Outsourcing in Biopharmaceutical Industry: India's Value Proposition



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Abstract: *In this paper we discuss the rationale behind biopharmaceutical outsourcing. We then discuss the benefits, challenges, current trends and market opportunities. From January 2005, India has agreed to comply with the product patent protection in accordance with the obligation under the TRIPS Agreement of the WTO. This has created new opportunities as well as challenges for the Indian biopharmaceutical companies. We analyze the value proposition of India as a suitable destination for outsourcing in biopharmaceutical industry in this new business environment. This research will help managers to understand the benefits of biopharmaceutical outsourcing along with its challenges under the current business scenario. Hence, this study is timely and relevant from both an academic and a practitioner's perspective.*

1. Introduction

In today's global economy, outsourcing has become a very common phenomenon (Alvares et al., 1995; Greaver, 1999; Squires, 2004). While outsourcing has been studied in traditional manufacturing and information technology sectors (Earl, 1996; Hirschheim and Lacity, 1993; Lacity and Wilcocks 1995, Lacity and Hirschheim, 1993), it is still in the nascent stage when applied to the biopharmaceutical industry (Bell, 2003; McKelvey 2000). By outsourcing, management can focus their critical resources and competencies on developing new drugs through research and development, improving market share, gaining competitive advantage, generating more profits, and achieving higher customer satisfaction (McCoy and Francois, 2003). Many large pharmaceutical companies have outsourced many of their business processes. Factors like lower costs, improved productivity, higher quality, higher customer satisfaction, time to market, and ability to focus on core areas are some of the benefits of outsourcing. However, there are many challenges and risks associated with biopharmaceutical outsourcing.

There are three major aspects of the proposed research that are summarized by the following questions.

1. *What are the benefits of outsourcing in biopharmaceutical industry?*
2. *What are the major factors that contribute to risk in global biopharmaceutical outsourcing?*
3. *What is the value proposition of India as suitable destination for outsourcing in biopharmaceutical industry?*

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Globalization and Competition

Technological advances, especially in the areas of communications and transportation have had a profound impact on the business and geographic scope of organization. Additionally, the opening up of previously closed economies and the emergence of new markets such as India, China, and the former Eastern bloc countries along with a proliferation of multi-lateral trade agreements are presenting tremendous opportunities for firms in their constant quest for increasing efficiencies and profits. Hence, previous limitations on the boundaries of firms are made practically non-existent and tasks that could be accomplished earlier only within the firm are now possible by coordinating with vendors or cooperating with a customer regardless of geographical distances.

Vertically integrated and internal value chains within atomistic organizations are now being replaced almost entirely by inter-firm cooperation on a broad and far-reaching scale with the objective of achieving greater efficiencies and returns on investment. Within the pharmaceutical industry, projects are now carried out across several organizations by larger teams of researchers with varied skills and backgrounds from different countries to solve complex problems and make rapid advances in drug discovery, genomics, bioinformatics and pharmaceutical manufacturing (Valazza, and Wada, 2001). As a result, new products, new technologies and services are developed more quickly and meeting the specific needs of the firm by taking advantage of global cooperation in the form of strategic joint ventures, outsourcing, or some variants of teams having complementary skills and lower costs (Valazza, 1998).

Collaboration

For the present day pharmaceutical industry, collaboration is an increasingly important and essential business model. Vendors work with clients to share the *development work* and hence the associated *risk* to improve newly created products, custom products, technologies and services. This is particularly important for bio-informatics tools vendors as it is not always possible to create ubiquitous software tools that cater to different customers as there is always a need for customization and tweaking during technical development to suit individual requirements (Kim and Buchanan, 2003).

For biotechnology and pharmaceutical companies, the magnitude in the cost of development of viable products is extremely prohibitive to restrict selling only to local markets. Hence, there is a real need for access to new markets to sustain profits and long term growth. There is a global market for similar health concerns in every part of the world such as hypertension, migraines, obesity, allergies, and life extension etc., presenting opportunities for firms in developing countries in terms of partnerships and outsourcing vendor relationships with North American and European drug firms which have had a head start over the former (U.S. Department of Commerce, 2003).

Bio-Pharmaceutical Industry Problems

High cost drug discovery economics is only a part of the problem faced by the pharmaceutical industry which is also characterized by escalated investment expenses for research and development, length of time for FDA approval and time to market and higher commercialization costs (Stefan, 2001). The total investments

need to almost double to sustain previous double digit growth rates. Price containment tactics imposed by medical insurance companies, rising consumer unrest over the high prices, and increased competitive intensity have exacerbated market pressures on pharmaceutical firms to decrease costs of drugs, research and development investments, while generating higher and higher returns on investments (DiMasi et al., 2003).

The traditional "bigger-the-better" model of pharmaceutical companies with massive investments in the organization and waiting for the discovery of the next lottery drug, casts serious doubts on the sustainability and longevity of such organizations in the present business conditions in spite of favorable outlook on the growth of this industry (Polastro and Tulcinsky, 2000). The most difficult challenge is the impending expiry of patent rights to several of the blockbuster drugs in the market, potentially resulting in severe loss of revenue for the original innovators. Furthermore, many companies seem to be operating on borrowed time in anticipation of the next blockbuster drug. According to industry sources, drugs accounting for almost 25% of the total sales translating to nearly 80 billion dollars are set to lose patent rights in the next 5 years and are open for competition from generic drugs. The pressure is higher than ever for the need to shorten drug development time and speed-to-market (Robbins, 2000).

2. Benefits of Outsourcing in Biopharmaceutical Industry

The pace of new techniques in drug discovery are invented faster than can be mastered by any individual company, and planning carefully the scope of outsourcing within the research and development agenda can have excellent payoffs in terms of utilizing locally non-existent technology, cost and overall product development time.

We now examine in detail the true benefits of outsourcing as a strategic business decision to acquire specialized and complementary assets/ technologies not existent within the firm.

Reduce R&D Costs and Improved Margins

Major pharmaceutical industries spend up to 20% of the total sales in R&D and have traditionally sought to reduce spending by engaging in selective outsourcing of fundamental research activities to universities, government laboratories and research institutes. Hundreds of independent new generation biotechnology companies have been innovating new technologies aimed at drug discovery and development, outnumbering the total number of pharmaceutical products available in the market (Douglas, 2002).

Biotech firms have strategically reoriented themselves as "drug discovery tools companies" aiming to provide research services to drug discovery companies, and research spending by biotech firms alone was estimated to be about $11 billion in a report prepared by *Ernst & Young* for the Biotechnology Industry Organization (Ernst & Young, 2000). It is practically impossible for any single medium and small sized pharmaceutical company to beat the pace of innovation at the applied research level and stay ahead of the external firms creating innovation in their respective core competencies.

When the Swedish biotech firm KabiGen decided to make its foray into genetic engineering for the manufacture of pharmaceutical products, they did not have any resident expertise but were keen not to miss the commercial potential of this new technology. KabiGen decided to jump start into the new technical trajectory by contracting R&D work to Genentech who had developed research competences and different genetic engineering techniques. Kabigen essentially funded Genentech to create new scientific techniques and absorbed the knowledge in-house. Without such innovative contracting, it would not have been possible for Kabigen to move quickly into the commercial trajectory of using genetic engineering into its pharmaceutical production system (McKelvey, 2000).

Teece's (1986) take on profiting from R&D is by allocating R&D resources towards new products that can be potentially commercialized quickly using the existing capabilities within the firm – the assets and revenues of the firm must condition and guide the R&D investment decisions.

Establishing Alliances and Outsourcing Contract Research

Expanding into international markets is an important strategy for American companies to optimize the potential for sustained revenue growth. Common healthcare needs of customers across the world directly translate into opportunity. According to the 2001 Biotechnology Industry survey report by the U.S. Department of Commerce, international markets accounted for approximately 16% of the total sales (which is about $8 billion in revenues) of biotechnology firms in 2001.

It is a clear strategy to reducing the risk in the complex and unpredictable process of drug development. It helps to target resources in creating innovation in new directions. The freely available human genome sequence data from the public project has triggered an explosion in the pace of research worldwide and an integrated structure with scope for outsourcing portions of R&D is the model of industry wide re-structuring.

Access to New International Markets

There are several strategies employed by multinational pharmaceuticals to increase their geographical reach and international participation such as direct export, licensing, international strategic alliances through partnerships and outsourcing agreements and Foreign Direct Investment (FDI). Direct export and licensing strategies are low risk ventures but control over the product is minimal and competitors can quickly duplicate and erode market share.

Strategic alliances are pursued when firms have complementary capabilities that when combined can result in competitive advantages, local firm's knowledge of government regulations and market conditions can be exploited to quickly access local channels of distribution and the relationship can be extended to manufacturing and sourcing of raw materials when the market conditions for the product or services are more clear.

For medium and small sized firms strategic outsourcing alliances paves the way to sharing complementary technologies in discovery processes, research, and manufacturing capabilities. Conditions for optimal scale of economies are created by bringing resources together.

Cost considerations are very important to be able to compete in international markets especially in Asian markets where the earning potential of consumers is enormously low in comparison with the American or European counterparts, it makes business sense to locally manufacture and leverage corporate high quality control, brand equity and best practices to capture market share.

Tapping Global Skills

When the task of sequencing the human genome was launched thirteen years ago, the complexity of this project originally estimated to take approximately 30 years. However global collaboration and utilization of global competencies among 16 research laboratories worldwide made it possible to complete this colossal task within 13 years since it started.

Most new innovations in any industry are dependent on computing power and software. No single R&D entity in the world can predict all the possible combinations of applying software and computing power to innovate all possible potential new products and processes.

A firm can strive to gain competitive advantage over its counterparts by discovering sources of lower cost or differentiation in any of its activities (Cullen, 2003) from any part of the world such as:

- New ideas and technologies
- Source of raw materials
- Efficient manufacturing capabilities
- Lower labor cost in other countries
- Lower R&D cost in other countries

Refocusing on Core Competencies

Diversified corporations aim to create and increase shareholder value by strategically orienting themselves as either focused on creating new and innovative products or as a services company adept at efficient business processes focusing on cost effective manufacturing solutions and logistics. The pharmaceutical industry is research and development intensive and hence product driven.

The U.S. Patent laws allows patenting of newly discovered drugs but not the extraction process of the drug, without offering protection from imitation by a difference in just a single molecule. Product differentiation and advertising placed high importance on the adoption and market demand. Hence pharmaceutical companies invested in their own manufacturing capabilities, sales and distribution channels as none of these segments were easily available in the external market at competitive prices.

The critical task for the management in the most simplified terms is to create new drugs that almost have no side effects, and inventing new drugs that customers need, but none exist in the market. This of course is a highly difficult and deceptive task. The changed market conditions have given rise to a wide range of diversified companies specializing in different segments of the drug discovery process creating a highly competitive atmosphere and the entry of generics has further intensified the competitive nature.

Refocusing on core competencies allow to compete rigorously, for some companies it might be more suitable to outsource their marketing, sales and distribution functions, while other companies find it more suitable to license drug compounds from other companies and capitalize on their own brand equity, established marketing and sales networks and geographical reach. For example, Novartis Pharma, a Swiss pharmaceutical major signed a license with a lesser known company Sigma Tau to develop, manufacture and commercialize the drug compound Gimatecan having therapeutic values for the treatment of cancer (Novartis Media Release).

Time to Market

Time to market is a very critical factor and is often the biggest deciding factor between success and failure of the product as first-to-market wins the allegiance of the market. For example Pfizer's Viagra generated sales of 1.9 billion dollars in 2003 alone and still owns a major share of the market in spite of at least two new entrants Cialis and Levitra to challenge its market dominance.

The early phase of the research can be isolated into its constituent steps of chemical, biological screening services involving isolation of compound using latest computational power and automated high speed screening by opportunistically outsourcing relevant areas can result in shorter development time.

Many of the phases that are typically executed in a serial fashion can be done in parallel, by outsourcing operations management to companies that excel in providing efficient drug development timelines by conducting as many steps in parallel. The ability of the external company to detect toxicity of specific compounds, and perform target validation efficiently can save time and speed up the process. Outsourcing makes it possible for the sponsoring company to concurrently run multiple promising projects due to the additional resources pooled in from the vendor.

In terms of aiming to reduce the time span of the product development life cycle, much potential results from new technological innovations that are made available almost continually by vendor biotech companies focused on innovating tools for drug discovery and establishing outsourcing alliances with such organizations can lead to successful completion of project within or exceeding timescales.

3. Risk Factors

In this section, we discuss various risk factors that are specific to biopharmaceutical outsourcing.

Protecting IP through Patents

In the biotech and pharmaceutical industry, firms hope to earn money through new innovations and creating new technology rather than end product differentiation unlike in other industries such as consumer goods or automobiles where innovations are more easily duplicated and they rely on product value competition. Patents are highly effective and remain the single most effective strategy of biotech companies to protect their intellectual property rights.

The U.S. Patent system is a "give and take" bargain agreement between the inventor and the government. The inventor has to fully disclose to the public "the invention" in exchange for a government protected exclusive right to exploit the

invention in the U.S. for a limited time period (Blaug, et al., 2003). Patenting allows the inventors to fully exploit the commercial potentials of their inventions without risking theft of their R&D effort by other competing firms.

Given the higher levels of investment and risk needed for the development of commercially viable inventions and processes related to drug discovery and development, the time period of patent protection for patents involving drugs is much higher (20 years) and a request for a further extension of patent rights for a few more years can be filed when nearing the end of patent life.

FDA Regulations

Biotech and pharmaceutical companies choosing to take advantage of contracting firms for outsourcing any activity in the drug development need to be cautious in ensuring the compliance of regulatory requirements of FDA. Vendor firms provide a means of access to resources and expertise without high capital investment costs in equipment. It does not necessarily mean that the FDA regulatory requirements are adhered to unless specified in the contracts and the contract firm has inherent capabilities and methodologies in place for such compliance requirements.

If the contract firm violates FDA regulations, there are potential implications of significant liability to the client and there is a risk of attracting legal sanctions and involves product seizure, court injunction and penalties. To mitigate such risks, the client company should take precautionary measures of interviewing references, review the vendor's regulatory files and establishment inspection reports at the FDA and consider track records of earlier dealings with the FDA (Kim and Buchanan, 2003).

Maintaining Quality

A quality agreement between the contractor and the client, clarifying in significant detail the quality and regulatory compliance obligations is an important instrument in maintaining quality concerns during outsourcing. The agreement must specify the documents that are expected from the contractor, address the communication of deviations and responsibilities of corrective actions, roles and responsibilities of audits and inspections, and communication of complaints and recalls of raw materials etc., "Guidance for Industry – Cooperative Manufacturing Arrangements for Licensed Biologics" document published by the FDA provides some excellent examples of Quality Agreements in the biotech industry (FDA, 1999).

Pitfalls to Avoid

- "One size fits all", every outsourcing contract is unique and different.
- Outsourcing is not an opportunity to offload internal problems, not knowing what to expect will only lead to uncertainty in evaluating the level of success of the result.

4. Tapping Offshore Resources – India

Western multinational companies are attracted to India today more than ever before as it offers a way to reduce costs in every industry, from software development to insurance claims-processing, and from customer care call centers to income tax

returns preparation. The second most important reason most large companies propose to expand abroad is in search of specialized capabilities that are not available locally.

A study by a group of researchers (Chung et al., 2002) find "knowledge seeking" is highly prevalent among companies associated in Research & Development-intensive industries such as pharmaceuticals, semiconductors and electronics. In fact, their research shows that *drug makers are twice as likely to seek knowledge abroad as companies in any other industry*.

Bio-pharmaceutical industry in India – a Background

India is one of the largest and cheapest producers of therapeutic drugs in the world; It stands foremost among the third world and has excellent technology, R&D and production facilities; a wide range of quality medicines are made locally for most medical conditions ranging from common fever to specialized antibiotics and vaccines (Maria, Ruet and Zerah, 2003).

Traditionally the industry has been only excelling in reverse engineering and tweaking of drugs focused to sell in the domestic market. However, with the product patent rights regime going into effect from 2005, the major players in this industry

Table 1: *Key Bio Pharmaceutical Companies focusing on Research & Development in India*

Company Name	Research and Development Efforts
Ranbaxy	NCE's Filed: 8 at various stages INDs filed: 4 (Benign prostatic hyperplasia and Anti-Inflammation)
Dr. Reddy's Laboratory	INDs filed: Anti diabetic compound Licensed To: Novo Novordisk (Danish Multinational) Currently: Working on new compounds for cancer treatments.
Wockhardt	INDs filed: Anti Infectives (WCK-771)
Lupin	INDs: Anti Migraine, Anti psoriasis, Anti TB
Nicholas Piramal	IND: Expects to file in Cardiovascular and oncology areas.
Shantha Biotechnics	Biotechnics has captured a 46% market share globally for the Hepatitis-B vaccine worth approximately $3 billion and has contracted with Pfizer for marketing the vaccine internationally. The company is doing research on a wide variety of other segments like: hepatitis-C, lung cancer, tissue plasminogen, etc.
Biocon	Biocon is one of the leading biotechnology companies in India having strong R&D capabilities in statins, immuno-suppressants, small molecules, recombinant proteins and offers a wide product range across key therapeutic segments such as diabetes, cancer and heart ailments. Biocon has FDA approved manufacturing capabilities and has filed for more than 100 patents.

[Source: Company websites]

are forcibly undergoing a strategic shift in their business models. They are moving from being copycat generic drug manufacturers to innovative drug firms in order to move higher in the value chain of the industry and have woken up to realizing the importance of original R&D work that could lead to filing for internationally patentable New Chemical Entities (NCE) to retain competitiveness.

Buoyed with the success of the IT services industry, the government is actively engaging to promote the bio-pharmaceutical industry by focusing efforts on R&D for creating new molecules, microbial enzymes, gene expression technologies and a range of genomics and proteomics related activities targeting export markets in drug discovery and development.

India has access to vast resources of well educated and talented workforce and a slew of research centers and world class laboratory facilities. There are a number of research activities in progress: Biocon, Dr. Reddy's Laboratories, and Ranbaxy are some of the leading companies that have filed for international patents as shown in Table 1. Indian companies have begun to successfully create strategic alliances with global heavy-weight pharmaceutical companies in the areas of drug discovery, development and manufacture. In addition to high growth rates (Table 2), as shown in Figure 1 India is also quickly emerging as a preferred destination for contracting research in biotech products such as recombinant techniques, enzymes aimed at drug discovery, diagnostics and contract manufacturing (Chorghade et al., 2001).

The presence of a large pool of research community that is fluent in English language (biggest outside of the U.S), biodiversity (presence of a large number of diverse ethnic population), a growing technologically sophisticated pharmaceutical industry (the industry is poised to grow at a rate of 25-30 percent) and India's signing of TRIPS with a pledge to fulfill the agreements has triggered a large number of western alliances with local Indian pharmaceutical and biotechnology firms and this trend is expected to continue. Some of the high profile partnerships are described in Table 3.

Smaller and intermediate size companies trying to make a foray into India must explore the possibilities of forming a strategic and gainful partnership based on complementary capabilities; success is hard to come by without such alliances as Indian firms are highly competitive, price and service-capability wise.

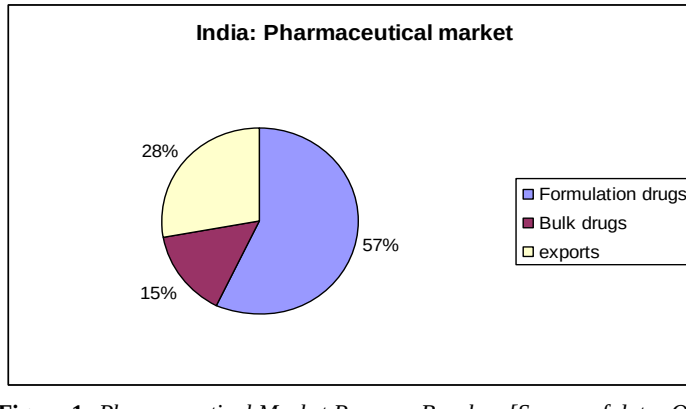


Figure 1: *Pharmaceutical Market Revenue Breakup [Source of data: OPPI]*

Table 2: *World Pharmaceutical Market Growth by Region (1998-2002)*

REGIONS	CAGR %1998-2002
North America	9.8%
Europe	5.8%
Japan	4.9%
Latin America & Caribbean	8.4%
Southeast Asia/China	11.0%
Eastern Europe	8.6%
Middle East	10.6%
Africa	3.3%
Indian Sub-Continent	8.6%
Australasia	9.8%
CIS	6.7%
Total World Market	**8.0%**

[Source: IMS HEALTH Global Pharma Forecast 1998-2002]

Table 3: *Foreign Partnerships with Indian Pharmaceutical and Biotechnology Firms*

Dabur Pharma and Abbot Laboratories
Austin and Shasun
Cipla and Abbot Laboratories
Dr. Reddy's Laboratories and Novo Nordisk (Danish Multinational)
Ranbaxy and GlaxoSmithkline for commercialization of products Ranbaxy and British Pharma for worldwide marketing rights Ranbaxy and Vecture – controlled drug delivery Ranbaxy and Eli Lily – marketing biotech based insulin products.
Nicholas and Piramal
Torrent and Novo Nordisk
Shantha Biotechnics and Pfizer
Biological E. Ltd and Amersham Pharmacia – DNA Microarrays

Table 4: *Advantages and Disadvantages of doing Clinical Trials in India*

Advantages:

- Large patient pool with a wide gene pool, quick patient enrollment reduces time.
- Incentives: 10 year tax break for R&D investments and no custom duty for materials imported for clinical trials.
- Availability of a large number of western-medicine style educated physicians, medical practitioners and nurses.
- Low costs: patient recruitment costs, infrastructure costs and physician costs are lower.

Disadvantages:

- Intellectual property protection challenges
- Issues on lack of ethics during patient recruitment and testing
- Documentation standards are not geared for FDA quality
- Reforms on regulatory affairs are unclear
- No single window clearance, need to deal with multiple agencies for approvals

There is an enormous scope for outsourcing and cooperative joint ventures in the areas of contract research for drug discovery, design, synthesis and manufacture (of pre-designed) combi-chem libraries, formulation development, chemistry and biology services, clinical trials and technical documentation writing according to regulatory guidelines, contract manufacturing of drugs coming off patent (sunset drug compounds) etc,.

Many of the Western biotech and pharmaceutical majors have large libraries of therapeutic compounds and molecules but never prioritized for commercial development because of its lower market potentials. Strategic partnerships with Indian companies can bring low cost clinical trials and manufacturing capabilities yielding new revenues with minimal investment and risk.

Clinical Trials

Conducting clinical trials forms a significant portion of the drug development costs and is time intensive. A heterogeneous pool of genes and the availability of a large number of patients have attracted a number of companies such as Pfizer and GlaxoSmithkline to conduct clinical trials in India. According to estimates by Kotak securities (2003) it is 40-50% cheaper to conduct clinical trials in India compared to developed markets due to the availability of a large number of physicians, good clinical practices training and the speed of patient recruitments.

However, while most multinational companies conducting clinical trials in India, do so through their fully owned subsidiaries, the design and the protocols of the clinical trials is still not done in India but in their other facilities. Only tasks with clearly defined inputs and outcomes are executed in India. Pfizer, Eli-Lily, Astra Zeneca are few of the international companies that are successfully conducting clinical trials in India. The sponsoring client company has to take the initiative to design the protocols, monitoring criteria, and pre define data management guidelines. There are very few independent Contract Research Organizations that are already

capable of doing these tasks from start to finish without handholding. If a client is seriously pursuing clinical practices in India, the following are the leading companies specializing in this area and can be explored for potential joint venture partners or outsourcing:

- Clinigene International Pvt. Ltd.
- Lotus labs Pvt. Ltd.
- Siro Clinpharm

Advantages and disadvantages of doing clinical trials in India are listed in Table 4.

Contract Research Services

The Department of Biotechnology (DBT) in India has been instrumental in creating basic infrastructural facilities to accelerate R&D in the areas of molecular biology and modern biotechnology. Numerous national laboratories and university grants has resulted in a large number of fundamental research projects in the areas of functional genomics, microbial genomics, human genome diversity, pharmacogenomics, proteomics, stem cells, bio-computing etc., and has resulted in a large pool of talented research (Patel, 1997; Rudolph and McIntire, 1996).

The programs initiated by the DBT have developed screening programs for a wide range of prevalent genetic diseases such as sickle cell anemia, thalassemia etc., and also resulted in several indigenous diagnostic technologies using genome information for diseases such as AIDS and vaccines for rabies and malaria. Reliance Life Sciences and the National Center for Biological Sciences are among the 8 institutions in 5 countries that have been identified by National Institute of Health (NIH) in US as sources of embryonic stem cells eligible for U.S government federal funding.

International pharmaceutical companies however have been very apprehensive of making any significant R&D investments in India, mainly because of earlier bad experiences with weak intellectual property protection laws. There is a change in attitude and mind set since the signing of WTO and it remains to be seen how the industry shapes up post January 2005.

Presently, only few private Indian biotech companies such as Syngene, Aurigene, Shantha Biotechnics etc., have undertaken contract research services for European and American clients and much of the R&D capabilities lie in the government owned public laboratories and there is scope for many improvements in the areas of regulatory procedures, world class training on GCP (Good Clinical Procedures) and intellectual property protection before the R&D capabilities of India can be fully exploited.

Contract Manufacturing Services

According to OPPI, there are about 60 (FDA Approved) drug manufacturing plants in India which is ranked second only to the U.S and correspondingly the world no. 2 in Drug Master Filings (DMF), which is manufacturing of bulk drugs for supplying to other large generic drug makers and for self consumption. Kotak Securities reports, India accounted for 34% of the global DMF filings in 2003 (compared to 2.4% in 1991). India offers an excellent manufacturing base at

internationally competitive prices and there is a large pool of scientific talent and engineering base.

Bioinformatics and IT Services

Bioinformatics and IT services are extensively used in all the phases of drug discovery and development, as the services and standards are beginning to be matured with well defined processes in place, bio-pharmaceutical firms are beginning to treat 'bio-informatics' as a more standardized component not central to their core competency (drug discovery) and are outsourcing bio-informatics projects to vendors specializing in it.

While the global bioinformatics market is estimated to be $0.8 to $14.6 billion (U.S. Department of Commerce), the Indian market is estimated to be a miniscule $2.2 million (Confederation of Indian Industries). The Indian bioinformatics market is estimated to grow to approximately $15-20 million by 2006 (Prabhu and Bhugwadia, 2003), and IDC India predicts a more exponential growth to nearly $130 million mainly from distributed computing, storage and data handling, data mining, geno-typing, DNA-Sequencing applications, and software services.

India's Advantages in Bioinformatics

The numbers indicate that the bioinformatics industry in India is clearly still in its infancy state but the business conditions offer a tremendous opportunity in view of the presence of the strong Information Technology knowledge and skills and the local presence of a large number of biotechnology and pharmaceutical companies that are hungry for innovative low cost bio-informatics solutions targeting a range of activities from drug discovery to data management.

The government has been careful not to miss the bio-informatics opportunity and was instrumental in establishing the Department of Biotechnology India (DBT) way back in 1986 to oversee the establishment of necessary infrastructure by creating Biotechnology Information System (BTIS) network that connects 57 research centers across the country to provide state of the art tools, education, and information in bioinformatics. There are many centers of excellence that have developed expertise and intellectual properties in computer simulation, molecular modeling and bio computational applications. Many specialized educational programs have been introduced in the universities by DBT to meet the challenge of skilled technical professionals.

India's Challenges in Bioinformatics

The key to realizing the bio-informatics revolution in India is the technical expertise and skill of manpower, vertical knowledge in IT and superficial knowledge of life sciences is not enough. Substantial levels of development skills are necessary to integrate disparate fields of life sciences, mathematical knowledge with the latest in Information Technology. The management challenges of such complicated projects are not trivial either. There is a shortage of this highly specialized workforce to be able to duplicate the low cost success stories in standalone IT applications.

The entry barriers to small companies are high and the venture capitals and other sources of funding are difficult to attain since product development time and Return-on-Investments (ROI) are longer. Bioinformatics outsourcing activity is mainly done

within the US, mostly by small and medium size businesses as large companies tend to have the capability within the firm. Convincing companies to outsource projects to India can prove a significant marketing challenge.

Intellectual Property (IP) Development and Protection

The Indian Patent Act was passed in 1970 to protect intellectual property, the laws were formed to limit the influence of powerful multinational drug firms from monopoly, and there were many elements of safeguards introduced to ensure easier access to drugs by common people. Product patents were not protected and only the process by which the product was manufactured is patentable and the duration of such patent enforcement existed only for 7 years instead of 14 years elsewhere.

It allowed India to produce generic drugs at a fraction of the cost compared to Europe and America, leading to a rapid increase in the domestic production of generic drugs and bulk formulations, many of which were reverse engineered and molecular level tweaked copies of block buster drugs. The domestic pharmaceutical industry has grown its market share from 25% in 1970 to almost 70% presently.

The loopholes in the patent laws largely prevented global pharmaceuticals to view Indian market with suspect and have prevented any significantly large deals in the subcontinent. India's entry into the WTO fold in 1995 and its agreeing to ratify all the obligations of patent laws from 2005 has forced a paradigm shift in the perspectives of the global biotech and pharmaceutical multinationals.

See Tables 5 & 6 for relevant Indian laws and the implications of India's membership in the WTO.

Table 5: *Laws Related To Patents for Drugs in India*

Indian Patent Act (1970):
• Does not recognize product patents, but only process patents
• Process patents are applicable to all inventions related to medicine and food and valid for a period of only 7 years and a compulsory licensing regime.
WTO (1995):
• India's signing of the WTO (World Trade Organization) agreements obliges it to comply with TRIPS (Trade Related Intellectual Property Rights).
• TRIPS imposes product patents in all the fields of technology effective from January 2005, the span of the patent protection increases to 20 years and there is no compulsory licensing (unless there are exceptions.)

Table 6: *As a WTO signatory, the obligations to be fulfilled by India*

Patents filed before July 1, 1995	**Patents filed after July 1, 1995**
• Not valid in India	• Need license from inventor for sale or manufacture in India.
• Only existing process patents are protected.	• A drug compound patented after July 1, 1995 approved to market before TRIPS takes into effect, 5 year market exclusivity is allowed to the company in India.

Regulatory Affairs

Indian companies aiming at the global market use the USFDA guidelines for drug approvals which is considered the most rigorous approval process. There is an absolute lack of one single agency that takes the responsibility to ensure the safety, efficacy, and quality of drugs in India. There are multiple agencies that are seriously understaffed which oversee the drug approval process and take an indeterminate time to evaluate new drug applications (NDA). The Prime Minister's commission on the sluggish growth of the biotech industry in spite of $500 million expenditure by the government identified complex drug approval system as the main constraint (Maria, Ruet, and Zerah, 2003).

There have been some significant efforts to reform the regulatory affairs related to drug development and clinical trials in India on the lines of the FDA; the Indian government has made it compulsory to follow the technical requirements mandated by ICH (International Conference of Harmonization) for registering all pharmaceutical products intended for human use. Compulsory following of Good Clinical Practice guidelines for clinical researches designed to be conducted in India has been mandated.

Until recently, the Indian government regulations for drugs required clinical trials for new drugs not discovered in India must be one phase behind the rest of the world and phase II and phase III trials for new drugs were not allowed simultaneously. There have been recent amendments in the Indian drugs and cosmetics act (schedule Y) to describe newer guidelines similar to the FDA's for clinical trials and allows simultaneous Phase II and III trials. However the recommendation to allow Phase I trials of new foreign drugs in India concurrently with those that are conducted abroad is yet to be ratified.

Key Reforms

In response to the Indian biotech and pharmaceutical industries pleas, the government has taken some positive measures to increase R&D activities and encourage foreign participation in the industry. There are proposals to

- Scrap the price control tactics of the government as this is a major discouraging factor for R&D investments for new drugs which warrants huge capital investments. Price control reduces return on investments and stretches the time span during which the costs can be recovered. However, the government is willing to reduce the number of drugs in the purview of price control and gradually move away from price control on bulk drugs.
- Allow conducting of Phase1 trials in India simultaneously while being carried elsewhere as this will lead to faster access to new drugs in India and promote the growth of clinical trials business revenue in India due to significant costs savings factor.
- Reform and streamline the regulatory agencies to grant approvals in a timely predictable manner and encourage a single agency for approvals on the lines of the USFDA.
- Reform the potency of the patent protection agency by strengthening of the appropriate legal frameworks and higher penalty for violations. Increase the size of patent specialist staff which is currently grossly understaffed to handle quicker processing of patent applications.

Bioethics

In spite of the existence of some laws and legislations to protect bio-ethics for humans, India lacks the frameworks, mechanisms and appropriate provisions for strict enforcement of the legal requirements. There have been many instances of violation of the poverty, illiteracy and ignorance of certain sections of people to be recruited as clinical trial patients and treated as guinea pigs without proper consent and information. International companies conducting clinical trials in India need to ensure the vendor company's compliance and historical credibility of confirming to international norms in order to protect itself against public backlash due to negligence.

Genuine Risks and Concerns

In spite of the enormous potential for India to grow in the area of biotechnology, the immediate benefits for multinational firms may not be high. There are many challenges in securing good infrastructure such as faster transportation, power and bandwidth. The IT industry has thrived and prevailed in spite of the enormous shortcomings by operating as small islands of prosperity by building their own captive infrastructure such as local power generation and facilities. However, the investments needed for similar operations of bio-pharmaceutical companies are much higher and the returns take much longer.

There is widespread corruption while dealing with government organizations for logistics and establishment. It is very important for smaller and medium sized firms establishing offices in India to use the services of companies that specialize in providing legalities, logistics and tax areas. Choice of the right vendor who has historical credibility and can help make things happen, a partner with a comprehensive set of capabilities that can be customized to the client's specific needs will decide the success or failure of off-shoring endeavors. Many participants of our survey have expressed discontentment on the bureaucratic problems and have had exited from the Indian market, in spite of having the advantage of being people from Indian origin. Table 7 lists the SWOT analysis for India and Table 8 highlights key players in the Indian pharmaceutical/bioinformatics sectors.

5. Conclusions

In many large biopharmaceutical organizations, outsourcing is a very common trend and will continue to grow in the future. Some of the main benefits are reducing R&D costs, improved profit margins, establishing global alliances for contract research and well as tapping into new markets, access to global skills and time to market the product. We have discussed the major risk factors associated with outsourcing. In addition, we also analyzed the value proposition of India as a major player in the area of biotechnology outsourcing. India provides some good opportunities for global pharmaceutical and biotechnology companies as a possible resource for contract research, clinical trials, contract manufacturing and bioinformatics. However, there are some challenges also which we discussed. This research will help managers to understand the benefits of biotechnology outsourcing along with its challenges. Hence, this study is timely and relevant from both an academic and a practitioner's perspective.

Table 7: *SWOT Analysis of the Bio-pharmaceutical Industry in India*

Strengths	Weaknesses	Opportunities	Threats
• Ratification of WTO and TRIPS from 2005 • Access to skilled workforce in chemistry and biology • Access to skilled low cost workforce in bioinformatics • Large domestic market • Low costs for human resources, training, research, development and manufacturing • Low cost for conducting clinical trials • Knowledge of English translates into quicker adoption of new technology and skills • Democratic government • Presence of a large number of multinational companies that can enhance product value. • 10 year tax break for R&D investments • Advantage of time zone can be exploited for faster turnaround (U.S.:12 to 12.5 hrs Europe: 4 to 6 hrs)	• Non recognition for product patents until 2005 • Lack of world class infrastructure to protect intellectual property • Lower profit margins • Purchasing power of the people is low • Multiple regulatory agencies • People are knowledgeable in basic sciences but need more training • Lack of ethics	• Rising middle class society is increasing the purchasing power (about 300-400 million people are middle class) • Streamlining of regulatory agencies by adopting FDA style guidelines • Product patent recognition from 2005 • Potential for sourcing skills in the areas of research, development, bioinformatics and manufacturing. • Higher opportunities for export of locally manufactured generics • Development of the quality of skilled and intellectual talent • Inflow of new drugs and technology with confident participation of international companies • Stronger Intellectual properties protection will lead to effective utilization of skills and prevent brain drain. • Attract more FDI, Foreign equities can now own up to 74% (was previously 51%)	• Cost of new drugs will increase beyond 2005 and hence unaffordable for a major portion of the population. • The Indian patent office is highly understaffed and needs reforms to handle patent issues beyond 2005. • Loopholes in enforcement agencies • Bureaucracy and corruption • Infrastructure taken for granted in the west can prove to be a big problem. • Threat of China in the global context.

Indian companies are undergoing a major strategic shift from generics manufacturing under protectionist regimes to compete with innovative international firms in preparation for the WTO regime. There is a large gap in terms of over-

lapping subject domain knowledge, vertical and complementary competencies to be covered before being able to compete with the international bio-pharmaceutical majors. Companies need to focus on developing non-infringing product processes and drugs coming off patent to further strengthen the generics market.

Key industry alliances for joint development of drugs and processes will be critical to business success and establishing credibility in the global market for many small to medium sized businesses. The transition from being a leader in IT services to areas of competencies in life sciences to capitalize in the bioinformatics is the most important challenge to achieve a synergistic business success

Currently, international joint-venture partnerships and global offshore outsourcing to India is prevalent only in contract manufacturing, chemical and biological screening services and peripheral bioinformatics services. This situation might change in the near future but issues concerning infrastructure and procuring international raw materials in a timely fashion without bureaucratic delays still remain an important impediment.

Finally, the push to innovate to create new drug molecules, proteins, and intellectual property will be critical for long term success. Medium and small size firms looking towards cutting costs can definitely take advantage of many benefits offered by India, the knowledge, willingness and skills are definitely available but not to the extent where it can be totally expected to be delivered without some "handholding", the cost advantages are significant to ignore and worth the effort if done properly.

Table 8: *Key Players in India*

Pharmaceuticals	**Biotech**	**Multinationals**	**Bio-informatics**
Ranbaxy	Biocon Ltd.	Abbot Laboratories	Accelrys India
Cipla	Panacea Biotec	Burroughs Wellcome	Avesthagen
Dr. Reddy's Labs	Wipro Health Sciences	GlaxoSmithkline	Cytogenomics
Zydus Cadila	Wockhardt	Novartis India	Genotypic Tech
Nicholas Piramal	Haffkine	Pfizer	Kshema Technologies
Sun Pharmaceuticals	Reliance Life Sciences	GlaxoSmithkline	Strand Genomics

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Appendix A: *Summary of Key Regulatory Agencies in India*

ICMR: Indian Council for Medical Research

Role: Evaluation of new drug applications. Biotech drugs are reviewed under an expert panel.

DGCI: Drug Controller General of India

Role: DGCI is the executive head of the CDSCO and provides a number of clearances during the conducting of clinical trials. DGCI has also announced the guidelines for GCP based on ICH.

CDSCO: Central Drug Standard Control Organization

Role: Ascertain efficacy, safety and quality of drugs.

FDCA: Food and Drug Control Administration

Role: State regulatory body involved in regulating counterfeit drugs etc.

Appendix B: *Summary of Guidelines for Drug Discovery Clinical Practices and Retail Sales*

Drug and Cosmetics Act:

Governs the drug approval process in India.

Schedule V: Standards about patents for proprietary therapeutic medicines

Guidelines on conducting of clinical trials for new drugs

Drugs Prices Control Order:

The DPCO provides the government the power to fix the maximum retail prices of certain bulk drugs and drug formulations. It ensures that the drug is available to the population at an affordable price. The National Pharmaceutical Pricing Authority (NPPA) takes the authority to collect data and study the pricing structure to fix the ceiling prices. It is estimated that only about 35% of the total available drugs in India are governed by the DPCO. [Source: http://www.nppaindia.nic.in]

ICH-GCP

The Good Clinical Practices prescribed by the International Conference for Harmonization

The Environment Protection Act

The EPA serves to protect the pollution of the environment by genetically modified organisms and other biotech pollution.