Biotech
GlaxoSmithKline	7	Large	Pharma
Lilly	6	Large	Pharma
Bristol-Myers Squibb	4	Large	Pharma
Codexis	4	Small	Biotech
Pfizer	4	Large	Pharma
Mallinckrodt	3	Large	Devices
Mayne Pharma	3	Medium	Generics
Novartis	3	Large	Pharma
Par Pharmaceutical	3	Small	Generics
Taro Pharmaceuticals	3	Medium	Generics
Watson Pharmaceuticals	3	Large	Generics

Most noteworthy among the firms that are most active is the Akorn group whose strategy appears to be to source all of their products in India and use their U.S. base for regulatory and marketing activities only. Gilead's presence is only to protect its market position of its HIV drug Viread (tenofovir disoproxil fumarate) and would most likely not otherwise have participated in the joint agreement with its 11 Indian licensees. The alliances of these 13 companies represent 26.3% of the total deals while 54.9% of deals are with single-deal firms.

The landscape for Indian firms is much denser as shown in Table 6.

Table 6: The most active Indian companies in deal making

Indian Party	Number of	Size	Primary

	Deals with Western Firms		Product Focus
Ranbaxy Laboratories	31	Large	Pharma
Jubilant Biosys	21	Medium	CRO
Nicholas Piramal	16	Medium	Pharma
Dr. Reddy's Laboratories	15	Medium	Pharma
Strand Genomics	15	Small	Lab Tools
Biocon Ltd.	11	Medium	Biotech
Serum Institute of India	8	Large	Pharma
Glenmark Pharmaceuticals	7	Large	Pharma
Strides Arcolab	7	Medium	CMO
Zydus Cadila	7	Medium	Generics
Matrix Laboratories	6	Medium	Generics
Orchid Chemicals & Pharmaceuticals	6	Medium	Generics

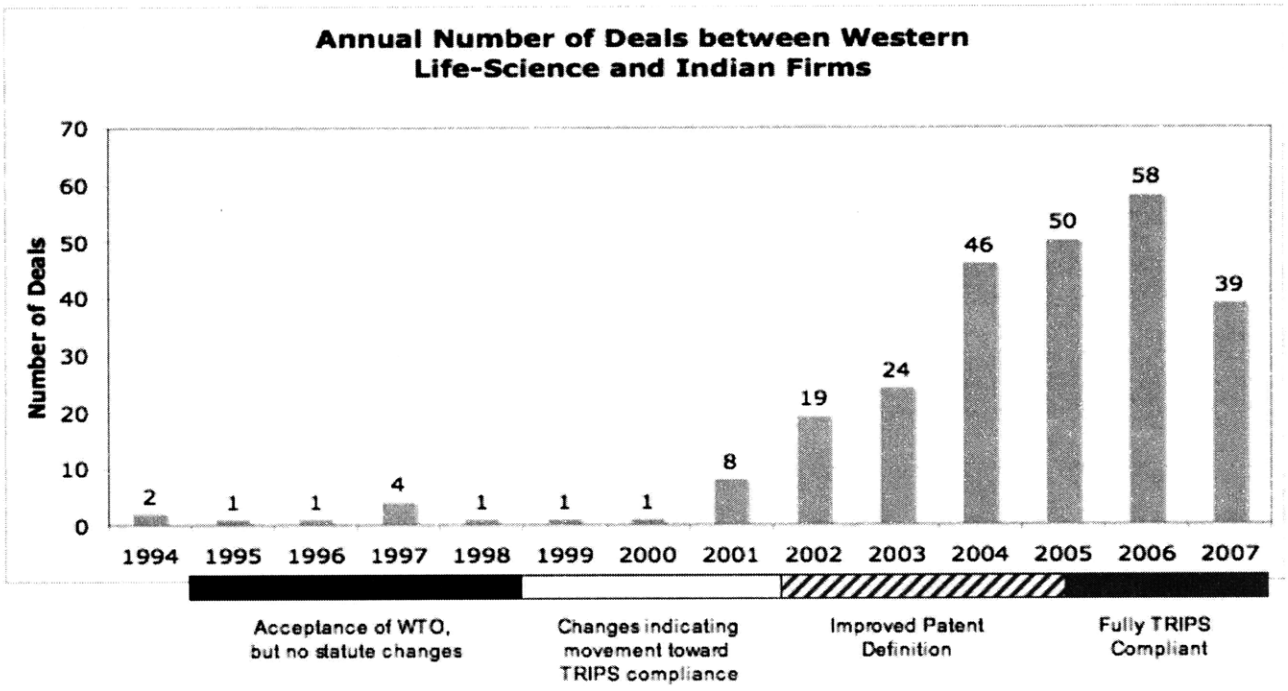
The most active firms in the partnering space are also some of the most global of Indian firms—the same firms that made the Indian Pharmaceutical Industry a global leader in generic drug production. The 12 firms listed in Table 6 represent 58.9% of the partnering deals while 15.9% of the deals were with Indian partners having only a single deal.

Question 2: How has deal activity been affected by TRIPS compliance?

Deal activity between multinationals and Indian firms has closely tracked India's acceptance and implementation of the WTO agreement. Figure 1 shows the deal activity for the dataset beginning in 1994 through the first half of 2007 with the major patent law changes superimposed under the year. The rate of activity has clearly increased with the number of deals tripling from 2001 to 2003, and then nearly doubling again from 2003 to 2004.

Figure 1: Number of deals between Multinationals and Indian firms with major modifications in the patent laws to comply with WTO and TRIPS guidelines highlighted

(n=255)



Given the extremely high rate of deal activity in the life science space, these deals represents a small fraction of the overall worldwide activity, but clearly life science companies have recognized the opportunity in India and have reacted to by increasing their deal consummation in the region. There are many drivers of deal growth beyond the effects of increased knowledge about India in the west. These effects include India's torrid GDP growth, increased deal making across all industries, increasing numbers of alliances in the life sciences, and the large cash reserves of MPCs increasing their ability to finance alliances. What the data makes clear is that as the Indian Parliament has updated the patent laws, there is a mechanistic increase in the number of alliances that are taking place between domestic Indian firms and foreign life science companies.

As Figure 1 shows, the level of activity was relatively flat through 2000. For the six years subsequent to the signing of the WTO agreement and the verbal commitments the Indian government made to comply

with the TRIPS accords, deal activity remained almost non-existent. Until the Indian parliament began enacting reforms in statutes which included substantive improvement in the definition of an innovation in 2002 that deal activity was quantitatively affected. This data demonstrates the importance of legal implementation versus paying lip service to changing IP laws, and the rewards that can be reaped on account of these material changes.

Question 2a: Have the characteristics of the firms entering deals changed before and after TRIPS compliance?

TRIPS clearly had an upward effect on the general level of activity in the licensing space in India, and the next question to answer is whether the changes in IP law had an effect on the types of firms that went to India to find a partner. Figure 2 follows Figure 1 but breaks down the deal activity by the focus of the multinational firm.

Figure 2: Deal activity by Multinational focus 1994-2007 (n=255)

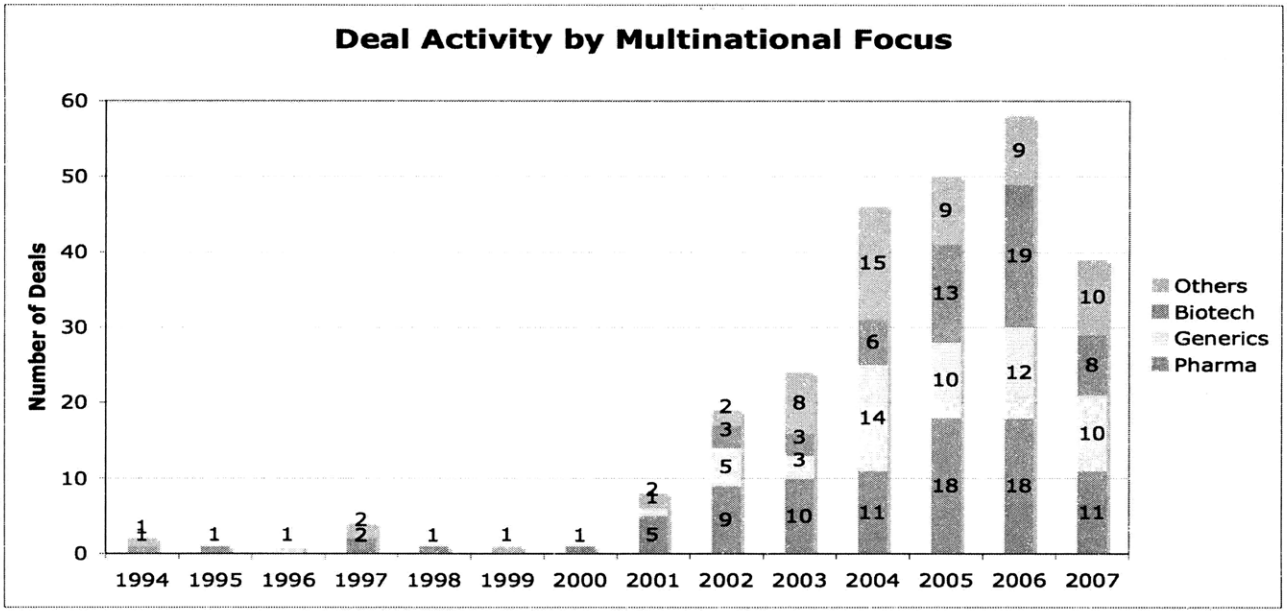


Figure 2 shows that pharmaceutical companies led the wave of alliance making into India and its rate of deal making grew until 2005 and has held relatively stable since then. In 2001, pharmaceutical companies made 62.5% of the deals with India, and in 2007, those companies participated in only 27.5% of the deals. Biotechnology firms on the other hand have steadily increased their proportion of the consummated deals, while generics have maintained their proportion of the total deals at 20-25% of the total alliances since 2004. TRIPS compliance stimulated an increased in the absolute number of alliances by multinationals in the country while decreasing the relative role played by pharmaceutical companies.

Question 2b: Have the types of deals changed and in what ways?

Alliances entered by companies are motivated either for learning more about a specific question, or about capitalizing on the lessons of earlier explorations. In their study of biotechnology research initiatives, Rothaermel and Deeds (2004)—which included firms forming alliances from 1973 to 1997—

showed that 42% of their alliances were exploratory with the balance being exploitative. Of the deals entered by multi-national pharmaceutical and biotechnology firms with Indian partners, 25.7% were exploratory in nature from 1994 through 2007. Pharmaceutical companies had 29% that were exploratory and 20.4% of the biotechnology company alliances were of an exploratory nature. Given that the current sample pulls from both pre and post-TRIPS time periods it is not surprising that there are fewer exploratory alliances as compared to the Rothaermel and Deeds work. Biotechnology firms are underrepresented in the sample because of the high transaction costs associated with entering into alliances with India, and it is unsurprising that biotechnology firms have a lower proportion of exploratory deals also due to the risks and transaction costs associated with entering alliances in an unfamiliar IP regime. As shown in Figure 2, Generics companies make up the third most active group in India. Alliances formed by generics companies were characterized into exploratory or exploitive based on whether the product constituting the focus of the deal has been developed or not. In other words, if the alliance is a transfer of a production methodology, then it is exploitive; otherwise it is exploratory as the production development constitutes the area of exploration for the firms in the alliance.

The strengthened IP regime the Indian parliament approved in 2005 was initiated to stimulate domestic research and development as well as international cooperation with domestic firms. Table 7 shows the effect that TRIPS compliant IP laws have had on pharmaceutical, biotechnology, and generics firms on the types of deals they entered with domestic Indian firms. Theses strengthened IP laws stimulated pharmaceutical firms to initiate alliances focused on products prior to the IND stage at a statistically significant level. The proportion of exploratory biotechnology deals decreased after TRIPS compliance at a significant level and this remains unexplained, although it was insignificant using the Chi-square

test. Generic companies, on the other hand, have not seen a significant change in the types of deals they pursue in India.

Table 7: Number of deals where the primary focus of the alliance is exploitation vs. exploration before and after TRIPS compliance

	Pharmaceutical Companies		Biotech Companies		Generics Companies	
	1996-2005	***2006-2007***	***1996-2005***	***2006-2007***	***1996-2005***	***2006-2007***
Number of Exploit alliances (Ratio)	46 (.81)	18 (.67)	24 (.89)	15 (.52)	20 (.59)	14 (.64)
Number of Explore alliances (Ratio)	11 (.19)	9 (.33)	3 (.11)	14 (.48)	14 (.41)	8 (.136)
	57	27	27	29	34	22
P-Value	0.00257**		0.02477*		0.641	
Chi-Squared	0.0051*		0.0495*		0.130	
	**Significant at p<0.005 level		*Significant at p<0.05 level			

To further illustrate the effect that TRIPS compliance has had on deal making, one need only look at Eli Lilly's six alliances with Indian firms. Eli Lilly has earned the industry's respect by consistently pursuing novel licensing and collaboration agreements across function, geographies, and partner types. This has solidified their reputation as a standard-setting licensing firm (Windhover, May 2008). Although Lilly is aggressive with their efforts, the data in Table 8 shows that they are careful to structure their deals to be supported by legal institutions. Prior to TRIPS compliance, Lilly was engaging only in supply agreements to exploit the cost advantages of Indian manufacturing and marketing agreements to increase the market access of Lilly's drugs in the Indian market. These first forays into the region came subsequent to legislative activity indicating IP protections were emerging after the 2002 acts. Subsequent to 2005, however, Lilly immediately initiated the drug discovery alliance with Jubilant Organosys which covered many activities that are explorative in nature. They continued to push the

envelope and initiated two additional drug discovery deals with Suven Life Sciences and Nicholas Piramal. Drug discovery alliances put the greatest amount of Intellectual Property at risk, require the highest levels of collaboration, and are the areas that are most fraught with IP enforcement risk. The deal with Nicholas Piramal has an extended horizon, includes the transfer of considerable risk, and contains many long-term provisions for remuneration of the Indian firm for their investment of resources.

Table 8: Eli Lilly deals with India: The effect of strengthened IP protection

Deal Date	Indian Partner	Nature of relationship	Deal Details
June, 2003	Shasun Chemicals & Drugs	Supply Contract	Suppliy agreement for Cycloserine for Multidrug-Resistant TB. Shasun to provide bulk API to Eli Lilly while Lilly is making available the necessary manufacturing know-how, providing financial assistance for the purchase of equipment and/or conversion of manufacturing facilities and technical training for various steps in manufacturing processes (Lilly)
July, 2004	Nicholas Piramal	License	A license to market and sell injectable cardiac stimulant, Dobutrex (Dobutamine) brand in India. Dobutrex is an off-patent branded generic product.
January, 2005	Elder Pharmaceuticals	License	A license to market and sell Tobraneg (Tobramycin) injectionable antibiotic in India. Price: 1.25x of sales.
January, 2006	Jubilant Organosys	Collaboration	5-year drug discovery services agreement for three drug programs in the initial stages of drug discovery.
August, 2006	Suven Life Sciences	Collaboration	GPCR drug discovery for CNS targets. Suven will perform pre-clinical research in exchange for research funding and future development milestone payments.
January, 2007	Nicholas Piramal	Collaboration	Drug Development Agreement. NPIL responsible for all pre-clinical and clinical payments while Lilly retains a call-back option on the transferred metabolic disorders drug. Contract included provision to work on four additional drugs.

Looking at alliances from another perspective is to examine how an Indian firm's deals have evolved over the course of the changes in IP laws. Nicholas Piramal has focused on a strategy of developing novel, patent-protected therapeutics based on the Western model since it's inception. As Table 12 shows, despite having Intellectual Property form the basis of its strategy was insufficient to attract MPCs as collaborative research partners in the absence of a strong IP regime. Subsequent to TRIPS compliance, however, Nicholas Piramal has now entered into five collaborative agreements where significant IP generation is possible. In the absence of IP-strengthening laws, these alliances would not have been consummated. The company is also entering into alliances with a diversity of company

characteristics from large pharmaceutical groups like Eli Lilly and Merck, but also with biotechnology companies like Biogen and BioSyntech. Companies such as Nicholas Piramal will continue to learn about the drug discovery process and stimulate the domestic Indian firms toward more innovative world-class work.

Table 9: Nicholas Piramal deals with MPCs: The effect of strengthened IP protection

Deal Date	MPC Partner	Nature of relationship	Deal Details
November, 2002	Biogen Idec	License	Marketing and distribution agreement for multiple sclerosis drug Avonex in Nepal & India.
January, 2003	Minrad	License	Marketing and distribution agreement for generic products inhaled anesthetics Isoflurane, Enflurane, Sevoflurane in 11 emerging markets.
December, 2003	Advanced Medical Optics	License	Contract Manufacturing for Neutralizing Tablets, Fill form & Seal Solution Products
July, 2004	Lilly	License	A license to market and sell injectable cardiac stimulant, Dobutrex (Dobutamine) brand in India. Dobutrex is an off-patent branded generic product.
August, 2004	Genzyme	License	5-year marketing and distribution of osteoarthritic Synvisc Viscose in India.
August, 2004	Ethypharm	License	Technology transfer agreement for the manufacture of pain reliever Paracetamol Flash Tablets. Raw material will be sourced from Ethypharm, and NPIL will manufacture and sell finished product in Indian market under it's own name.
December, 2004	Rhodia	Asset Purchase	NPIL acquired the global inhalation anaesthetic business for $14M. Rhodia will continue to manufacture products for 2 years, and NPIL owns the global sales and marketing rights.
July, 2005	BioSyntech	Equity	Exclusive rights for current and future products of Biosyntech, exclusive rights for marketing, sales and distribution of current and future products of BioSyntech for India, Pakistan, Sri Lanka, Bangladesh, Laos, Cambodia, Vietnam and the Philippines in exchange for equity private placement.
October, 2005	AstraZeneca	Collaboration	Drug Discovery Development & Collaboration the Companies will establish a framework for future collaboration for development of processes for the manufacture of intermediates, active ingredients or bulk drugs for supply to AstraZeneca. The Development and Know-how Agreement does not have a fixed tenure
October, 2005	Avecia	Acquisition	Acquisition of Avecia for $19M. The acquisition gives NPIL access to Avecia's customer-list and new technologies used in the synthesis of products
December, 2005	Pfizer Animal Health	License	7-year manufacturing supply agreement for process development and scale-up services.
June, 2006	Pfizer	Asset Purchase	Acq. of Pfizer's UK manufacturing facility. Plan to use the European assets to manufacture niche high-value drugs, while keeping lower cost manufacturing in India.
November, 2006	Biosyntech	Collaboration	Phase II clinical development plan for BST-InPod for chronic foot pain to generate clinical data at a lower cost in India.

January, 2007	Lilly	Collaboration	Drug Development Agreement. NPIL responsible for all pre-clinical and clinical payments while Lilly retains a call-back option on the transferred metabolic disorders drug. Contract included provision to work on four additional drugs.
January, 2007	Napo Pharmaceuticals	Collaboration	Plant Screening Agreement for diabetes drug discovery. NPIL will utilize its high throughput screening facility and natural product chemistry expertise along with biological testing capabilities to identify active compounds from Napo's library of medicinal plant extracts from tropical regions. NPIL and Napo will jointly own the products developed under the agreement.
November, 2007	Merck	Collaboration	Cancer drug discovery collaboration. NPIL will be responsible for taking two selected targets provided by Merck from the discovery stage to mid-stage clinical trials. Merck will pay $175M per target plus royalties.

To further illustrate the ways in which deals have changed is to examine whether the types of contracts have changed as a result of the IP law changes. The Exploit vs. Explore framework captures some of the differences between the contracts, but it speaks more to the stage of development of the product. Firms may enter into straightforward marketing alliances for products yet to be named, which would qualify as an exploratory alliance because both firms will learn more about the target of their alliance, but the shared learning may limited at the initial stages. The alliance between Alchemia and Dr. Reddy's for synthetic heparin is an example of such:

> *"Australian drug development company Alchemia Limited (ASX: ACL) today announced the appointment of Dr Reddy's Laboratories Limited (NYSE: RDY) as its marketing partner for synthetic heparin (fondaparinux sodium). Alchemia has granted Dr Reddy's the exclusive rights to market its synthetic heparin in North America, with first right of refusal to market the product in the European Union once GlaxoSmithKline's branded product, Arixtra(R)'s market exclusivity expires in 2012. Dr Reddy's will be responsible for the development of the API as well as finished product and all regulatory filings including the submission of an Abbreviated New Drug Application (ANDA)."*
>
> Alchemia Press Release, April 26th, 2007

As the Press Release states, the product is yet to be developed and registered which expands the possibilities for shared learning of the product through it's development, but as a licensing agreement the amount of learning between firms may be more limited than in research collaborations. The converse of this is late-stage collaborations. Both parties to the alliance may share more lessons than the early-stage alliance, but as a late-stage product, the sharing may be more robust and the inter-firm learning

more exploratory for later-stage products. In these deals, the firms are exploiting the lessons learned in the early stage, but may continue to learn about the markets and the best methods for manufacturing and distributing therapeutic targets. The alliance between Lupin and Allergan on the marketing and sales of their product is such a deal:

> *"Lupin Limited today announced that its wholly owned subsidiary Lupin Pharmaceuticals, Inc. has entered into an agreement with Allergan, Inc. (NYSE:AGN) in the United States to promote Zymar (gatifloxacin ophthalmic solution) 0.3% in the pediatric specialty area Under the terms of the agreement, Lupin Pharmaceuticals' pediatric sales force will promote ZymarTM to high volume pediatric prescribers. Lupin Pharmaceuticals has created a dedicated national pediatric sales force in the US to promote its recently approved product Suprax".*
>
> Lupin Limited Press Release, March 29th, 2004

The Zymar product is late-stage making the alliance an exploitive deal, but the two companies will be collaborating and sharing learning about the market for pediatric ophthalmic products. This is one such example of a collaboration that has the potential of expanding the learning possibilities for the organizations that would be characterized as exploiting alliances based on the stage of the product. A comparison of the types of alliances that have been entered by the companies before and after the implementation of the TRIPS compliance is listed in Table 10. This analysis compares licensing agreements with the more collaborative joint ventures and collaborations grouped into a single group to strengthen the conclusions that can be drawn from the data.

Table 10: Difference in ratios of Collaborations and Joint Ventures vs. Licensing alliances for pharmaceutical, biotechnology, and generics companies before and after TRIPS compliance

	Pharmaceutical Companies		Biotech Companies		Generics Companies	
	1996-2005	***2006-2007***	***1996-2005***	***2006-2007***	***1996-2005***	***2006-2007***
Number of Collaborations and Joint Ventures (Ratio)	9 (.19)	13 (.59)	8 (.31)	3 (.12)	6 (.24)	5 (.36)
Number of Licensing Alliances (Ratio)	38 (.81)	9 (.41)	18 (.69)	22 (.88)	19 (.76)	9 (.64)

	47	22	26	25	25	14
Difference in Ratio (After TRIPS vs. Before)	0.399**		-0.19		0.117	
P-Value of Difference in Ratios	0.00045		0.0667		0.2177	
Chi-Squared P-Value	0.00091		0.10328		0.4355	
	**Significant at p<0.005 level		*Significant at p<0.05 level			

Table 10 clearly shows that TRIPS compliance has stimulated pharmaceutical companies to align more closely with domestic Indian firms in the governance of the alliances that they form. Interestingly, there has been a downward trend in the number of collaborations undertaken by biotechnology firms, but this does not reach statistical significance. This trend remains unexplained.

Merck and Eli Lilly have entered the Indian market with strongly collaborative, long-term research and development partnerships enabled by the TRIPS compliance legislation. On November 16, 2006 Merck announced a partnership with Advinus Pharmaceuticals of Bangalore, India to develop two drug leads through Phase I clinical trials. On January 12, 2007 Eli Lilly announced an alliance with Nicholas Piramal to develop clinical lead through Phase IIb clinical trials. Structurally, both of the deals leave open the option of collaboration on additional programs and include sophisticated milestone payment schemes, callback options, sales royalties, and intellectual property agreements that have usually been the hallmark of deals between western biotechnology partners and MPCs (For example GSK's CEEDD deals with Theravance, Exilixis, and Chemocentryx). Table 11 highlights the important and relevant aspects of these two post-TRIPS deals.

Table 11: Deal highlights from two post-TRIPS deals demonstrating a high degree of integration, collaboration, and potential for intellectual property generation

Parties	*Specific Deal Terms*
Advinus/Merck	• Development program on two metabolic drug targets for up to 5 years time • Advinus will develop drug leads through Phase I clinical trials when Merck retains right of first refusal • Upfront payment, and development milestone payments totaling up to $74.5M • Advinus has royalty rights on any commercial products resulting from the collaboration • Merck retains rights on all IP generated • Agreement may expand to cover up to 8 additional targets
Nicholas Piramal/Eli Lilly	• Drug development collaboration for "multiple candidates in multiple therapeutic areas" • First candidate is preclinical drug candidate for metabolic disorders • NPIL responsible for all aspects of pre-clinical and clinical development through Phase II • Lilly retains a call-back option on each program after completion of Phase II trials • If Lilly does not call back the drug, NPIL retains all development and commercialization rights • If Lilly calls back the drug candidate, NPIL eligible for US$100M in milestones plus sales royalties • NPIL retains regional marketing rights for commercialized products

Discussion

The goal of this analysis was to shed light on the extent of deal making in the Indian life science industry. Using a scan of a database of alliances, some initial conclusions can be drawn. One of the most interesting initial observations is the lack of dispersion among the domestic Indian firms that are entering into partnerships. While 180 Western firms have dipped their toe into the waters of the Indian market, only 75 domestic firms have participated in deals. There may be several reasons for this phenomenon, which include a paucity of professionally managed domestic companies, the multinationals inability to identify alternative potential partners beyond those that have experience establishing alliances, and the accretive reputation effects subsequent to a company establishing its first alliance.

A surprise result of the analysis is the limited role that biotechnology companies have played in the initial exploration of India as a region for partnering. The reasons for their limited role remain to be

explored more fully, but it appears that strategic considerations have trumped the need for low-cost labor. Given the cost advantages and the energy with which pharmaceuticals have pursued deals that India would make a very attractive alliance target for biotechnology firms looking for creative ways of doing business in the pursuit of efficiency. Biotechnology companies, however, may not have the resources, time, and legal acumen to comfortably pursue an agreement with a developing-economy company. In addition, biotechnology companies are more susceptible to IP risk given their lack of a diversified portfolio. Therefore, it appears that these considerations have limited the involvement of biotechnology firms prior to fully TRIPS compliance patent laws. With more and more companies enjoying successful collaborations with India, more deal activity by the biotechnology sector is to be expected.

An additional surprise was the scattered appearance of the major multinational pharmaceutical companies in their involvement in collaborations with India. Some of the largest companies in the space like J&J, Sanofi-Aventis, and Schering-Plough are notable absences among the Top-20 Pharmaceutical players as are Amgen and Genentech on the biotechnology side. Glaxo has been especially active in forming alliances in the country, while AstraZeneca has pursued licensing agreements as well as setting up wholly owned research and development facilities. Merck, GSK, and BMS have the most aggressive, longest term, and most capital-intensive agreements, which are focused on drug discovery in defined therapeutic areas with their respective partners Advinus, Ranbaxy, and Biocon. This analysis did not consider those firms that are pursuing an organic strategy seeding and growing facilities within India. The question is whether the other organizations that did not show up in this analysis have pursued the subsidiary strategy or whether they have waited to enter the Indian market until the Intellectual Property questions are fully resolved.

This analysis clearly demonstrates that India's patent transformation initiated in 1995 with its acceptance of the WTO and culminating in its passage of the 2005 patent law reforms have been one of the driving forces in increasing the number of alliances between multinational life science companies and domestic Indian firms. TRIPS compliance has stimulated more research-oriented collaborations between pharmaceutical companies, and stimulated biotechnology companies to engage more actively with Indian firms. While pharmaceutical companies initially led the movement, biotechnology has become more active in creating alliances with Indian companies. Furthermore, the TRIPS compliance appears to be instrumental in stimulating multinationals to move more IP sensitive activities to India.

Bibliography

1. Aghion, Philippe and Jean Tirole, "Opening the black box of innovation", *European Economic Review*, Volume 38 (1994) : 701-710.
2. Aghion, Philippe, Mathias Dewatripont, and Patrick Rey, "On partial contracting", *European Economic Review*, Volume 46 (2002) : 745-753.
3. Arora, Asish and Marco Ceccagnoli, "Patent Protection, Complementary Assets, and Firms' Incentives or Technology Licensing", (December 2004).
4. Arora, Asish, Lee Branstetter, and Chirantan Chatterjee, "Strong Medicine: Patent Reform and the Emergence of a Research-Driven Pharmaceutical Industry in India", *Conference Draft for NBER Conference on Location of Biopharmaceutical Activity March 6-8, 2008*, 2008
5. Basheer, Shamnad, "'Policy Style' Reasoning at the Indian Patent Office", *Intellectual Property Quarterly*, No. 3. (2005) : 309-323
6. Bhalla, Vikram, Simon Goodall, Bart Janssens, Rachel Lee, Carol Liao, Kim Wagner, John Wong, "Tapping China and India to Reinvigorate the Global Biopharmaceutical Industry", *BCG Report*, August 2006.
7. DiMasi, Joseph, Ronald W Hansen, Henry G Grabows, "The price of innovation: new estimates of drug development costs" *Journal of Health Economics*, Volume 22 (March 2003) : 151-185.
8. Frew, Sarah, Rahim Rezaie, Stephen M Sammut, Monali Ray, Abdallah S Daar, and Peter A Singer, "India's health biotech sector at a crossroads", *Nature Biotechnology*, Volume 25, (April 2007): 403-417.
9. Guedj, Ilan and David Scharfstein, "Organizational scope and investment: Evidence from the drug development strategies and performance of biopharmaceutical firms", *National Bureau of Economic Research Working Paper*. Working Paper 10933, (2004).

10. Grindley, D.J. and David J. Teece, Managing Intellectual Capital: Licensing and Cross-licensing in Semiconductors and Electronics, 1997.

11. India. Parliament. Ministry of Law and Justice. Legislative Department. The Patents (Amendment) Act, 2005.

12. Koza, Mitchell P, and Arie Y. Lewin, "The Co-evolution of Strategic Alliances", *Organization Science*, Volume 9, Number 3 (May-June 1998): 255-264.

13. Kumar, Nagesh, "Intellectual Property Protection, Market Orientation and Location of Overseas R&D Activities by Multinational Enterprises", *World Development*, Volume 24, Number 4 (1996): 673-688.

14. Levin, Richard C, Alvin K. Klevorick, Richard R. Nelson, and Sidney G. Winter, "Appropriating the Returns from Industrial Research and Development", *Brookings Papers on Economic Activity*, Volume 18, Issue 1987-3: 783-832.

15. Licking, Ellen Foster, "Lilly and Merck lead the way with Asian FIPNet strategies", *In Vivo*. May 2008.

16. March, James, "Exploration and Exploitation in Organizational Learning", *Organization Science*, Volume 2, Number 1 (1991): 71-87.

17. Pisano, Gary, "The R&D boundaries of the firm: an empirical analysis-research and development-Technology, Organizations, and Innovation", *Administrative Science Quarterly*, March1990.

18. Pore, Mridula, Yu Pu, Lakshman Pernenkil, and Charles L. Cooney, "Offshoring in the Pharmaceutical Industry", *Working Paper from the 'Workshop on the Offshoring of Engineering: Facts, Myths, Unknowns and Implications', October 24-25, 2006, Washington, DC.* 2007.

19. Rosenkopf, Lori, and Atul Nerkar, "Beyond Local Search: Boundary-Spanning, Exploration, and Impact in the Optical Disk Industry", *Strategic Management Journal*, Volume 22 (2001): 287-306.

20. Rothaermal, Frank T., and David L. Deeds. "Exploration and Exploitation Alliances in Biotechnology: A System of New Product Development", *Strategic Management Journal*, Volume 25 (2004): 201-221.

21. Varadarajan, Cunningham. "Strategic alliances: A synthesis of conceptual foundations". *Journal of the Academy of Marketing Science*. Volume 23, Number 4 (1995): 282-296.

22. Williamson, Oliver E. *Markets and Hierarchies, analysis and antitrust implications: a study in the economics of internal organization.* 1975.

23. Yalamanchili, Vijay, "State of India's TRIPS-Compliant Patent Regime", *Biotechnology Law Report*, June 2007.

Tables and Figures

Table 12: Categories into which each deal participant was slotted

Category	Category Description	Bins
Geography	The location of the party's registration	Indian Western Non-Western
Focus	The primary business of the most senior organization	Pharma Biotech Generics Contract Manufacturing Contract Research Medical Device Lab Tools
Size	The number of employees of the most senior organization	Small (less than 1,000) Medium (less than 10,000) Large (larger than 10,000)
Ownership	Whether the organization is publicly traded or if it is privately owned	Public Private

Conflicts of Interest

The author has worked for the following firms for the following terms:

-Novartis Pharmaceuticals: October 2001-June 2003

-Vanda Pharmaceuticals: June 2003-July 2005

-Johnson & Johnson Corporation: May 2006-August 2006

-Bain & Company on a major Pharmaceutical client not previously identified, but specifically referenced in this report: June 2007-August 2007