

DESTINATION INDIA

THE RIGHT CHOICE FOR THE PHARMACEUTICAL INDUSTRY

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INTRODUCTION

THE drugs and pharmaceutical industry has an important place in the Indian economy due to its positive technological spillovers to other sectors of the economy. The industry grew at 7.2 percent and contributed 1.3 percent to GDP in 2004. It recorded \$4 billion in domestic sales (about 1.5 percent of the global pharmaceutical sales) and over \$3 billion in exports in 2003-04 (Government of India, *Economic Survey, 2004-05*). Thus, the pharmaceutical industry is a sun-rise industry with vast opportunities for both the domestic and foreign players. With the changes in the regulatory environment regarding patent laws, the spotlight is now on India for contract research, joint ventures and alliances.

An Overview of India's Pharmaceutical Industry

The Indian pharmaceutical industry is highly fragmented with over 23,000 units, Only around 250 of them are in the organized sector. The industry has been characterized by tight price controls as well as weak patent laws. While price regulation has restricted profitability, weak patent laws have facilitated growth in the industry. In fact, the industry has been competing on its capability of reverse-engineering¹ patented products that are produced by foreign companies and then selling them at lower prices. However, this option will no longer be available to them since India has to recognize both the product and the process patents under the World Trade Organization (WTO) regime and the industry will have to boost its in-house R&D and develop original molecules along with developing generic drugs.

The Indian pharmaceutical industry produces bulk drugs belonging to all major therapeutic groups. Bulk drugs are the key acting ingredients with medicinal properties that form the basic raw materials for formulations² and account for roughly one-fifth of the industry output while formulations account for the rest. Some pharmaceutical firms are tapping the low-cost low-risk and medium returns overseas generics markets and also undertaking various initiatives for new chemical entities (NCEs) and novel drug delivery systems (NDDS) that are improvements on the available drugs like lower side-effects or easier dosage forms.

The government has controlled pharmaceutical prices since 1970 under the Drug Price Control Order (DPCO), 1970 to make available essential drugs at affordable prices. Due to complaints from the pharmaceutical companies regarding regulation of prices, now the National Pharmaceutical Pricing Authority is responsible for monitoring prices. The National Drug Authority has been set up to ensure quality consciousness and to check the proliferation of substandard drugs. Moreover, the government

1 Reverse-engineering is a method of using the functional aspects and underlying ideas of a product to develop a similar or identical product.

2 Bulk drugs are the active chemical ingredients used to manufacture formulations or finished products.

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in recognition of the pharmaceutical industry as a knowledge-based industry, has extended the facility of availing 125 percent weighted tax deduction for R&D up to March 31, 2005. This is in addition to new drugs being exempted from DPCO for 10 years.

TRIPs Regulations

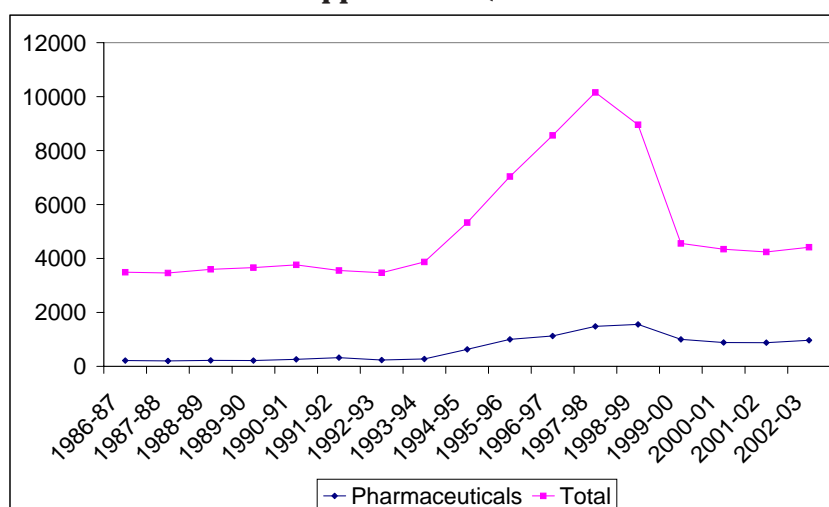
The most important governmental intervention in the pharmaceutical industry relates to the amendment of the Patent Act 1970. The 1970 Act had abolished product patents, reduced the patent term and recognized only process patents for pharmaceuticals. But, India being a signatory to the WTO is also party to the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPs). In order to honour its commitment under TRIPs, India introduced product patents³ from January 1, 2005 through the passage of the Patents (Third Amendment) Act in March 2005. Regarding the effect of TRIPs on prices, it is expected that the prices of patented drugs would rise. It is true that pharmaceutical companies should be rewarded for their efforts at research and inventions through patents, but in a country like India, the burden of rising drug prices for the overwhelming majority of the population will be enormous given the existing meagre facilities for healthcare and medication. Thus, the patent regime should be such that it balances the interests of producers and consumers in a way that ultimately enhances social welfare.

However, the immediate effect of product patents in India may be less severe than expected since many off-patented therapeutic equivalents are available to the consumer and only about 3 per cent of the drugs marketed in India are patented (Panchal, 2005). Further, many of the currently patented drugs are likely to go off patent in the next few years, clearing the way to follow the reverse-engineering strategy. But at the same time, new drugs would come under patent protection and the extension of the patent period would limit the availability of products to reverse-engineer.

R&D and Patenting Activity

There is evidence to show that R&D efforts and patenting activity have been stimulated with the signing of TRIPs and the enforcement of stronger patent protection rights in India. Figure 3.1 shows

Figure 1: Number of Patent Applications (other than PCT National Phase)



Source: Government of India, Annual Reports of the Controller General of Patents, Designs, Trademarks and Geographical Indications, *Intellectual Property*, various years.

3 Product patents confer on the owner the right to prevent third parties not having his consent from making, using, offering for sale, selling or importing the product whereas process patents confer on the owner the right to prevent third parties not having his consent from using the process and from using, offering for sale, selling or importing the product obtained directly by that process.

the trend in patent applications filed under Section 155 of the Patents Act, 1970 from 1986-2003. These applications are filed at the national patent offices and do not include the patents filed under the Patent Cooperation Treaty (PCT) and designated to India. The graph shows a steep rise in both pharmaceutical as well as total patent applications after the setting up of the WTO in 1995. There is a fall in total patent applications after 1999 that can be attributed to India's signing the PCT in December 1998. Instead of filing national and international patents separately, it is now more convenient for Indian and foreign innovators to file a single patent at an international patent office and designate the countries in which they want to protect their innovation including India.

Patent applications filed in the U.S. are also an important index of domestic inventive activity and Indian firms are spending huge resources to secure non-infringing process patents in foreign countries. After tapping the developing countries, they are trying to access developed countries with drug master filings (DMFs) for bulk actives supply and abbreviated new drug applications (ANDAs) for formulations.

In order to make an early entry into the U.S. market for a drug going off patent, Indian firms have filed ANDAs⁴ under Paragraph II and Paragraph III. They are moving up the value chain and securing exclusivity status. Under their aggressive strategy of filing ANDAs in the U.S. market, sales in the U.S. market started growing faster than any others (Kothari, 2003). Table 1 lists some of the top brandname drugs, their innovator firms and sales in 2002. It is noteworthy that of the top 10 blockbuster drugs, eight of them have Indian challengers waiting in the wings to produce the generic versions of these drugs when their patents expire. Firms like Ranbaxy Laboratories, Cipla and Sun Pharmaceuticals have created a pipeline of ANDA filings to maintain their hold in the U.S. market. Paragraph IV filings are also becoming increasingly popular among generic drug firms since the first generic applicant to file an ANDA containing a Paragraph IV certification is eligible for 180 days of marketing exclusivity. In fact, recently, Ranbaxy Laboratories has challenged the U.S. drug manufacturer Pfizer regarding its patent on the blockbuster cholesterol drug Lipitor, which is the best-selling drug in the world. If the court ruling in the U.S. favours Ranbaxy, the Indian company will earn up to \$800 million from a generic version of the drug with exclusive marketing rights for six months (Zamiska, 2005).

Table 1: Blockbuster Drugs and Indian Challengers

Brandname drug	Innovator	Sales in 2002 (\$ bn)	Indian challenger(s)
Lipitor	Pfizer	8.0	Ranbaxy
Zocor	Merck	5.6	Ranbaxy, Biocon
Prilosec/Losec	AstraZeneca	4.6	Dr Reddy's, Cipla
Norvasc	Pfizer	3.8	Dr Reddy's, Matrix
Zyprexa	Eli Lilly	3.7	Dr Reddy's
Paxil/Seroxad	GlaxoSmithKline	3.1	Dr Reddy's
Celebrex	Merck	3.0	Cipla
Zoloft	Pfizer	2.7	Dr Reddy's, Cipla

Source: *Chemical and Engineering News*, January 19, 2004, 82(3), pp.48-50.

4 The Hatch-Waxman Act provides ANDA filings for four categories: (i) Paragraph I filing- when the required patent information is not filed by the innovator, the FDA immediately approves the ANDA. (ii) Paragraph II filing- when the patent expires, the FDA approves the ANDA. (iii) Paragraph III filing- when the patent has not expired and the approval is sought after patent expiration. (iv) Paragraph IV filing- when the patent is invalid or will not infringe by the generic drug for which the generic drug ANDA applicant is seeking approval. It signals the intention of the ANDA applicant to market a bioequivalent version of a brand before patent expiration on the grounds that the patent is invalid, not infringed or unenforceable. In response, a brand company has the right (if done within 45 days) to initiate patent infringement litigation to block generic entry with a 30-month stay.

For the year 2003, the Indian pharmaceutical industry filed 126 DMFs with the USFDA, accounting for a third of the total global filings, higher than Spain, Italy, China and Israel (OPPI, 2004). Further, India has the largest number of USFDA approved manufacturing plants outside the U.S. However, a comparison of global and Indian R&D expenditures leaves much to be desired. While the global pharmaceutical R&D spending hovers around 10-16 per cent of turnover, the R&D expenditure (unweighted) by the Indian pharmaceutical industry as a whole is only 1.9 per cent of the industry's turnover although some research-based companies are spending over 6 percent of sales on R&D (OPPI, 2004). Thus, there is an urgent need to step up R&D expenditure so as to compete effectively with MNCs.

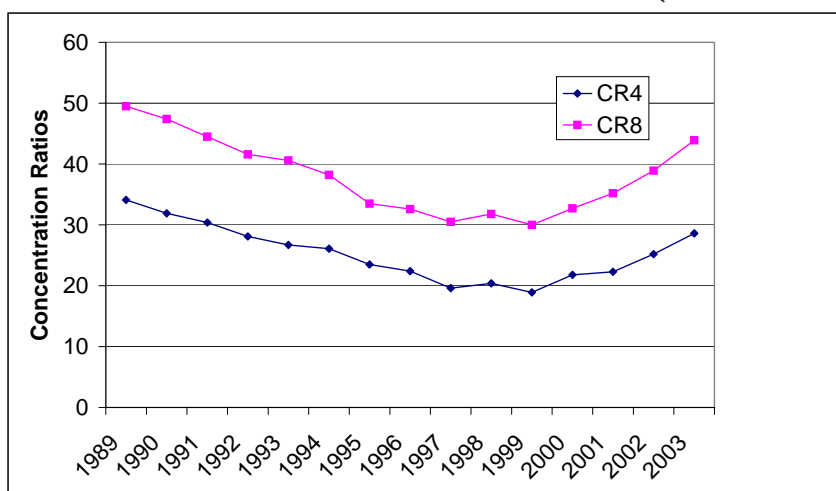
Market Structure

The recent WTO regulations have given an impetus to a major restructuring of corporate strategies in the industry, with an unmistakable trend towards consolidation. The industry has been swept by a wave of mergers and acquisitions (M&As) in its attempt to come to terms with the new WTO dispensation. This is particularly true of the Indian affiliates of MNCs that have formed alliances based on the mergers undertaken by their parent firms. M&As lead to synergies by pooling resources and exploiting economies of scale.

On the flip side, small manufacturers that were dependent only on the marketing of process innovations are likely to face survival concerns after the introduction of product patent rights in 2005. But, even these smaller firms with low research capability have an opportunity to gain by reorienting themselves as contract manufacturers for the large pharmaceutical MNCs, provided they are able to compete with other low-cost locations like China. On the whole, the emerging industry dynamics point towards greater consolidation in the future. This is clear from Figure 2, which depicts the trend in the CRs⁵ for the largest four and eight firms. The graph follows a U-shape, falling from 1988-89 up to 1995-96 and then rising thereafter. Thus, with the establishment of the WTO in 1995, the trend towards decentralization was reversed in the Indian pharmaceutical industry. This is as expected since the world pharmaceutical industry is an oligopoly investing huge amounts for R&D and as the Indian pharmaceutical industry becomes more research-intensive, it is likely to adopt an oligopolistic market structure.

Figure 2: Trends in CR4 and CR8

(1988-89 to 2002-03 (percent))



Source: Centre for Monitoring Indian Economy's Prowess database.

5 Concentration ratios or CRs are defined as the percentage of total industry sales contributed to the largest few firms.

Foreign Direct Investment

The pharmaceutical industry has been selected as one of the sunrise areas where concerted efforts are being made to attract foreign direct investment (FDI). The Government of India has not only abolished industrial licensing for bulk drugs, intermediates and formulations, but has allowed automatic FDI approvals up to 100 percent foreign ownership. During 1991-2004, the drugs and pharmaceutical sector attracted nearly Rs 35 billion in FDI inflows (see Table 2).

Hitherto, the fear of not recognizing product patents in India made MNCs shy away from comprehensive technology transfer to their Indian affiliates. Since the problem of software piracy was brought under control in India, the software industry witnessed massive inflow of FDI but the lack of intellectual property protection prevented the inflow of FDI in the pharmaceutical and biotech industry. Now with the introduction of a stricter patent regime, greater technology transfer is expected. Table 2 compares the FDI inflows into India for the drug and pharmaceutical sector with all sectors after the liberalization of the economy in August 1991. As is clear from Table 2, the share of the drugs and pharmaceuticals sector in FDI inflows has more than doubled from 1.43 percent for the period 1991-99 to 3.57 percent for the period of 2000-04. Thus, there has been a significant improvement in FDI inflows after the year 1999, when steps were taken to amend the Patent Act 1970 for the first time. The figure for 2004 is especially striking since it shows a marked jump in FDI, probably in anticipation of the enforcement of product patents from January 2005 onwards.

The rise in FDI inflows can also be attributed to the expected decline in profitability of pharmaceutical majors owing to shrinking sales growth and mounting costs. Sales growth is shrinking as a large number of blockbuster drugs go off patent. According to one estimate, 42 of 52 blockbuster drugs amounting to \$ 82 billion in sales, will lose patent protection by 2010 (Kothari, 2003). At the same time, R&D costs are mounting due to the rising number of tests and the period of exclusivity for a new drug is falling due to the intensified competition in the pharmaceutical market place with me-too drugs entering the market before patent expiration. India has an important role to play in the global division of labour by providing the base for outsourcing to bring down costs of manufacturing and R&D through contract research. The source of comparative advantage for the Indian pharmaceutical industry lies in the vast pool of skilled manpower in the country. The industry has access to highly qualified specialists in the fields of molecular biology, biotechnology and chemistry and that too at very competitive costs. While research in Indian pharmaceutical industry has mainly focussed on the anti-infective segment,

Table 2: FDI Inflows into India

(Rs. million)

Year	Pharmaceuticals	All sectors	Share of pharmaceuticals (%)
Aug 1991-Dec 1999	8221.75	576821.15	1.43
2000	2079.88	123537.34	1.68
2001	4081.79	167777.54	2.43
2002	2510.52	181955.56	1.38
2003	2793.28	116171.7	2.40
2004	15711.08	172665.2	9.10
Total	35398.3	1338930	2.64

Source: Government of India, Department of Industrial Policy and Promotion, Ministry of Commerce and Industry, Secretariat for Industrial Assistance, *SIA Newsletter*, various issues.

some companies have started basic research as well. Further, MNCs have also started using India as a base for conducting certain stages of basic research, including clinical trials due to low costs, scientific talent and a diverse pool of patients.

Major Indian pharmaceutical firms like Ranbaxy Laboratories, Dr Reddy's Laboratories, Cipla, Wockhardt and Sun Pharmaceuticals have started developing strategies and capabilities to strengthen R&D efforts. These firms have benefited patients in India and many poor countries by providing them access to affordable drugs and treatments. Witness the case of the fall in prices of antiretroviral AIDS drugs from nearly \$10,000-12,000 per patient per year to \$350 for 'Doctors without Borders' and \$600 for governments, thanks to the development of the "cocktail" therapy of three drugs developed by Cipla (Zimmerman and Pesta, 2001).

The Indian pharmaceutical industry is also increasingly complying with good manufacturing practices (GMP)⁶ and investing in R&D for diseases like malaria and tuberculosis that are peculiar to tropical countries. Further, for greater market access, Indian companies have started acquiring foreign firms. A study of some of the major pharmaceutical companies' annual reports showed the following foreign acquisitions: Ranbaxy acquired Ohm Laboratories of the U.S. in 1995 and RPG Aventis of France in 2004 for over \$80 million; Sun Pharmaceuticals acquired Caraco of the U.S. in 1997 and increased its stakes further in 2003; Wockhardt acquired Wallis of the U.K. in 1998; Dr Reddy's Laboratories acquired BMS of the U.K. in 2002 and Trigenesis of the U.S. in 2004.

Exports

The rising exports of Indian pharmaceutical manufacturers are an indicator of local technological capability, particularly in process innovations. With their cost-effective process innovations and reverse-engineering of brandname drugs, Indian firms have emerged as competitive suppliers in the world for a large number of generic drugs. Moreover, since least developed countries have an additional 10 years to provide product patents after 2005, Indian firms can continue to service the markets in these 49 countries till 2016 by setting up manufacturing bases for on-patent drugs in these countries.

A revealed comparative advantage index considers the intrinsic advantage of a particular export commodity in world markets. Balassa's index of revealed comparative advantage (*BRCA*) compares the export share of a given sector in a country with the export share of that sector in the world market (Balassa, 1965, 1979 and 1986). However, this index cannot distinguish between improvements in factor endowments and pursuit of appropriate trade policies. Vollrath's index of revealed comparative advantage (*VRCA*) takes into account both the significance of a country's export in a given sector and that country's total export in the world market (Vollrath, 1991). The *BRCA* and *VCRA* are calculated as follows:

$$BRCA_{ij} = \frac{\left[\frac{X_{ij}}{\sum_j X_{ij}} \right]}{\left[\frac{\sum_i X_{ij}}{\sum_j \sum_i X_{ij}} \right]}$$

6 GMP refers to the Good Manufacturing Practices Regulations of the USFDA that require the manufacturers, processors and packagers of pharmaceuticals to ensure that their manufacturing processes are safe, pure and devoid of contamination.

$$VRCA_{ij} = \frac{\left\{ \frac{X_{ij}}{\sum_i X_{ij} - X_{ij}} \right\}}{\left\{ \frac{\sum_j X_{ij} - X_{ij}}{\left(\sum_j \sum_i X_{ij} - \sum_j X_{ij} \right) - \left(\sum_i X_{ij} - X_{ij} \right)} \right\}}$$

where X_{ij} is the exports of sector i from country j , $\sum_i X_{ij}$ is the total exports of country j , $\sum_j X_{ij}$ is the world exports of sector i and $\sum_j \sum_i X_{ij}$ are the total world exports.

Table 3 computes the Balassa's index of revealed comparative advantage (BRCA) and Vollrath's index of revealed comparative advantage (VRCA) for Indian pharmaceutical exports and finds that both the indices are quite high being greater than unity for all the years. Thus, India has a comparative advantage in pharmaceutical exports due to its known ability for low-cost reverse-engineering of brandname drugs to produce generic drugs.

Despite this proven comparative advantage, Indian pharmaceutical exports contribute a negligible share to world pharmaceutical exports, hovering around 1 percent of world pharmaceutical exports (Table 3). Further, exports of generics from India are likely to face competition from other countries, particularly for generic drugs whose market is highly price sensitive. Some of India's main competitors include China, South Korea, Taiwan and Brazil. Thus, to face this competition successfully, Indian pharmaceutical firms will have to intensify R&D efforts and improve efficiency.

Table 3: Comparative Advantage of Indian Exports of Medicinal and Pharmaceutical Products (SITC 541)

	Indian pharma exports (\$ mn)	Total Indian exports (\$ mn)	Share of pharma exports in total India's exports (%)	World pharma exports	Share of India in world pharma exports (%)	Balassa's RCA Index	Vollrath's RCA Index
1992	431.2	19641	2.20	49829.4	0.87	1.63	1.65
1993	482.9	21573	2.24	51778.6	0.93	1.60	1.63
1994	585.8	25022	2.34	59723.7	0.98	1.66	1.68
1995	724.2	30628	2.36	71997.5	1.00	1.61	1.63
1996	814	33107	2.46	77833.9	1.04	1.62	1.64
1997	947.2	35006	2.71	83616.9	1.13	1.71	1.74
1998	933.7	33463	2.79	94572.1	0.98	1.54	1.56
1999	1068.2	35666	2.99	104870.4	1.02	1.55	1.57
2000	1255.2	42378	2.96	107481.7	1.17	1.67	1.69
2001	1348.2	43338	3.11	132797	1.02	1.36	1.38
2002	1760	49293	3.56	151861.6	1.16	1.43	1.45

Source: United Nations, *International Trade Statistics Yearbook*, various years.

Conclusion

The twin dose of economic liberalization and strong patent regime has rejuvenated the Indian pharmaceutical industry. The export focus of Indian firms, propelled by the recognition of process patents in different countries, has made them penetrate a number of countries based on their low cost structure. They are now concentrating not only on off-patent drugs but also on undertaking contract research. The pharmaceutical industry is in the transition phase ready to face new challenges that could bring major changes in its business environment. For long-term solutions, the industry will have to build up its R&D facilities as well as make sustained efforts to attract FDI for technical collaborations. Moreover, it is imperative that the deregulation and decontrol of the industry should proceed in such a manner that prices of essential drugs remain affordable to consumers since this industry has direct implications for healthcare and social welfare. But, with stronger patent laws, contract research, joint ventures and clinical trials at a fraction of the cost in India as compared to developed countries, India is the right choice for pharmaceutical FDI in the near term.

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