ICRA Management Consulting Services Limited

IMaCS Research & Analytics

Industry Comment

THE INDIAN PHARMACEUTICALS INDUSTRY

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TABLE OF CONTENTS

INDUSTRY OVERVIEW

Background

The Indian pharmaceutical industry is one of the developing world's largest and amongst the most developed. Further, the Indian pharmaceutical industry is one of the world's largest and most developed, ranking fourth in volume terms and thirteenth in value terms. The country accounts for an estimated 8% of global production and 2% of world markets in pharmaceuticals. Most of the domestic pharmaceutical drug requirements are met by the domestic industry. In the segment of Active Pharmaceutical Ingredients (APIs) India ranks third in the world producing about 500 different APIs.

The Indian pharmaceutical sector is emerging as one of the major contributors to Indian exports with export earnings rising from a negligible amount in early 1990s to Rs. 291.40 billion (US$7.24 billion) in FY2008. Exports of drugs, pharmaceuticals & fine chemicals have grown at a compounded annual growth rate (CAGR) of 17.8% during FY2004-08. The Indian domestic pharmaceutical market size is estimated at Rs. 433 billion (US$10.76 billion) in 2008 and is expected to grow at a high annual rate of 9.5-10% till 2010 and thereafter at a CAGR of 9.5% till 2015. The industry contributes to the Government exchequer in terms of sales tax; excise duty and import duty; and ccrporate tax on profit before tax (at 30%) and dividends. In terms of employment, the industry is estimated to provide employment (directly and indirectly, through distribution trade and ancillary industry) to around 3 million people.

Over the last 30 years, India's pharmaceutical industry has evolved from almost non-existent to a world leader in the production of high quality and bio-equivalent generic drugs. India has achieved a worldwide reputation for producing high quality, low cost generic drugs. The industry currently meets India's demand for bulk drugs and nearly all its demand for formulations, with the remainder supplied by foreign multinational corporations (MNCs).

India's pharmaceutical industry is one of the fastest growing segments of the Indian economy with an average annual growth rate of 13-15% during 2003-07. The surge in production has been driven by legislative reforms, the growth in contract manufacturing and outsourcing, value added foreign acquisitions and joint ventures, India's mastery of reverse engineering of patented drug molecules, and India's efforts to comply with its World Trade Organization (WTO) Trade Related Intellectual Property Agreement (TRIPs) obligations.

When India joined the WTO in 1995, its pharmaceutical exports were valued at less than US$600 million. By FY2008, its exports had grown to US$7.2 billion and accounted for more than 61% of industry turnover. Currently, Indian pharmaceutical companies produce between 20 and 22% of the world's generic drugs (in value terms) and offer 60,000 finished medicines and nearly 400 bulk drugs used in formulations.

With changes in India's patent laws in the early 1970s, Indian drug producers became experts in 'reverse engineering' and increased its supply of less expensive copies of the world's best-selling

patent protected drugs. India's pharmaceutical industry grew and prospered in a highly regulated environment with government price controls on a significant number of formulations and bulk drugs. In January 2005, India amended its patent laws governing pharmaceuticals, bringing them into conformance with the WTO TRIPs agreement. Under the new patent law, Indian drug markers can no longer manufacture and market reverse-engineered versions of drugs patented by foreign drug producers. To replace sales lost to TRIPs compliance, many of India's leading pharmaceutical producers have increased their exports of generic drugs to the US and Western Europe and entered into research and development agreements, mergers and acquisitions, and other alliances with foreign pharmaceutical firms.

India's Pharmaceutical Industry: Independence to 2008

At the time of independence in 1947, India's pharmaceutical market was dominated by Western MNCs that controlled between 80 and 90% of the market primarily through importation. Approximately 99% of all pharmaceutical products under patent in India at the time were held by foreign companies and domestic Indian drug prices were among the highest in the world. The Indian pharmaceutical market remained import-dependent through the 1960s until the government initiated policies stressing self-reliance through local production. At that time, 8 of India's top 10 pharmaceutical firms, based on sales, were subsidiaries of MNCs.

To facilitate an independent supply of pharmaceutical products in the domestic market, the Government of India (GoI) founded 5 state-owned pharmaceutical companies. Today, India is the world's fifth largest producer of bulk drugs. Government policy culminated in various actions including: the abolition of product patents on food, chemicals, and drugs; the institution of process patents; the limitation of multinational equity share in India pharmaceutical companies, and the imposition of price controls on certain formulations and bulk drugs. Subsequently, most foreign pharmaceutical manufacturers abandoned the Indian market due to the absence of legal mechanisms to protect their patented products. Accordingly, the share of the domestic Indian market held by foreign drug manufacturers declined to less than 20% in 2006-07. As the MNCs abandoned the Indian market, local firms rushed in to fill the void, and by 1990, India was self-sufficient in the production of formulations and nearly self-sufficient in the production of bulk drugs.

REGULATORY ENVIRONMENT

To end the dominance of foreign drug companies, the GoI has enacted a series of policies designed to foster self-sufficiency in the production of basic drugs. Because these measures lowered barriers to entry, thousands of medium and small Indian pharmaceutical companies entered the market challenging the MNCs for control. These actions laid the foundation for today's highly competitive domestic industry that is capable of offering some of the lowest drug prices in the world.

These policies ended India's dependence on expensive foreign drugs, fostered the development of a competitive pharmaceutical industry, and guaranteed the Indian public access to inexpensive drugs.

Nonetheless, the Indian pharmaceutical industry also became one of the country's most heavily regulated. The industry currently faces restrictions on imports, high tariff rates, ration requirements, and equity ceilings for foreign participation.

The Indian Patent Act, 1970

The Act's stated objective was to foster the development of an indigenous Indian pharmaceutical industry and to guarantee that the Indian public had access to low-cost drugs. The Act replaced intellectual property rights laws left over from the British colonial era and ended India's recognition of Western-style `product' patent protection for pharmaceuticals, agricultural products, and atomic energy. Product-specific patents were disregarded in favour of manufacturing `process' patents that allowed Indian companies' to reverse engineer or copy foreign patented drugs without paying a licensing fee. Technically, a chemical compound (a pharmaceutical product) can be obtained through different processes and methods. From a legal perspective, product patent protection would prevent all other processes and methods from producing the same chemical product. In contrast, under process patent protection, a second producer can produce the same chemical product provided that an alternative method is used.

Thus the Indian Patent Act, 1970 allowed the domestic industry build up considerable competencies and offer a large number of cheaper "copycat" generic versions legally in India at a fraction of the cost of the drug in the West, as long as they employed a production process that differed from that used by the patent owner. The Act protected process patents for 7 years instead of the usual 15 years needed to develop and test new drugs.

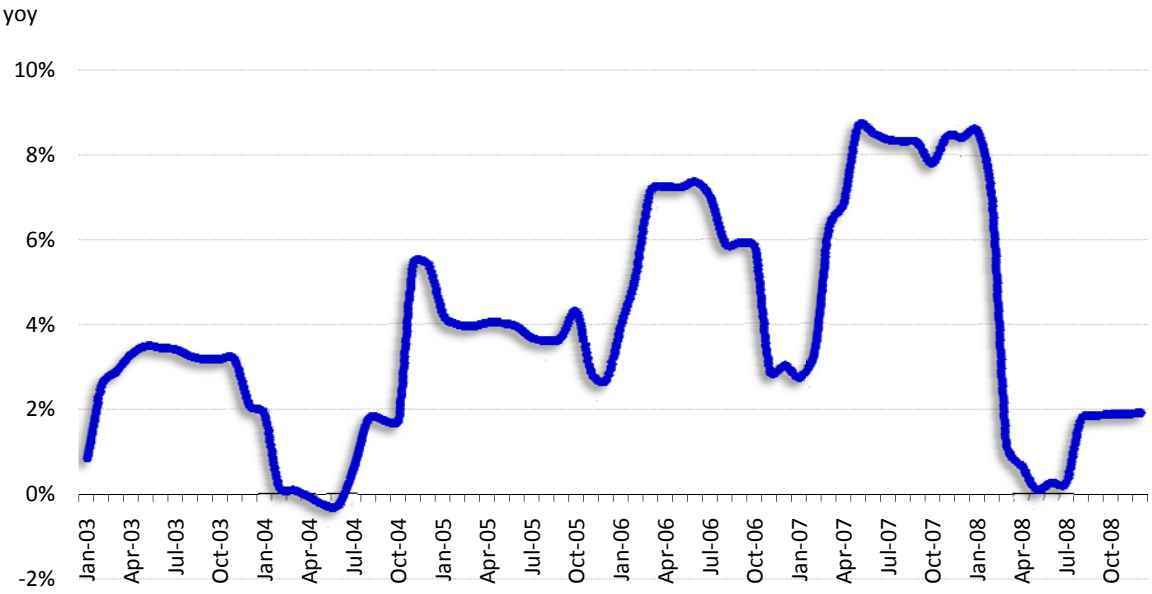
Drug Price Control Order, 1970 (DPCO)

The Drug Price Control Order (DPCO) was introduced when most of India's drugs were under strict price controls. Since its introduction, the number of bulk drugs under price controls gradually declined from 347 in 1987 to 163 in 1994 to 74 in 1995. In 2005, the government capped prices on 74 bulk drugs and 260 formulations that account for approximately 25% of India's retail pharmaceutical market. Trade margins for these drugs were capped at 8% for retailers and 16% for wholesalers. The National Pharmaceutical Pricing Authority (NPPA), founded in 1997, is responsible for monitoring prices using the DPCO to fix ceiling prices on drugs and ensure that no Indian company in a monopoly position takes advantages of its monopolistic position by profiteering. In June 2006, the National Pharmaceutical Policy 2006 (Part A) proposed to add price controls on 354 specific drugs listed as essential medicines. The new policy will cap margins on generic drugs at 15% for wholesalers and 35% for retailers. It will also enforce a 5% price cut on more than 75 commonly-used medicines resulting from import duty reductions of 5 to 7.5% on certain APIs. The NPPA controls ceiling prices for controlled bulk drugs in all intra-industry transactions as well as the retail ceiling prices for controlled formulations. Consequent upon reduction in excise duty on drugs and pharmaceuticals from 16% to 8% in the Union Budget for 2008-09 and a reduction in the rate of abatement on drugs and pharmaceuticals from 42.5% to 35.5%, the prices of scheduled formulation packs have been

revised downwards by the NPPA. The NPPA has revised the Equivalent Maximum Retail Price (MRP) (inclusive of all taxes) of all Scheduled formulation packs downward. All manufacturers are required to reduce the Equivalent MRP (inclusive of Excise duty & all taxes) by 4.58%. The reduction in prices of such scheduled packs shall however not apply on those categories of scheduled formulation packs where no excise duty has been actually paid to the GoI and therefore no excise duty shall be chargeable in the MRP of these scheduled formulation packs.

Consequent upon the reduction in the rate of Excise duty on medicines from 8% to 4% with effect from December 7, 2008, all manufacturers and marketing companies of formulations packs have been advised to ensure that the benefit of this excise duty reduction and the reduced rate of abatement is passed on to the consumers through reduced MRP. Accordingly, the NPPA has noted that prices of all non-scheduled packs must accordingly be reduced downwards by 2.84% except in those categories of non-scheduled formulation packs where no excise duty has been actually paid to the Government and, therefore, no excise duty shall be chargeable in the MRP of such non-scheduled packs. The NPPA expects that the above reduction in MRP would be complied with by way of reduced MRP and that necessary revised price lists would be submitted to NPPA forthwith. NPPA shall accordingly monitor the limit of 10% increase in prices per annum of non-scheduled packs based on the reduced MRP for all such packs where the batch of the formulation pack has been cleared by the manufacturer through the competent excise authorities on or after December 7, 2008.

Monthly Change in WPI for Drugs and Medicines



Patents (Amendment) Act 2005

The Agreement on Trade-Related Aspects of Intellectual Property Rights (The TRIPS Agreement), concluded during the Uruguay Round negotiations, has led to some changes in the development of pharmaceutical industries. The TRIPS Agreement, which came into effect on January 1, 1995, sets out the minimum standards of protection for all WTO Members. A key legal requirement of

the TRIPS Agreement is for all WTO Members to replace process patent protection with product patent protection in all fields including pharmaceuticals.

With respect to its patent-related obligations, India decided to use the additional transitional provisions in article 65.4 of TRIPS; thus giving itself a final compliance date of January 1, 2005 for product patents in exempt technologies, notably pharmaceutical products. As a result, India's compliance with the TRIPS Agreement proceeded in several stages. The Patents (Amendment) Act, 1999 introduced the `mail-box' system and set up a system of exclusive market rights (EMRs) to be retrospective from January 1, 1995. Article 70.8 of TRIPs requires countries that do not currently provide TRIPS-mandated patent protection for pharmaceutical, chemical or agricultural products to establish a filing system to establish a priority date for these applications for such future review when patent protection becomes available in that country-a kind of pipeline protection. In addition, EMRs are available to the applicant for a period of five years following marketing approval or the issuance of a product patent, whichever period is shorter. The Patent (Amendment) Act, 2002 introduced 64 changes to the Patent Act of 1970, the most important ones of these being the extension of patent term from 14 to 20 years, and the reversal of burden of proof from patent holder to alleged infringer. The final set of changes to make India's patent regime comply with the TRIPS Agreement in toto were first contained in the Indian Patent Ordinance of 2004, that was replaced by the Indian Patent (Amendments) Act, 2005 (IPA, 2005). Under the Act:

- None of the drugs, presently in the Indian market or those that have been patented prior to January 1, 1995 any where in the world, can be patented in India.
- For drugs presently being manufactured in India and discovered/patented after January 1, 1995 and also granted patent in India: such drugs will continue to be produced subject to a payment of reasonable royalty. The price of all such medicines should rise proportionate to the royalty payments. However, India's existing price control mechanism can control such cases if the increase is beyond permissible levels.
- New drugs (post-2005) which get patented in India and they are not being produced in India at present: If their therapeutic equivalents are available in India, then such drugs could be reasonably priced. However, in the case of a `blockbuster' drug the prices can go far beyond the reasonable levels. In such a situation, price control mechanism can be used to take care of the situation. Alternatively, compulsory licensing (CL), as provided for under the TRIPS Agreement, or the threat of its use, could be used as a price-leveraging instrument to ensure affordable access to patented medicines.

The Act states that anything that falls within the purview of 'invention' will be patentable in India. `New invention' means any invention or technology which has not been anticipated by publication in any document or used in the country or elsewhere in the world before the date of filing of patent application with complete specification, i.e., the subject matter has not fallen in public domain or that it does not form part of the state of the art. The term of the patent in case of international applications field under the Patent Cooperation Treaty designating India, shall be 20 years from the international filing date accorded under the Patent Cooperation Treaty. Certain changes have been introduced in the provisions relating to CL. In this respect a provision has been introduced that allows CL to be available for manufacture and export of patented pharmaceutical products to any country having insufficient manufacturing capacity in the

pharmaceutical sector for the concerned product to address public health problems, provided CL has been granted by such country. The GoI estimated that only 3% of the existing formulation market may be impacted following enforcement of product patents by innovators once such patents are granted.

Although protection would be available prospectively, the life of patent (20 years) would be computed from the date of application, thus reducing the effective life of the patent. Assuming that newly patented drugs are made available in India, it is likely that the newly patented drugs will be expensive, at least in the therapeutic categories where there are no generics available to offer price competition. However, the definition of patentability, as contained in the IPA, 2005 and its effectiveness in dealing with `ever-greening', will play a large role in determining the nature of competition that Indian firms will be able to put up in the generics market. The new section 3 of the IPA, 2005 contains an explanation that was inserted specifically to deal with the problem of ever-greening. The explanation reads as follows: `For purposes of this clause, Salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations, and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy'. salts, esters, ethers, polymorphs, metabolites ...shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy'. However, this puts much of the onus to prevent ever-greening on patent examiners (through pre-grant oppositions) and/or courts. The lack of capacity in India's patent offices may have more adverse consequences for the domestic industry in terms of patent litigation following grant of patents that should not have been granted, than for the mailbox applicants.
At present, nearly 97% of all drugs manufactured in India are off patent and therefore will not be affected by this Act. It also introduced a provision establishing CL for exports to least developed countries with insufficient pharmaceutical manufacturing capacities.

INDUSTRY PRODUCTION AND STRUCTURE

Overview

The Indian pharmaceutical industry can be said to have begun with the setting up of `Bengal Chemical and Pharmaceutical Works' in Calcutta (now Kolkata). Subsequently institutes like Kings Institute of Preventive Medicine in Chennai, Pasteur Institute in Coonoor, the Central Drug Research Institute in Kasauli and others were set up. Post-independence, many other public sector companies such as Hindustan Antibiotics Ltd. and Indian Drugs and Pharmaceuticals Ltd. were set up to reduce the imports of important antibiotics and also to meet the county's demand from indigenous production.

The industry is conspicuous by the large presence of private sector which has captured a substantial share in the domestic & external market due to factors such as conducive regulatory environment, past patent policies, low cost of innovation, access to funds from banks to corporate manufacturers, low cost of setting up and running high technology manufacturing facilities, etc. The public sector as in many other sectors contributed to strategic areas but has

gradually been overtaken by the private players—an indication of the latter's emerging competitiveness and entrepreneurial capabilities. Indian owned firms currently account for 70% of the domestic market, up from less than 20% in 1970. In 2006, nine of the top 10 companies in India were domestically owned, compared with just four in 1994.

The expertise that the Indian pharmaceutical sector developed in reverse engineering and production of generics can be directly attributed to the effects of Governmental policy such as the Patents Act, 1970 which played a major role in shaping the industry and bringing it to the present enviable position. The Act of 1970 excluded product patents on pharmaceuticals, allowing the mushrooming of a vigorous generics industry in India which could meet not only domestic demand for drugs at lower prices but could also export cheaper drugs to other Third World countries. Further, the government policies restricted imports of finished formulations, imposed high tariff rates and introduced strict price control regulation through the Drugs Price Control Order.

Nearly four decades of protection has enabled the Indian pharmaceutical industry to perfect its scientific and manufacturing capabilities, allowing many of its leading companies to move up the value-added chain. India's pharmaceutical industry consists of large, medium, and small companies and is one of the world's most price competitive. It is also highly fragmented with more than 20,000 domestic production units. Because of low barriers to entry and low capital requirements, the number of domestic pharmaceutical firms engaged in the formal and informal sectors expanded dramatically from 2,257 in 1970 to more than 20,000 in 2007-08. Because many of these companies focus of producing similar generic drugs, with possibly hundreds of companies producing the same drug, the industry is characterised by fierce competition and high volumes, razor-thin profit margins, overcapacity, and declining prices.

India's pharmaceutical firms can be differentiated by size, annual sales, function, export markets, and R&D capabilities.

Industry Structure

Grouping	Number of firms	Description
Group 1	100	Largest firms, includes both wholly-owned Indian firms and subsidiaries of MNCs; have annual revenues of at least Rs. 30 billion; have brand recognition and are engaged in developing R&D capabilities; responsible for recent wave of cross-border acquisitions and alliances; export to regulated, semi-regulated, and unregulated markets.
Group 2	200	Mid-size firms with annual revenues between Rs. 10-30 billion; they have limited investment capabilities and primarily serve the domestic Indian market. They are generic drug producers that subsist mainly on reverse engineering of patented and off-patent drugs (primarily bulk drugs and APIs); also includes niche players specializing in contract research (CRAMS) and contract clinical trials in segments of the market where they have a competitive advantage; export to semi-regulated and unregulated markets.
Group 3	5,700	Smallest firms with annual revenues of less than Rs. 10 billion; primarily perform contract manufacturing services for MNCs or domestic firms. Many have been adversely affected and have been forced to close their doors due to revised Good Manufacturing Practices set by Schedule M of India's Drug and Cosmetic Act, 1940 that came into effect from July 1, 2005. Those affected cannot meet production standards of regulated market regulators and their production will be limited to the domestic, semi-regulated, and unregulated markets.

The vast majority of India's pharmaceutical firms are small by global standards with annual revenues of less than Rs. 200 million (US$4 million). Approximately 80% of them are engaging in some type of contract manufacturing or outsourcing. The largest 250 companies control nearly 70% of the domestic market with the top 10 controlling approximately 40%.

The domestic Indian pharmaceutical industry consists of both domestic companies and subsidiaries of MNCs. In the 1970s, the vast majority of foreign pharmaceutical companies abandoned the Indian market during the `process' patent era due to inadequate product protection, government price controls, growing domestic competition, and declining prices and profitability. Consequently, the share of India's market controlled by multinationals dropped to less than 19% by 2007.

In the absence of government protection, India's leading drug producers are moving toward new drug discovery rather continuing to rely solely on copying patented foreign drugs. Industry experts project that by 2010, Indian firms could produce six of the top 10 drugs scheduled to lose their patent protection.

Indian pharmaceutical companies now supply nearly all the country's demand for formulations and nearly 70% of its demand for bulk drugs. Indian firms produce nearly 60,000 generic brands in 60 therapeutic categories and between 350 and 400 bulk drugs. Approximately 80% of domestic production consists of formulations, and more than 85% of those formulations are sold in the domestic market, whereas at least 60% of bulk drug production is exported. Nearly 97% of India's drug market consists of second-and-third generation drugs no longer subject to patent protection in the developed countries. Some patented, lifesaving drugs continue to be

imported, primarily from developed countries, especially the US, Germany, the United Kingdom, and France.

Therapeutic Segments

India has the world's third-largest API manufacturing industry valued at nearly Rs. 100 billion in 2006. Currently, India's drug industry produces more than 400 different APIs and is among the world's top 5 API producers accounting for approximately 6.5% of the world's API production. Italy's Chemical Pharmaceutical Generic Association (CPA) projects that India's share of the world API market will grow to 10.5% by 2010 as patented blockbuster drugs lose their patent protection. The CPA also expects that the domestic Indian market for APIs, both generic and branded, will rise from US$755 million in 2005 to US$1.9 billion in 2010. According to IMS, the leading APIs were antiinfectives, and gastrointestinal, cardiovascular, and respiratory drugs. In terms of volume of sales, the gastrointestinal and cardiac segments saw the highest rates of growth and accounted for the largest number of new drug launches.

Major Therapeutic Segments

	Value (US$ million)					3-year CAGR	Share (2005)
Grouping	2001	2002	2003	2004	2005		
Alimentary Tract & Metabolism	811	883	1,007	1,107	1,230	11.7%	26.4%
Anti-infectives	853	900	960	1,000	1,059	5.6%	22.7%
Cardiovascular	432	487	564	659	732	14.5%	15.7%
Respiratory	325	343	402	418	433	8.1%	9.3%
CNS	242	248	297	321	353	12.5%	7.6%
Musculo-skeletal system	217	240	267	295	297	7.4%	6.4%
Women's Health	132	146	168	195	212	13.2%	4.5%
Dermatology	124	126	151	167	188	14.3%	4.0%
Cancer	16	19	27	36	44	32.3%	0.9%
Others	88	95	104	106	113	6.0%	2.4%
Total	3,240	3,487	3,948	4,304	4,660	10.1%	100.0%

In 2005-06, the strongest performance was recorded by products indicated for the treatment of alimentary tract and metabolism related disorders, which accrued sales of US$1,230 million, representing a market share of 26.4%. The bulk of sales captured within this therapeutic area are believed to be by vitamins, products indicated for the treatment of diabetes, anti-ulcerants and antacids.

Anti-infectives are positioned at number two with a share of 22.7%, attributable to India's epidemiology that continues to feature a strong prevalence of infectious and communicable diseases. This therapeutic area garnered sales of US$1,059m in 2005-06. The cardiovascular therapy area has expanded at a strong CAGR of 14.1% over the period of 2001-05, representing 16% of the market in 2005-06. This strong performance is attributed to the high prevalence of risk factors of cardiovascular disease, thus generating strong demand. Despite CNS disorders representing a modest 7.6% of the market, this therapy area witnessed a strong growth rate

recorded at 10.1% for 2004-06. However, majority of sales in this therapeutic area are accounted by analgesics, most of which are available as OTC products in India.

Therapies for respiratory disorders accounted for a strong 9.4% of the market having captured sales of US$433 million in 2005. In spite of the recent increased availability of domestically manufactured generics and inhalation devices, growth in this market remains low. The lowest market share was reported by cancer therapies, which account for a mere 1% of the market. Despite the strong presence of domestically manufactured, cheaper versions of cancer drugs, treatments for cancer remain extremely expensive in the Indian market, which when combined with limited availability of reimbursements and/or subsidies, render these treatments unaffordable for the majority of patients.

Leading Indian Pharmaceutical Manufacturers

India's leading pharmaceutical companies are striving to compete not only in the domestic Indian market, but also in the global market for both generic drugs and original products. Sales for India's largest 200 pharmaceutical companies grew from US$7.9 billion in 2004-05 to US$8.6 billion in 2005-06, or by 9%. By 2006-07, 9 of the top 10 Indian drug makers were Indian-owned firms accounting for more than 44% of total industry sales. India's top five pharmaceutical companies, in terms of sales, are Ranbaxy Laboratories, Dr. Reddy's Laboratories, Aurobindo Pharmaceutical, GSK-India, and Cipla. These companies manufacture a wide range of generic drugs (branded and non-branded), intermediates, and active pharmaceutical ingredients (APIs).

Leading Manufacturers

2007-08

Company	Rs. Million			Margins	
	Net Sales	Operating Profit	Net Profit	Operating Margin	Net Margin
Domestic					
Ranbaxy Labs.	44,286	4,292	6,177	9.7%	13.9%
Cipla	39,979	6,054	7,014	15.1%	17.5%
Dr Reddy's Labs	33,652	4,758	4,752	14.1%	14.1%
Sun Pharma	31,519	9,633	10,140	30.6%	32.2%
Lupin	25,236	2,666	4,434	10.6%	17.6%
Aurobindo Pharma	22,182	2,699	2,908	12.2%	13.1%
Piramal Health	19,139	3,986	3,015	20.8%	15.8%
Cadila Health	16,427	2,314	2,362	14.1%	14.4%
Glenmark Pharma	13,713	4,515	3,890	32.9%	28.4%
Orchid Chemicals	12,389	3,255	1,845	26.3%	14.9%
Wockhardt	12,218	2,107	2,139	17.2%	17.5%
Ipca Labs	11,035	1,646	1,411	14.9%	12.8%
Divi's Lab	10,332	3,847	3,536	37.2%	34.2%
Alembic	9,901	1,233	1,122	12.5%	11.3%
Torrent Pharma	9,846	2,211	1,555	22.5%	15.8%
Matrix Labs	9,521	-3,208	-2,984	-33.7%	-31.3%
Alkem Lab	8,950	1,254	1,441	14.0%	16.1%
Intas Pharma	7,542	192	610	2.5%	8.1%
Nectar Lifescn.	7,360	1,187	837	16.1%	11.4%
Foreign					
Glaxosmith Kline	16,653	5,062	5,766	30.4%	34.6%
Aventis Pharma	8,640	1,234	1,444	14.3%	16.7%
Pfizer	7,100	1,217	3,389	17.1%	47.7%
Abbott India	6,953	724	629	10.4%	9.0%
Novartis India	5,531	1,025	972	18.5%	17.6%
Wyeth	3,297	1,124	815	34.1%	24.7%
Merck	3,126	647	688	20.7%	22.0%
Astrazeneca	3,027	992	615	32.8%	20.3%

In terms of total sales, Ranbaxy Laboratories is India's largest pharmaceutical company and one of the world's top ten generic drug makers. Ranbaxy is a vertically integrated company with a presence across the pharmaceutical value chain, offering a range of unbranded and branded generics, active pharmaceutical ingredients, and biotechnology products. Cipla, India's second-largest pharmaceutical company, is best known for its anti-AIDs drugs, and Dr. Reddy's Laboratories, India's third-largest pharmaceutical company, also rely heavily on exports as its revenues.

Principal products of India's leading drug manufacturers

Company	Principal Products: bulk and generic drugs
Ranbaxy Labs	Anti-infectives, cardiovascular, gastrointestinal, central nervous (diazepam, midazolan), ophthalmic & ointments, urologicals, nutritionals, sex hormones, analgesics, anti-asthma, cough & cold, vaccines.
Dr. Reddy's	Cardiovascular, gastrointestinal, anti-infectives, pain management
Cipla	Antibiotics, anti-asthmatics, anti-AIDs and TB drugs, anabolic steroids, analgesics-antipyretics, antacids, anti-arthritis, anti-inflammatory, anti-cancer, antidepressant agents, anti-diabetic, anti-epileptic, anti-fungal, anti-malarial.
Wockhardt	Anti-infectives, pain management, nutraceuticals
Pfizer India	Nutritionals, cough syrup, anti-arthritis, anti-infectives, cardiovascular
Sun Pharma	Neuro-psychiatry, cardiovascular, gastrointestinal, diabetic, gynaecological, anti-allergic, antidepressants, cholesterol reducers, anti-asthma, Parkinson, ADD, pain.
GSK	Anti-infective, anti-inflammatory, analgesic, gastro-enterological, anti-allergic, dermatological.
Lupin	Tuberculosis medication, antibiotics, cardiovascular.
Cadila	Cardiovascular, gastrointestinal, anti-inflammatory/analgesic, antibiotics/anti-infectives, vaccines/immunomodulators, anti-diabetics; vitamins.
Nicholas Piramal	Analgesics-anti-inflammatory, antibiotics, antifungal, antihistamines, antiseptics, cardiovascular, central nervous system, diabetic, dermatologic, endocrinologic, gastro-enterological, vitamins, pulmonary-respiratory, trauma-emergency, gastrointestinal, NSAIDs.
Aurobindo Pharmaceuticals	Antibiotics, anti-retrovirals, cardiovascular, central nervous system, gastro-enterological, anti-allergy.

Many of the world's leading pharmaceutical companies have subsidiaries or other operations in India. Multinational companies like GlaxoSmithKline (GSK) Baxter, Aventis, Pfizer, Novartis, Wyeth, and Merck have been active in India's pharmaceutical market mainly through subsidiaries. The re-introduction of product patents precipitated the return of a large number of other MNCs, some of whom left during the process patent era. MNC pharmaceutical companies have also been attracted by tax holidays, the deduction of capital R&D expenditures, and other financial incentives offered by the Indian government. Industry sources indicate that the most significant challenges facing MNCs are the uncertainly over pharmaceutical price controls and data exclusivity.

There are approximately 34 foreign drug companies engaged in the Indian pharmaceutical market and among them are 15 of the world's 20 largest pharmaceutical companies. According to FICCI, although MNCs have not launched new products they have invested in new production facilities and R&D centres and many are engaged in contract manufacturing, clinical trials, and other forms of outsourcing.

However, many industry experts believe that the return of the world's leading pharmaceutical companies will gradually erode India's cost advantages. According to the Organization of Pharmaceutical Producers of India, multinational drug companies currently command 24% of the domestic Indian market, through their share could rise to 40% by 2010.

GSK-India, a 51% subsidiary of GSK Plc (UK), is the largest foreign company in India's pharmaceutical market, its fourth largest pharmaceutical company, and leading prescription drug supplier. GSK-India operates two Indian manufacturing plants. GSK-India is among India's

leading suppliers of anti-infective, anti-inflammatory, analgesic, gastro-enterological, anti-allergic, and dermatological drugs. GSK-India announced plans to extend its product line by launching several antibiotic, cancer, and cardiovascular products in India in the near term.

Likewise, MNCs dominate India's OTC (over the counter) drug market, with Pfizer accounting for 5.1% of the market, Sanofi-Aventis for 5.0%, and Johnson & Johnson for 4.8%. These companies offer analgesics, cough and cold preparations, indigestion medicines, skin care products, and vitamins and minerals. Other foreign multinationals active in India's pharmaceutical market include: Bristol-Myers Squibb, Eli Lilly, Boehringer, Bayer, Chiton Corp, Abbott, AstraZeneca, Janssen, and Roche.

Contract Research and Manufacturing, Outsourcing, and Other Services

The passage of the Patents (Amendment) Act 2005 has significant implications for both Indian and multinational companies competing in the Indian market. Leading Indian companies are moving away from a reliance on the domestic market to the development new drugs, exports to regulated markets, and cooperative agreements with MNCs. Facing lagging sales of patented drugs by MNCs in their home markets, declining R&D revenues, and rising costs, many MNCs have turned to contract manufacturing and research services (CRAMS), co-marketing alliances, outsourcing of research and clinical trials to reduce costs, increase development capacity, and trim the 'time to market' for new drugs. These strategies permit MNCs to focus on their core profit making activities (competencies), such as drug discoveries and marketing, rather than on manufacturing.

India has emerged as the principal destination for global pharmaceutical companies across the pharmaceutical value chain. Indian pharmaceutical companies have two basic options: compete with MNCs for vanilla generics and new chemical entities (new drugs) or co-operate.

Strategic Options for Indian Companies

Option to compete	Option to cooperate
❑ Market and sell plain vanilla and speciality generics.	❑ Provide contract manufacturing for MNCs
❑ Develop low risk NDAs	❑ Supply APIs to MNCs
❑ Develop follow-on biologics	❑ Partner with MNCs for their sales channels
❑ Challenge IPRs on regulated markets	❑ Provide clinical outsourcing for MNCs
❑ Invest in R&D for proprietary NCEs.	❑ R&D collaboration

Subcontracting in India has gradually moved up the value-added chain from intermediates and APIs to new drug discovery, clinical trials, marketing, and sales. According to India's Federation of Indian Chambers of Commerce and Industry (FICCI), many Indian companies, especially those without the resources for R&D, are embracing custom manufacturing, contract research, and marketing alliances to remain profitable. Others are planning to manufacture and export vanilla generics to regulated markets before eventually producing either more difficult to manufacture generics or new chemical entities (proprietary drugs).

CRAMS can be divided into 3 basic segments: the production of intermediates, active pharmaceutical ingredients for new chemical entities, and the manufacture of generic drugs. India has emerged as one of the world's leading CRAMS providers for MNC innovator companies and now accounts for between 6 and 7% of the global market and many expect India will command at least 15% of the market by 2009-10. Although CRAMS is still in its nascent stages in India, it represents a significant opportunity for medium-sized Indian pharmaceutical companies.

In 2005-06, the Indian CRAMS market was estimated at US$532 million with contract manufacturing accounting for nearly 84% of the total. The remainder consisted mainly of contract research (not including clinical trails). Both contract research and contract manufacturing grew by more than 40% in 2005 and 2006, and industry experts maintain that Indian companies have the capacity to gain between 35 and 40 percent of the global CRAMS market. The Associated Chambers of Commerce and Industry of India (Assocham) projects that the domestic Indian CRAMS market will reach $900 million by 2010 and the demand for contract clinical trials will grow from US$100 million in 2005 to US$200 million in 2007 and to US$1 billion by 2010.

India's competitive advantage lies in its lower production and research costs, its large pool of low cost technical and scientifically trained personnel, and the large number of US Food and Drug Administration (FDA) certified plants. Other important factors include the popularity of outsourcing non-critical business functions to India by MNCs, the reintroduction of product patents for pharmaceuticals, the growing importance of R&D related to drug discovery by Indian drug companies, and the growing demand for generic drugs in developed markets. It is estimated that manufacturing costs in India are between 30 and 40 percent lower than those in the US and Western Europe and labour costs are one-seventh of that in the US.

Western pharmaceutical companies are now outsourcing a wide range of activities including: the manufacture of APIs, chemical intermediates, and formulations; clinical research and clinical testing; and packaging and labelling. The Indian market for contract outsourcing has been driven by the need of leading MNC pharmaceutical companies to reduce production costs and increase revenues. These companies have shifted portions of the production, research & development, clinical trials, packaging and labelling, stability testing, and other types of drug development and discovery activities to India. Leading drug firms like Pfizer, AstraZeneca, Novartis, and Eli Lilly have already begun shifting a portion of these activities to India. The Chemical Pharmaceutical Generic Associations also predicted that this segment will reach US$1 billion by 2010. The Association indicated that India dwarfs its nearest rivals, Italy (US$60-$70 million) and Spain (US$25 million to $33 million), and projected that contract research in India will grow at an annual rate of between 20 percent to 25 percent. Clinical trials represent 65% of this market and new drug discovery makes up the remaining 35%. Companies active in India's contract research market include: a limited number of multinational corporations, subsidiaries of large international contract research firms (Quintiles, Covance), joint ventures and tie-ins between Indian and foreign companies, and stand-alone and offshoots of Indian companies. Several multinationals active in the Indian market have designated India as a hub for their production of

active pharmaceutical ingredients and finished formulations. Divi Labs, Shasun Chemicals & Drugs, and Dishman Pharmaceuticals are among India's leading contract research firms.

Clinical Trials

Industry-sponsored clinical research has traditionally been carried out in relatively wealthy locations in North America, Western Europe and Oceania. However, in recent years, a shift in clinical trials to so-called emerging regions, especially in Eastern European, Latin American and Asian countries, has been noted. Clinical trials increasingly occur on a global scale as industry and government sponsors in wealthy countries move trials to less wealthy countries. Since 2002, the number of active Food and Drug Administration (FDA)–regulated investigators based outside the US has grown by 15% annually, whereas the number of US-based investigators has declined by 5.5%.

Country-specific data on trial participation reveals considerable heterogeneity across geographical regions. The US dominates by a large margin, having more than eight times the number of trial sites than second-place Germany. The top five countries are all in traditional regions (North America, Western Europe and Oceania) and together host 66% of all trial sites. Countries in emerging regions (Eastern Europe, Latin America, Asia, Middle East and Africa) are mostly small players when analysed individually (each with less than 2% global share), but as a group they host 17% of actively recruiting sites. Eastern Europe and Latin America generally currently host more sites than Asia. However, emerging nations such as India and China have grown rapidly from an almost negligible base in just several years. Their high average relative annual growth rates, coupled with their very low density of trials and current levels of investment in clinical research infrastructure, suggest that they have potential to grow into major players in the future.

Country Trends in Participation in Biopharmaceutical Clinical Trials

Rank	Country	Number of sites	Share (%)	ARAGR (%)	Trial capacity	Trial density
1	United States	36,281	48.7	-6.5↓	43.7	120.3
2	Germany	4,214	5.7	11.7↑	10.9	51.2
3	France	3,226	4.3	-4.0↓	9.6	50.3
4	Canada	3,032	4.1	-12.0↓	8.6	92.2
5	Spain	2,076	2.8	14.9↑	6.8	46.4
6	Italy	2,039	2.7	8.1↑	6.7	34.6
7	Japan	2,002	2.7	10.3↑	33.4	15.7
8	United Kingdom	1,753	2.4	-9.9↓	7.6	29.1
9	Netherlands	1,394	1.9	2.1↑	6.8	85.0
10	Poland*	1,176	1.6	17.2↑	5.3	30.9
11	Australia	1,131	1.5	8.1↑	5.4	54.4
12	Russia*	1,084	1.5	33.0↑	5.8	7.7
13	Belgium	986	1.3	-9.4↓	5.2	94.8
14	Czech Republic*	799	1.1	24.6↑	4.5	77.6
15	Argentina*	757	1.0	26.9↑	4.8	19.0
16	India*	757	1.0	19.6↑	5.8	0.7
17	Brazil*	754	1.0	16.0↑	5.1	4.0
18	Sweden	739	1.0	-8.6↓	5.1	81.0
19	Mexico*	683	0.9	22.1↑	4.0	6.2
20	Hungary*	622	0.8	22.2↑	4.1	62.5
21	South Africa*	553	0.7	5.5↑	4.3	11.9
22	Austria	540	0.7	9.6↑	3.8	65.1
23	China*	533	0.7	47.0↑	5.3	0.4
24	Denmark	492	0.7	9.2↑	4.4	90.3
25	South Korea*	466	0.6	17.9↑	3.4	9.5

*Countries in emerging regions. ARAGR, average relative annual growth rate. Trial capacity is the number of sites in the country involved in large trials (20 or more sites) divided by the number of large trials in the country. Trial density is the number of recruiting sites on April 12th 2007 divided by the country population in millions.

Source: Nature

Through off-shoring of clinical trials, pharmaceutical and device companies can realise substantial cost savings. As a result, they are increasingly moving phase II and phase III trials to places such as India and South America. A first-rate academic medical centre in India charges approximately US$1,500-2,000 per case report, less than one tenth the cost at a second-tier center in the US. Since clinical research costs are driven by human labor, much of this cost difference is attributable to the lower salaries of physicians, nurses, and study coordinators in developing countries. Globalization of clinical trials may also shorten the timeline for clinical testing. The large pool of potential research participants and the lower cost of research in countries such as China and India provide opportunities to accelerate recruitment. Clinical testing in developing countries is also attractive to pharmaceutical and device companies because it can help them overcome regulatory barriers for drug approval in these countries in which the population size alone offers the promise of expanding markets. Widespread adoption of the International Conference on Harmonisation of Technical Requirements for Registration of

Pharmaceuticals for Human Use Good Clinical Practice (ICH-GCP) guidelines and stronger intellectual property protections in developing countries may also have contributed to the globalization of clinical research.

Overall, these trends have numerous public health, regulatory, economic and medical training implications. The globalisation of clinical trials can bring both health benefits and hazards to research subjects and the general population. Potential benefits include diffusion of medical knowledge and effective medical practice, and greater patient access to high quality medical care. Concerns include the possibly inadequate regulatory oversight of research activities in emerging regions and the difficulty in drawing valid scientific conclusions with pooled data from ethnically and culturally diverse populations. Additional areas of concern include ethical issues involving integrity of the informed consent process and suitability of the clinical research focus, and economic impacts from the shift of geographic allocation of clinical trails for the associated countries and companies.

Research and Development (R&D)

With the reintroduction of product patents, leading Indian pharmaceutical majors are altering their business strategies by placing greater focus on R&D and the discovery of new chemical entities. Traditionally, the vast majority of India's pharmaceutical R&D spending was concentrated on reverse engineering and the adaptation of patented foreign drugs to the Indian market. Most of the industry's funding went to research rather than to new drug discovery and development. Low levels of industry productivity and the relatively small size of India's pharmaceutical companies limited funding for R&D as they dedicated only less than 2% of their annual turnover to R&D compared with between 15 percent and 20 percent allocated by Western innovator companies.

After 2005, India's leading drug companies recognized that they could not survive as global players without significant R&D capabilities. Since 1995, total industry R&D spending has grown from nearly US$30 million to more than US$520 million in 2006-07. The vast majority of the industry's R&D spending is conducted by 15 companies whose R&D spending rose to US$210 million in 2006-07 from US$131 million in FY2004. R&D expenditures are expected to gradually rise to 9-11% of total industry spending by the end of 2008. Further, R&D spend of the leading companies has increased at a high rate in the recent past. In 2007, more than 175 companies had established R&D centres recognised by the Department of Scientific & Industrial Research. Around 15 companies are reported to be engaged in discovery research, spending around 10% of revenue on R&Ds. Ranbaxy, Dr. Reddy's Laboratories (DRL), Nicholas Piramal, and several other firms, have molecules in advanced stages of clinical testing, and the industry in total is reported to have about 60 compounds in various phases of development though no company has yet brought a drug to market. However, India's R&D expenditure as share of sales is miniscule compared with the average of 15% spent by global MNCs (around 18% in the US). In 2006, US R&D spending for the entire industry was estimated at US$55 billion. However, Indian companies have a lower cost-base, so the expenditure may `buy' more R&D in India than in North America or Europe.

Likewise, the vast majority of the industry's R&D expenditures on new drug discovery and development are conducted by a limited number of companies, with Dr. Reddy's and Ranbaxy at the forefront. Others with significant R&D expenditures include Nicholas Piramal, Aurobindo Pharma, and Glenmark Pharma.

Driven by the dynamics of the market, leading foreign pharmaceutical companies have entered into R&D agreements with India's leading drug companies. Facing spiralling costs and patent expiries for blockbuster drugs at home, many are looking to India as a low-cost alternative, especially due to the large number of US FDA-approved plants located in India. MNCs have been attracted by India's low costs for new drug discovery and many of these firms have founded state-of-the-art research facilities in India.

Whereas new drug discovery costs between US$100-1,000 million, the same process in India only costs approximately US$10-100 million. Likewise, clinical trials in India cost approximately US$20 million while the cost abroad would ranges between $300 million and $350 million.

Emerging R&D and Business Strategies

Emerging strategies of Indian firms are a natural response to an industrial and regulatory climate that still is not fully able to cater to the needs and concerns thrown up by tough international competition, and the losses induced by the restrictions placed on them by the new patent regime. They are a mix of both cooperative and competitive strategies, in order to adapt and capitalize on opportunities created by the new industrial environment. These emerging firm strategies portray a scenario that is very different from what was observed in several Latin American countries, where local firms mainly adopted cooperative strategies upon entry of foreign MNCs, thereby leading to vertical integration (as a result of acquisitions) and steep increases in drug prices. The behaviour of the Indian industry is more in keeping with what one would expect to see in an environment where a well-to-do local industry with clearly established areas of expertise is faced with strong international competition. Newer technologies and evolving market structures (in this case, as induced by the product patent regime and strong competition from global firms) almost always create new market segments and niches with many opportunities for specializations that the Indian industry is quick to capitalize upon, although this will also be accompanied by a high degree of consolidation in the industry in the coming years.

On the whole, each one of the three firm groups are using a combination of competitive and collaborative options to deal with pressures imposed by India's full-scale TRIPS compliance.

Group 1 firms are keen on having their own intellectual property protection in order to establish themselves within India and other regulated markets worldwide, as they are capable of investing in R&D. These firms, which have a turnover of over Rs. 30 billion, perform two main kinds of pharmaceutical activity: generics production and innovative R&D. These two are overlapping, i.e. firms are venturing into innovative options of generic production such as specialty generics and are also keenly developing their own marketing infrastructure within India and other regulated markets. The need to set up marketing infrastructure abroad has led

to several international acquisitions and alliances by Indian firms in the EU and the US in recent times. The experience of group 1 companies has been that while the entry barriers to regulated markets for the supply of generics are very high, the monetary returns and the ease of business that follows entry into these markets are both higher than in the semi-regulated and unregulated markets worldwide. Added profits earned by the sale of generic products in regulated markets make it possible for group 1 companies to make larger R&D investments. Group 1 companies in India are therefore choosing a mix of cooperative and competitive strategies to deal with challenges and opportunities post-2005.

Although most Indian companies clearly acknowledge that producing the next new blockbuster NCE (new chemical entity) in India is still some way off, most competitive strategies adopted by these companies are centred on enhancing their R&D focus. This includes the development of non-infringing processes, research on new chemical entities, generics and specialty generics for regulated markets, novel drug delivery systems and biopharmaceutical research. Cooperative strategies are predominantly focused on increasing internal technological competitiveness and higher revenues from greater sales in regulated markets by tapping the marketing networks of the non-Indian partners through collaborations. Some cooperative strategies are also geared towards helping MNCs use the marketing networks of Indian companies locally to market their products, in return for know-how or other desirable collaboration.

Group 2 companies have little or no investment capabilities to indulge in R&D, and will predictably remain pure generic suppliers or, at best, shift to niche activities in product development that involves minor modifications. Their main focus will be on specializing in order to make use of emerging opportunities for contract research and manufacturing (CRAM). Towards this end, group 2 companies are trying to establish themselves as niche players in CRAM by choosing specific areas where they can be competitive. Those who are planning to remain pure generic manufacturers are trying quickly to move in and capture shares in the semi-regulated and unregulated markets worldwide as the group 1 firms are gradually moving out of these markets into regulated markets.

In group 3 companies, contrary to popular misconceptions, it will mainly be the enactment of schedule M of the Indian Drugs and Cosmetics Act on minimum GMPs that will force unviable units to close down, as opposed to introduction of product patent protection. This segment of the industry will perhaps witness maximum consolidation in the next decade. Although many of the group 3 firms are also strategically aiming to benefit from contract manufacturing, either for larger Indian firms or even for foreign firms post-2005, only those who can upgrade their plants to at least the GMP standards as contained in schedule M of the Drugs and Cosmetics Act will tend to benefit. Even such a generalization has to be made with a note of caution, as the standards contained in schedule M of the Indian Drugs and Cosmetics Act are much below the WHO standards on GMPs. In this context, it remains unclear as to whether group 3 companies that do upgrade their facilities to the standards specified under schedule M can indeed target manufacturing for MNCs/firms operating outside India. In order to be able to manufacture for foreign partners from regulated markets, standards of foreign inspectors, such as the US FDA, will need to be met by group 3 firms, which are much more stringent than both the Indian and WHO standards on GMPs. It therefore seems more likely that most such companies that do

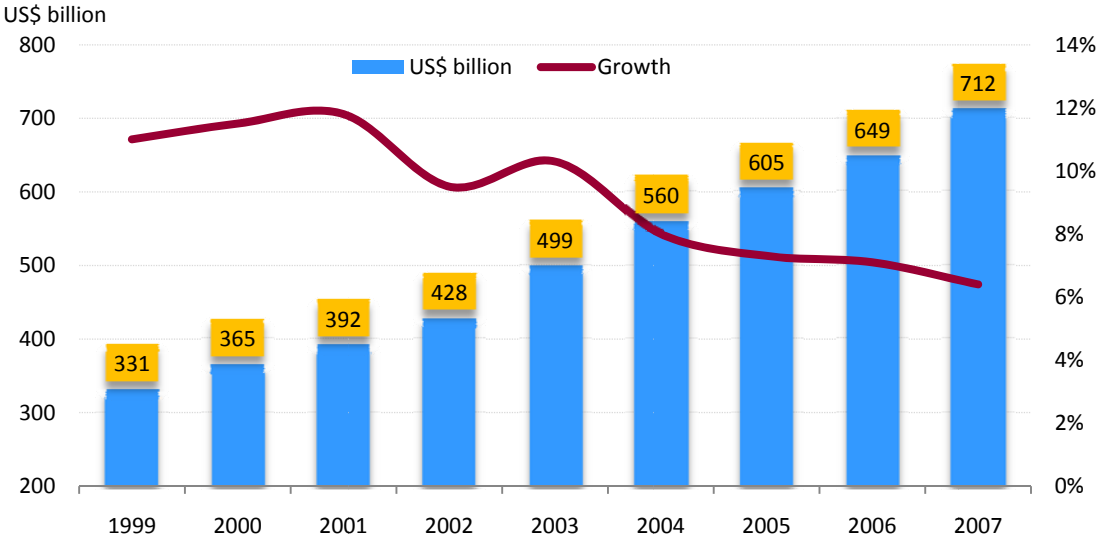
adhere to GMP standards as specified by schedule M will manufacture for group 2 companies in India who are looking at filling in the demand for generics in the unregulated and semi-regulated markets or foreign partners directly from the unregulated and semi-regulated markets. Alternatively, group 3 companies that comply with schedule M will also supply to companies that are targeting the domestic Indian market.

GLOBAL TRENDS

Increased Consumption with Increases in Per Capita Income

The global pharmaceutical market reached US$712 billion in 2007, up 6.4% from the previous year sales of US$649 billion. In general, income per capita is positively correlated across countries with the volume of pharmaceutical consumption and expenditure per capita. However, income is not the whole story. In fact, per capita income explains only one quarter of the variability observed in per capita volumes of consumption across countries, and even less of the variability in expenditure and retail price levels. This is consistent with findings from research indicating that pharmaceutical demand varies across countries and is relatively income-inelastic –meaning that expenditure changes with income, but not as fast as income does.

World Pharmaceutical Sales



The global pharmaceutical market is expected to grow 4.5-5.5% in 2009, a rate similar to forecast growth of 5% in 2008. IMS Health has predicted global pharmaceutical sales to surpass US$820 billion in 2009, reflecting sustained double-digit growth in key emerging countries tempered by a slower pace in more established markets. This includes the US, where growth is expected to be in the 1-2% range for both 2008 and 2009. In 2008, the US pharmaceutical market, the world's largest, is forecast to grow 1-2% to US$287-297 billion. Contributing to the slower growth is less-than-expected demand for recently introduced products, as well as the economic climate, which appears to be having an impact on doctor visits and pharmaceutical sales. In 2009, the expected 1-2% growth rate in the US will result in sales of US$292-302 billion, and reflects the impact of continuing patent expirations, fewer new product launches and a

tighter economy. The top five EU countries (France, Germany, Italy, Spain and the UK) are forecast to grow 3-4% in 2009, reaching sales of US$162-172 billion. In Europe, growth driven by the continued aging of the region's population and rising demand for preventive care will be tempered by the increased impact of health technology assessments, the use of contracting by payers as a means to control costs, and the decentralization of government healthcare budgets. Japan, the world's second-largest market, is expected to see higher growth of 4-5% in 2009, reaching US$84-88 billion.

By comparison, the emerging markets of China, Brazil, India, South Korea, Mexico, Turkey and Russia are forecast to grow at a combined 14-15% in 2009 to US$105-115 billion. Along with the pharmaceutical industry's increased focus on these high-growth markets, these countries are benefiting from greater government spending on healthcare and broader public and private healthcare funding – which is driving greater access to, and demand for, innovative medicines.

Out-of-pocket Payments Important Sources of Spending

Private sources play a bigger role in financing of pharmaceutical expenditures– accounting for 40%, on average – than of other components of health spending, although the bulk of pharmaceutical spending is publicly financed in almost all major countries, except in the US. Out-of-pocket spending is generally more significant than private health insurance, which is an important source of financing for drug spending in only a handful of countries (the US, Canada, and France).

High Market Concentration

The products of ten large firms account for much of the global pharmaceutical market. In 2007, the top ten pharmaceutical firms accounted for nearly half the value of global sales. The market for pharmaceutical products is increasingly a global one, with trade and policy practices making market segmentation and corresponding price differentiation by country difficult – particularly within Europe, where multinationals have encouraged their subsidiaries to set prices within narrow price corridors. New active ingredients are launched in an average of ten countries, although manufacturers often release multiple versions of their on-patent products in different markets to reflect consumer preferences and to reduce opportunities both for prospective buyers to make external price comparisons and for wholesalers to engage in parallel trade.

Key Markets

The US is the predominant market in terms of pharmaceutical sales value. With sales of US$278 billion in 2007, it accounted for 44% of world sales. It is worth noting that US companies invested a record US $58.8bn in 2007 in R&D.

Nine OECD countries account for about 80% of the value of global sales of pharmaceuticals. The US, with a 44% global share, is the world's largest market, followed by Japan, which accounts for 9% of global sales, France (6%), Germany (5%), the UK (4%), and Italy (4%).

Most Sales Revenues From On-Patent Products

Just ten therapeutic classes of drugs accounted for 36% of total global sales in 2006-07, a year in which approximately 105 original products were considered `blockbusters' i.e. each generating more than US$1 billion in annual sales. By contrast, generic products accounted for just 14% of the global market in terms of value, although more than 40% of products sold in several large markets, including the US, Germany and the UK, are generics.

Strong Growth in Generic Sales

Global prescription sales growth of generics drugs slowed to 3.6% to US$78 billion in the year ending September 2008. Although the global generics market has posted double-digit gains in recent years, growth slowed down in 2008 as manufacturers increasingly compete in fierce price battles within most of the world's major markets. This trend is very apparent in markets like the US and UK as generics companies contend with aggressive competition and cost-containment measures enforced by both private and government payers."

The top eight global markets—the U.S., Germany, France, the U.K., Canada, Italy, Spain and Japan—account for 84% of total generics sales. The US, the world's largest generics market with 42% of global sales, has experienced a 2.7% sales decline in the twelve months ending September 2008 while volume increased 5.4% during the same period. Generics products now account for 63.7% of the total US pharmaceutical market volume. The US generics market is currently valued at US$33 billion, compared with US$34 billion in 2007, reflecting declining prices and fewer blockbusters losing patent protection in 2008. However, generics sales rose 10.2% in Japan, 16.9% in France, 12.5% in Italy and 10.5% in Spain in the twelve months through September 2008.

The top 10 generics companies currently hold a 47% share of the generics market worldwide. The three leading generics manufacturers are Teva with 11% market share, Sandoz with 9%, and Mylan with 8%.

A major threat to the pharma market is increasing competition from generics, with over US$17 billion of branded drugs having lost exclusivity in 2007. The extent and rate of generic erosion following patent expiry varies across the 7 major markets, being most intense in the US, where it is estimated at 88% for standard oral solids two years after generic entry.

Total Generic Sales in the US/Major EU Countries

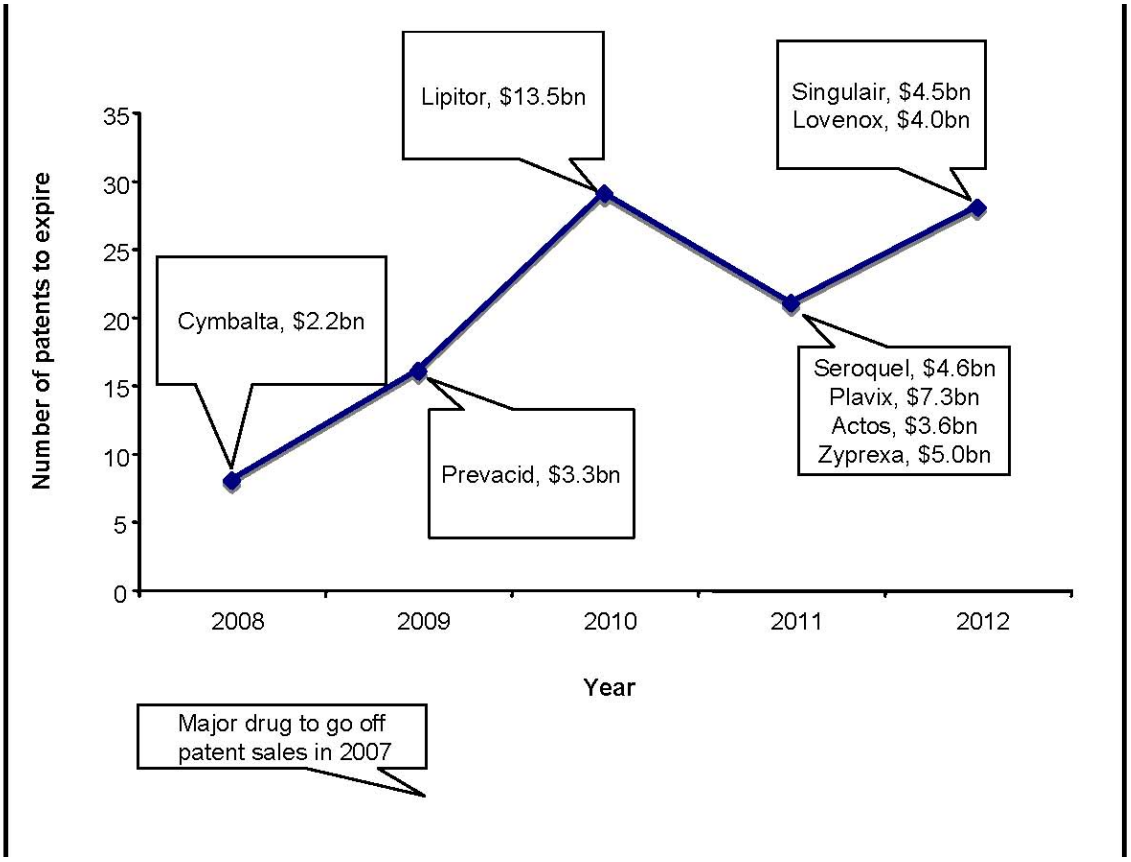
Country	Sales in 2007 (US$ million)	CAGR (2003-07)
US	25,435	13.0%
France	3,495	30.4%
Germany	3,475	11.5%
Italy	945	26.2%
Spain	1,326	23.8%
UK	4,449	15.0%

A major threat to the pharma market is increasing competition from generics, with over US$17 billion of branded drugs having lost exclusivity in 2007. Over the next 5 years, US$129 billion of branded pharmaceuticals are expected to face generic competition. In 2009, an additional US$24 billion of branded products, including anti-epileptics, proton pump inhibitors and anti-virals, will lose their market exclusivity in the top eight markets in 2009.

The generics industry has increased its sales at a more rapid rate than the rest of the pharmaceutical market. The extent and rate of generic erosion following patent expiry varies across the 7 major markets, being most intense in the US, where it is estimated at 88% for standard oral solids 2 years after generic entry. This compares with much lower erosion in Southern European countries (for example, 19% in Spain) where generic use is more limited. In the US, 103 drugs are due to go off patent during 2008–12, with total sales of US$62 billion in 2006.

Drug Patent Expiries in the US

2008-12



Several key blockbuster drugs are due to lose patent protection in the coming ten years including Lipitor which is currently the number one product by sales revenue in the world pharmaceutical market with sales revenue of US$13.5 billion in 2007 which has an estimated patent expiry in 2010. It is estimated that in the next five years alone drugs with sales of over US$120 billion are going to lose patent protection. This will begin a period of decline for blockbuster drugs and has already forced pharma companies to change their focus to specialty

drugs in niche indications rather than develop drugs to treat conditions that affect large numbers of patients, such as infectious diseases, GI disorders, high cholesterol, and high blood pressure.

Of the top ten pharma companies in the global pharmaceutical industry the majority are extremely reliant on their top 5 products to generate the bulk of the company's sales. It is interesting to note that Novartis, the fourth largest pharmaceutical company by global annual sales revenue, gained the smallest proportion of its revenue from its 5 leading products.

Sales contributions to the top 10 companies from their 5 leading product

2007

Company	Total Sales	Sales of Top 5 products	Revenue share of top 5 products
Pfizer	44,576	22,789	51.1%
GlaxoSmithKline	36,968	15,030	40.7%
Sanofi-Aventis	33,231	13,678	41.2%
Novartis	32,791	10,287	31.4%
AstraZeneca	30,053	17,480	58.2%
Johnson & Johnson	28,263	15,253	54.0%
Merck & Co	27,257	14,506	53.2%
Roche	26,690	13,002	48.7%
Abbott	17,276	8,904	51.5%
Lilly	16,694	10,678	64.0%

The challenges facing pharma have elicited immediate strategic responses by pharma, which have been to cut costs in order to improve profitability. This has been achieved through outsourcing, R&D efficiency and job cuts. Major global companies are increasingly turning to contract research organizations (CROs) and contract manufacturing organizations (CMOs) in the emerging markets or establishing their own facilities in countries such as India, China, South Korea, and Singapore.

Significant Variation in Prices

The prices manufacturers receive for their products vary across countries, although there is less variation in prices for the most innovative products. Japan, Switzerland and the US have particularly high ex-manufacturer prices for patented medicines. Japan and Switzerland also have high ex-manufacturer prices for generic products. Studies have found that ex-manufacturer prices vary according to national income per capita, although there are important exceptions. In particular, such prices are higher than expected in some low-income countries, including Mexico. Further, there is less cross-country variation in ex-manufacturer prices for those products representing significant innovation.

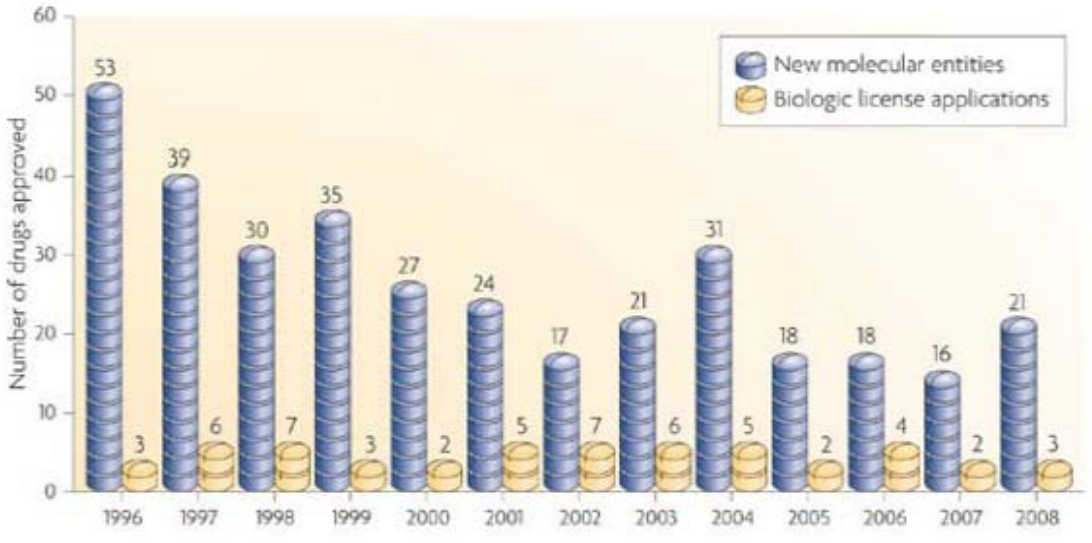
Falling R&D Productivity and Decline in Output of New Drugs

In spite of continuously increasing R&D investment, output of new drugs has declined and most pharmaceutical innovation has been incremental. Because most R&D initiatives are unsuccessful in bringing a new product to market, the total amount of investment per successful drug – an indication of the "productivity" of R&D spending in the pharmaceutical industry – is very large. A

decline in productivity has been evident since the mid-1990s, as increased R&D investment has coincided with a decline in the number of new chemical entities approved for marketing. As is true in other industries, most pharmaceutical innovation has been incremental, rather than radical. Most such innovation has little or no added therapeutic value over existing treatments.

It is widely believed that the pharma industry is facing an R&D productivity crisis with soaring costs and fewer product approvals. In the US drug approvals reached a peak in 1996 and have been decreasing in number in the years since then. US FDA approvals in 2008 totalled 21 new molecular entities (NMEs) and 3 biologic licence applications (BLAs) that were evaluated by the Center for Drug Evaluation and Research (CDER). Although the overall number of approvals increased in 2008, the number of agents given priority reviews—a reflection of their perceived potential to address unmet medical needs—was nine in both 2007 and 2008. The decline in approvals is partly attributable to the increased level of regulatory caution (in the wake of high-profile safety issues) and increased FDA workload. The increased level of regulatory caution appears to because less scientific and medical literature is available for novel drugs. Changes to FDA internal processes and increased workload may also be affected approvables. In recent years, the US FDA has been struggling to meet its Prescription Drug User Fee Act (PDUFA) goals to achieve review of 90% of NDAs and BLAs within 10 months for standard reviews and within 6 months for priority reviews. The reasons that the FDA has given for not meeting PDUFA goals include increased workload, in part related to the FDA Amendments Act (FDAAA) 2007, which introduced new authorities to require post-market studies, safety labelling changes, and risk evaluation and mitigation strategies (REMS).

FDA Drug Approvals



The data above indicate that the pharmaceutical industry has not been highly productive in achieving FDA approval of new drugs in the past few years. However, data for 2006 and 2007 also indicate that products from pharma that have reached Phase III trials have had a high rate of approval.

Pharma is also facing increasing drug development costs. In 2004-05, the total cost of bring a drug to market was as high as US$1.7 billion, with clinical trials costing approximately US$5,500, US$6,500 and more than US$7,600 per patient for Phase I, II, and III, respectively. One explanation for the increased expense of drug development is that clinical trials are taking longer than ever, with drugs in the US taking 7 years on average to pass through clinical development, an increase of 20.6% since 1999–2001. In contrast, the time taken for a drug to gain FDA approval has fallen by 50% from 3 years (1984–86) to 1.5 years (2002–04). As such, any delay in a drug's launch is extremely costly, and each day delayed could cost the manufacturer US$23 million in lost sales in the US and approximately US$37,000 per day in additional development costs. The most common reason for delayed launch is through longer clinical trials or regulatory non-approval leading to additional clinical development. Consequently it is vital that companies ensure that sufficient safety and efficacy data are attained before regulatory submission.

This large increase in costs can be largely attributed to the reduction in productivity. For every 13 compounds that are discovered only one will reach the market. The 12 compounds that fail to reach the market will of course use up valuable R&D investment and increase the total cost of the marketed product's development.

For every 13 compounds that are discovered only one will reach the market. The 12 compounds that fail to reach the market will of course impart a huge financial loss on the company. This is particularly the case if the product has reached the late stages of development as significant investment will have already been made. The problem of products failing in clinical trials is increasing. Between 2001 and 2006, the success rates of drugs entering Phases I, II and III progressing to launch have declined by 23%, 20% and 11% respectively. The likelihood of success and time to market on a per-compound basis vary widely across therapeutic areas.

Success Rates and Time to Market across Therapeutic Areas

Therapeutic area	Probability of approval (from Phase I)	Time in clinical development (months)
Hormones (excluding sex hormones)	65%	94
Antiparasitic	59%	103
Formulations	56%	83
Anti-infectives	50%	87
Musculoskeletal	44%	101
Dermatological	43%	86
Cardiovascular	42%	103
Alimentary and metabolic	40%	99
Blood and clotting	37%	106
Genitourinary (and sex hormones)	36%	90
Immunological	35%	98
Respiratory	35%	103
Neurological	32%	108
Anticancer	24%	108
Biotechnology	21%	100

Source: PharmaPredict

In an attempt to minimize such occurrences products are being discontinued in the earlier stages of drug development. The most common reasons for such failures include failure to demonstrate a significant difference from a placebo, safety issues and concerns or failure to demonstrate superior efficacy over the active competitor. To avoid late stage attrition pharma is increasingly looking to more innovative technologies in drug discovery to increase the rigor with which drugs are tested, such as ADMETox, and looking to select better targets for example through the use of RNAi. Recent failures or discontinued phase III clinical trials include:

Techniques to Maximise Profits

The pharmaceutical industry uses a range of techniques to maximise profits over a product's life cycle. Since marginal production costs are relatively low, maximising profits translates into maximising cash flows during the life of a product. In each market where sales would be expected to enhance a product's global profitability, pharmaceutical firms endeavour to launch products quickly at the price that maximises prospective profits. Firms try to extend the period of market exclusivity and to engage in promotional activities that aim both to capture as large a market share as possible and to increase the potential market. By some estimates, pharmaceutical marketing expenditures account for a share of firms' outlays that exceeds that of R&D expenditures. Furthermore, the costs of doing business in different countries vary, depending on factors such as the burden imposed by regulatory compliance, the types of marketing and/or advertising activities permitted and the exposure to liability for safety or quality problems.

In order to overcome spiralling R&D costs and reduced R&D productivity, the pharma industry is experimenting with a variety of different R&D strategies. This has mainly involved the migration away from internally driven R&D organizations through the establishment of centers of R&D excellences/disease focuses R&D centers towards an externally driven structure utilizing CROs locally, internationally and more recently in emerging markets to discover, optimize and clinically assess new candidates. In addition, companies are tapping into a number of external sources such as open source research, as well as establishing cooperatives (CRADAs) and private-public partnerships (PPPs). During the last decade the industry has in-licensed late stage products from biotechs and technology aggregators and more recently spun off R&D companies to attract investment to rejuvenate product portfolios and restore the status quo, make use of tax incentives and de-risk R&D strategies from the development of clinical candidates.

As noted above, pharma companies are increasingly turning to CROs and CMOs in the emerging markets or establishing their own facilities in countries such as India, China, South Korea and Singapore. These Asian countries have operating costs up to 50% lower than in the developed countries, and thus Asia is becoming the destination of choice for manufacturing APIs, conducting clinical trials and recently early stage R&D. However, as a result of concerns regarding IP protection, most manufacturing is centered on more mature products with companies uncertain of adequate IP protection and that widespread drug counterfeiting would present high risk to new, patent-protected drugs.

It is estimated that 20% of Pharma and Biotech's research budget of US$83 billion is spent on CROs. By 2010, global expenditure on CRO services is forecast to reach over US$26 billion by 2010 accounting for 22% of the pharma budget with the majority of outsourcing focusing on Phase III and drug discovery. China and India have emerged as top destinations for clinical trials due to their huge patient pools. Most global CROs are present in India or have formed alliances there: seven out of the top 10 CROs have local offices in India with leading companies such as Quintiles, Chiltern, ICON Clinical Research building up a significant Indian presence.

Mitigation Strategies for Genericization

Drug developers may utilize a variety of options to maximize product sales and minimize the impact of generic competition, including indication expansion, reformulation, second generation launch, Rx-to-OTC switch, own generic launch and divestiture.

Since generic entry very often entails a dramatic fall in revenues for original products, pharmaceutical companies have developed a set of strategies aimed at maximising patent life and/or countering generic entry and competition.

Pharmaceutical companies usually engage in so-called `strategic patenting', i.e. sequential filing of multiple patents for multiple attributes of a single product (basic composition, synthetic production, formulation, etc.). Companies often file applications for new patents just a few months before patent expiry of their existing on-patent products in order to maximize the duration of market exclusivity.

Companies also introduce line extensions. They create new formulations of existing products (new administration mode, extended release), new dosages, new molecule associations, and chemical derivatives of the original molecule (such as isomers, esters, active metabolites, etc.). Line extensions do not always offer a significant therapeutic advantage over the original product. When these products manage to reach the market before generic entry, they are likely to capture a part of the potential market for generics, particularly in cases where purchasers are not price-sensitive.

Further, in the 1990s many pharmaceutical companies engaged in aggressive strategies to protect their intellectual property rights, engaging in litigation with generic manufacturers for patent infringement. In the US, pharmaceutical companies were accused of having abused patent litigation in order to benefit from the additional months of exclusivity that were granted in case of litigation by the temporary suspension of generic sales. A few companies were condemned for violation of anti-trust law and required to pay damages to health insurance plans or patients for financial losses due to delayed generic entry.

Other strategies used by manufacturers to minimise losses from generic competition are the production of a generic by the originator company or by a licensee; a switch to OTC status in cases where the company can count on consumers' brand loyalty; and reduction of the original product's price.

The launch of authorized generics has become an increasingly common defense strategy for many pharmaceutical companies. Either through coming to a deal with a generics company or through the use of their own generics subsidiaries such as Novartis' Sandoz and Pfizer's Greenstone. Launching an authorized generic has the advantage in the US of receiving the 180 day market exclusivity granted to the first to market product. This ensures that there is only one competitor generic on the market for 180 days and also either gains them some form of royalties from the generic (in the case of a pharma/generic company deal) or where they have a generics subsidiary the originator gains all of the revenue. The strategy can also limit the reward earned by generics companies for challenging patents, thereby discouraging the practice. Going forward, continued use of this strategy by the branded pharmaceutical industry is likely to further reduce the threat of patent challenges, especially for smaller products with limited sales potential.

Therefore, many generics companies will become increasingly interested in collaborations involving an authorized generic and branded players will find no shortage of potential partners with which to implement this strategy. This is particularly true since overall, generics players with 180-day exclusivity periods have been unsuccessful in challenging the launch of authorized generics during those periods.

Smaller generics producers are experiencing significant margin pressure in this environment. At the same time, large companies are consolidating their operations in established markets or expanding into emerging ones through local acquisitions or partnerships. As a result, the generics industry is becoming more divided between large, high-performing companies extending their global footprint and smaller, local producers.

Widespread health insurance coverage distorts the market for pharmaceuticals

The coverage schemes that subsidise the amount individuals spend on pharmaceuticals and protect them against the risk of incurring high out-of-pocket costs also distort the pharmaceutical market, affecting both prices and volumes of consumption. They define the degree to which the pharmaceutical market is subsidised, with greater subsidies resulting in relatively lower consumer price elasticity of demand. While there is great cross-country variation in cost-sharing requirements, individuals in OECD countries typically bear much less than half the cost of their pharmaceutical consumption, resulting in consumption that is greater than it otherwise would be if individuals paid the full cost. Beyond this, coverage schemes differ importantly in the extent to which they seek to manage the volume and mix of pharmaceutical consumption, with many coverage schemes having few restrictions on choice by physicians and patients while others are active in efforts to affect physician, pharmacist and/or patient decision-making.

Promotional Strategies

Pharmaceutical companies engage in various activities to promote sales of their products. Promotional activities serve two purposes. The first is to try to attract market share away from competitors by increasing awareness of the product and its relative benefits. The second is to

expand the total market size of the product, which may include promoting alternative applications or increasing awareness of conditions for which the product might be used.

Promotion directed at physicians varies from detailing – office and hospital-based visits of sales representatives – to advertisements in medical journals, as well as gifts and free sample products. Pharmaceutical companies also play a large role in providing medical education and especially continuing medical education, by organising and sponsoring conferences and other events.

The significant role the pharmaceutical industry plays in educating physicians is highly contested. From the physician perspective, sales representatives are a readily available, well-educated and easily accessible source of targeted information about new drug therapies. On the other hand, sales representatives are unobjectively seeking to represent their products to the physicians as being better than any others on the market. The passive promotion of off-label use by manufacturers is another controversial technique used to promote sales. The effect of these promotional activities on physician prescribing behaviour is large, although this influence is not always acknowledged by physicians.

The role of consumer advertisements is increasing, although direct-to-consumer advertising (DTCA) is mainly directed at a few products; half of industry expenditures on DTCA in the US were for 20 drugs. DTCA is allowed only for OTC drugs in most countries, with the exception of the US and New Zealand. In those two countries, it is allowed for more drugs under specific guidelines. In the US, television and magazines are the most-used forms of media to promote pharmaceutical products. DTCA, however, cannot stand on its own and for a pharmaceutical promotion to be successful, professionals must also be targeted.

Professional detailing thus also plays an important role in preparing physicians for patient requests arising from DTCA, and increasingly the pharmaceutical industry provides physicians with free product samples to be given to consumers. The influence of the promotional activities is large in most countries. There are codes of practice between the pharmaceutical companies, medical associations and government, to ensure promotional activities to be carried out in a responsible, ethical and professional manner.

The importance of these promotional activities for sales can be surmised by the large amount of resources directed to promotion by the industry. In the US, promotional expenditures constitute 18% of the value of pharmaceutical sales. Providing free drug samples to physicians constitute by far the largest component of promotional spending (62% of total promotional spending). As an indication of the importance of promotional activities to pharmaceutical companies, 44% of the people employed by GlaxoSmithKline globally are involved in sales.

Trends in Disease Focus of Drug Development

Since the introduction of a policy by the International Committee of Medical Journal Editors (ICMJE) requiring that interventional clinical trials are registered in a public trial registry at their outset as a condition of publication, the US trials register (ClinicalTrials.gov) has become a truly

global register of industry-sponsored Phase II–IV clinical trials. This registry has provided new opportunities to analyse ongoing clinical trials and recent trends in the disease focus of drug development.

Thus, data from ClinicalTrials.gov for all `industry-sponsored' Phase II–IV interventional studies on November 2007, including trials that were first registered between October 2005 and September 2007, giving two full years of data.

Most registered trials were in oncology, followed by central nervous system (CNS) disorders, cardiology, infectious diseases, endocrinology, and respiratory disease. These six therapeutic areas accounted for around two-thirds of all protocols and over two-thirds of all sites. The number of registered trials for each area corresponds to the leading causes of deaths reported for developed countries. Among the six largest therapeutic areas, respiratory diseases, endocrinology and oncology showed a growth in the number of trials in the period analysed. The highest relative growth was seen for rheumatology (157.6%), and the lowest was for cardiology (74.3%). The number of studies increased for three of the top ten diseases: rheumatoid arthritis, asthma and hepatitis. Indeed, rheumatoid arthritis became the third most common disease for clinical trials. A considerable change in the focus of trials in therapeutic areas is therefore noticeable over just two consecutive years.

Highest ranked therapeutic/disease areas

2005-07

Therapeutic/ disease area	Year 1		Year 2		Total		Sites per protocols (n)	Growth* protocols (%)	Growth* sites (%)
	Protocols (n)	Sites (n)	Protocols (n)	Sites (n)	Protocols (n)	Sites (n)			
Oncology	405	13,375	419	10,520	824	23,895	29.0	103.5	78.7
CNS	337	10,141	333	5,753	670	15,894	23.7	98.8	53.2
Cardiology	346	11,166	257	6,888	603	18,054	29.9	74.3	61.7
Infectious	310	6,049	256	4,572	566	10,621	18.8	82.6	75.6
Endocrinology	272	11,120	276	5,677	548	16,797	30.7	101.5	51.1
Respiratory	144	4,637	160	4,237	304	8,874	29.2	111.1	91.4
GI and hepatology	120	5,173	108	3,016	228	8,189	35.9	90.0	58.3
Kidney/urology	94	2,560	114	2,231	208	4,791	23.0	121.3	87.1
Ophthalmology	85	526	92	865	177	1,391	7.9	108.2	164.4
Rheumatology	59	2,972	93	3,295	152	6,267	41.2	157.6	110.9

*Percentage increase: (number in Year 2)/(number in Year 1) × 100. CNS, central nervous system; GI, gastrointestinal.

Oncology is the largest therapeutic area in terms of clinical-trial activity, with more early phase trials than any other area, highlighting the strong industry focus on cancer at present. Anticancer drugs are the second largest therapy market, with US$41.4 billion in global pharmaceutical sales in 2007. This is marginally second to sales of lipid regulators, for which the market in this period was worth US$33.7 billion. Breast cancer and lung cancer (which are also the most prevalent cancers, together with prostate cancer and colorectal cancer), are the two cancers with the greatest amount of clinical-trial activity. Although the two leading cancer

indications show a decrease in the number of studies over the past 2 years, other cancer types showed strong growth.

The second largest therapeutic area is CNS disorders. The top two disorders for which trials are being conducted are depression and schizophrenia. Both indicate negative growth, with relatively few early phase trials. This might reflect the lack of success in the development of novel drugs for psychiatric diseases in the past two decades compared with other therapeutic areas. However, four other CNS diseases—multiple sclerosis, Alzheimer's disease, sleep disorders and attention-deficit/hyperactivity disorder—contradict the pattern, showing positive growth with relatively earlier phase trials, indicating a shift of focus within CNS diseases.

Cardiology is the third largest therapeutic area, although the number of trials for leading cardiovascular diseases showed a decrease. Hypertension ranks second overall for all diseases, but showed a decline in the number of trials, and only one out of every five studies on hypertension is a Phase II trial. For many decades the pharmaceutical industry has conducted large-scale cardiovascular clinical trials for conditions such as hypertension and atherosclerosis, and four cardiovascular drugs were among the top ten leading products by global sales in 2007. However, although age-standardized deaths rates have been reduced by half for heart disease, it is still the leading cause of death. This could be because it might now be considered financially risky to develop a new cardiology drug that will eventually need to compete with current strong market leaders, many of which soon will become generics. The need for large, long-term expensive trials might also make the area less favourable compared with others.

Infectious diseases accounted for the fourth largest number of trials, but also showed a decrease in the number of trials in the period studied. Most notably, bacterial-disease trials are decreasing in numbers, and so is the proportion of early phase trials in this area, thus underlining the diminishing industry focus on antibacterials in the past decade. Only one major infectious disease, hepatitis, showed a growth in the number of studies. Hepatitis, especially type B, is a major chronic disease in some countries.

The fifth largest therapeutic area was endocrinology, driven in particular by 356 new trials registered for diabetes, which is the top-ranked disease in terms of overall trials in the period analysed. This compares with 165 trials for hypertension, the second largest disease under trial. The prevalence of diabetes is also increasing, which is partly due to increased obesity. For such reasons, diabetes drugs were the fifth leading therapy class, accounting for US$24.1 billion in global pharmaceutical sales in 2007.

In endocrinology, obesity also had a strong growth in the number of trials, as well as a high proportion of early phase trials. So far, only a few weight-loss medications have been approved, but these are limited by side effects such as cardiac toxicity, hypertension, psychiatric symptoms and faecal incontinence. It is predicted that obesity therapies will become important, and a substantial number of new obesity drugs are in early clinical trials.

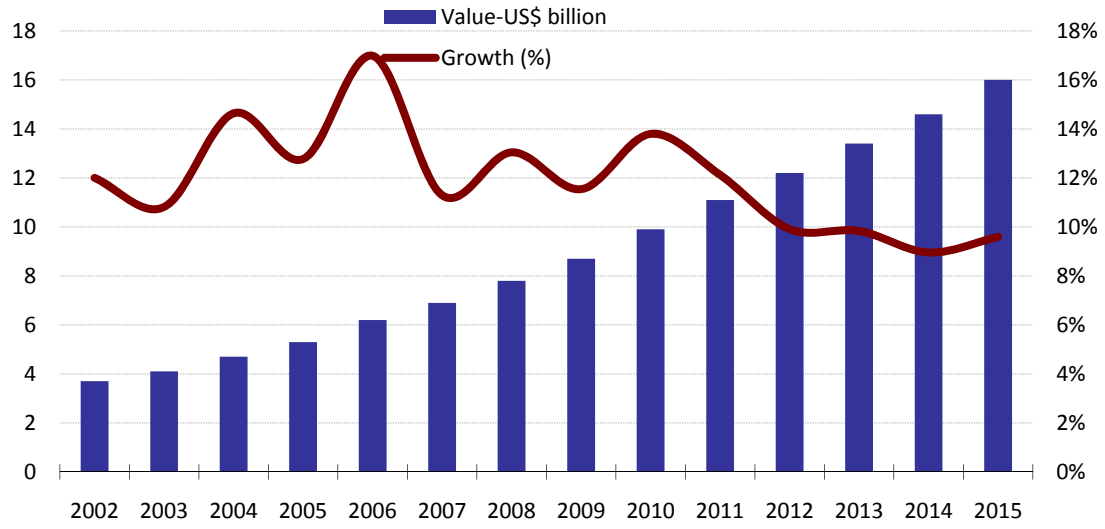
In summary, between 2005 and 2007, the US clinical trial registry indicated priority changes for sponsored clinical trials in various therapeutic areas— notably a growth in oncology trials and a decline in cardiology trials.

INDIAN MARKET

The Indian pharmaceutical market is small, both by Western standards and in terms of per capita consumption. Although India is the world's leading producer of generic drugs, its annual per capita consumption of pharmaceuticals is among the lowest in the world at approximately Rs. 190 (US$4.50) per person, as compared with US$820 in the US and US$13 in China in 2006. The value of India's pharmaceutical industry nearly doubled from US$3.2 billion in 2000 to more than US$10.8 billion in 2007-08, or by an average of 15-16% annually. The Indian domestic pharmaceutical market size is estimated at Rs. 433 billion (US$10.76 billion) in 2008 and is expected to grow at a high CAGR of 9.9%% till 2010 and thereafter at a CAGR of 9.5% till 2015. This growth is expected to be driven by: access to low cost, high volume generic drugs; mergers and acquisitions: industry consolidation; and India's growing importance as a pharmaceutical contract manufacturing and services location.

Estimated Retail Size of India's Domestic Pharmaceutical Industry

US$ billion



Approximately 80% of domestic industry production consists of formulations, with the remainder consisting of bulk drugs.

The development of the service industry in India and rapid growth of manufacturing exports in China has resulted in the creation of a booming middle class in these two countries. Although this social layer represents only a small fraction of the total population, it is expected to grow significantly, especially in India, provided economic growth is sustained in the mid-to-short term. The emerging middle class has growing disposable income and lifestyles that are becoming ever more Western, this has resulted in increasingly high prevalence of Western

lifestyle diseases. The middle class's preference for Western branded goods is also translated into preference for foreign pharmaceuticals over cheap domestic generic copies.

One of the key attractions of India and China is their huge population: even if only a fraction of the population has access to modern drugs, this represents a sizeable number of consumers. However, the increase in the elderly population compounded with increasingly Westernized lifestyles has meant epidemiological trends in emerging market countries are growing closer to those seen in Western markets, prompting a shift in therapeutic focus: sales of anti-infectives that traditionally dominate emerging markets are slowing down and are being taken over by the CNS, cardiovascular, gastrointestinal and metabolic agents. Sales of oncology drugs are still low compared to the major pharmaceutical markets, however, they are growing rapidly.

Although the patient potential of the emerging market countries is enormous, currently foreign companies tap into only a fraction of the consumers, as access to drugs is fairly poor in developing countries such as India and China. Recent economic growth seen in the emerging market countries is one of the key drivers of their pharmaceutical markets. Rising disposable income and the resulting increase in out-of-pocket expenditure on drugs, combined with investment in public health provision seen in some countries is leading to higher expenditure on pharmaceuticals, particularly modern Western drugs.

In the post-product patents era, India's domestic market is changing, reflecting rising disposable incomes in urban areas and changes in India's demographic profile. Leading drug companies are putting more emphasis on meeting a growing demand for high value low volume, Western-style "lifestyle" drugs for wealthy urban customers who make up approximately 12% of the market. This highly lucrative market segment includes drugs for "chronic" or "lifestyle" diseases have grown from 10 percent to 20 percent of the market in the mid-1990s to between 25 and 35 percent of the market presently. The demand for these drugs is growing at a faster rate, at 18%, than domestic demand for the acute drug segment (12%). India has often been called the world's diabetes capital and the rates of aliments like hypertension and high cholesterol are increasing annually. The lifestyle drug segment will fuel the growth of India's pharmaceutical industry and includes anti-diabetes, anti-ulcer, anti-depressants, cardiovascular, hypertension drugs, Alzheimers disease, osteoarthritis, and cancer.

Intense domestic competition, a growing reliance on exports by the largest producers, and India as a growing market for contract manufacturing, contract research and development, and clinical trials, were among the forces behind the industry's growth. Prescription drugs dominate the Indian market, accounting for 85% of India's pharmaceutical production. The Indian pharmaceutical industry accounts for the second largest number of Abbreviated New Drug Applications (ANDAs), is the world's leader in Drug Master Files (DMFs) applications with the U.S. Food and Drug Administration, and has the largest number of FDA-approved manufacturing plants (75) outside of the US.

Many of India's leading Indian pharmaceutical companies have also been certified by regulatory authorities in Australia, South Africa, and the EU.

EXPORTS

India is currently recognised as a high-quality, low-cost skilled producer of pharmaceuticals. It is seen not only as a manufacturing base for APIs and formulations, but also as an emerging hub for biotechnology, bioinformatics, contract research, clinical data management and clinical trials. The country's pharmaceutical industry, as evidenced in the paragraphs which follow, has shown tremendous progress in terms of infrastructure development, technology base creation and a wide range of production.

India exports full basket of pharmaceutical products comprising intermediates, APIs, Finished Dosage Combinations (FDCs), biopharmaceuticals, vaccines, clinical services, etc., to various parts of the world. The country has achieved the distinction of providing healthcare at very low cost while maintaining profitability.

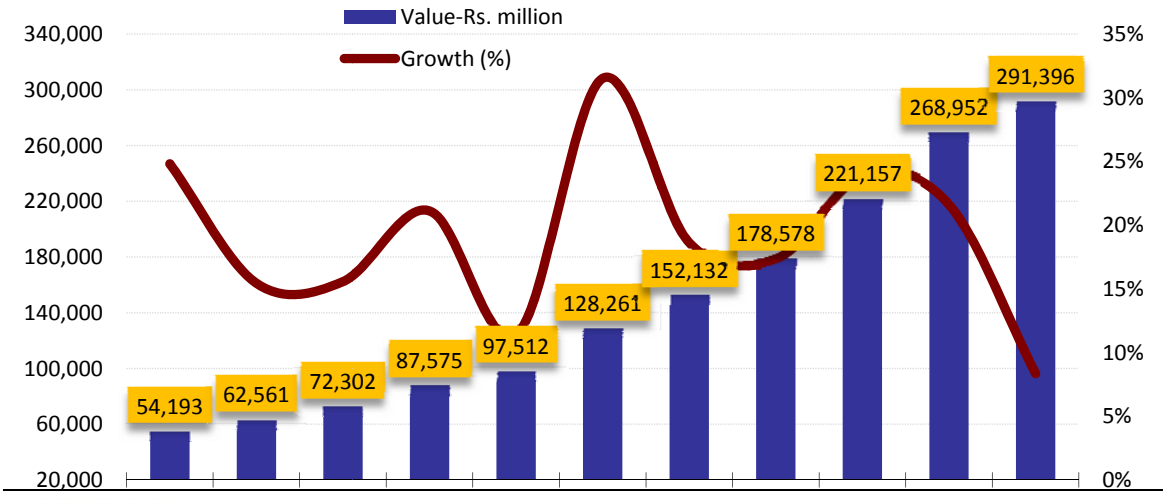
At present, India is among the top 20 pharmaceutical exporters world-wide and with the largest number of US FDA inspected plants outside the USA. Various other agencies like MHRA UK, MCA South Africa, TGA Australia, HPB Canada have approved scores of plants in India.

The export sales growth of pharmaceutical companies globally is driven by product innovation. This is on account of the fact that grant of product patent to the company that undertakes discovery and development of new chemical entity (NCE) allows it to be the sole marketer for the entire patent term (20 years in the US). Thus, such a player faces competition in that product only once the patent expires. Patent expiration for a major product can see revenues for the original patent-holder fall to 10% of pre-patent revenues within two years. The loss of patent protection for key products is increasingly important for assessing the future performance of major Indian pharmaceutical companies. The successful identification and exploitation of the opportunities afforded by patent expirations provides a major growth driver for the pharmaceutical companies who focus their business on the provision of generics.

India's exports of drugs and pharmaceuticals have registered strong growth during the last few years. Exports have increased at a 5-year CAGR of 18% to around Rs. 291 billion in FY2008.

India's Exports of Drugs and Pharmaceuticals

FY, Rs. million



Formulations contribute 55% while the rest 45% comes from bulk drugs.

Catgeory-Wise Exports of Bulk Drugs, Formulations, Ayurvedic, Unani, Homeo & Herbal Products

Rs. million

	2003	2004	2005	2006	2007	2008	5-year CAGR
Formulations	59,529	74,815	90,669	108,296	143,826	166,474	22.8%
Basic Drugs, Fine Chemicals & Intermediates	24,934	72,078	80,917	107,405	118,683	132,993	39.8%
Herbals	3,908	3,184	2,936	3,075	3,770	4,707	3.8%
Medicants & Medicaments of Ayurvedic System	7,439	1,928	3,998	2,331	2,595	3,214	-15.4%
Medicants & Medicaments of Homeopathic System	82	103	21	19	27	31	-17.9%
Medicants & Medicaments of Unani System	0	21	19	11	7	11	
Medicants & Medicaments of Siddha System	0	4	5	3	0	4	
Total	95,892	152,132	178,566	221,139	268,909	307,435	26.2%

According to UNCTAD, India is the second largest exporter of pharmaceuticals, amongst developing countries, after China. The growth in pharmaceutical exports from India has been driven by rising sales to Western countries that are increasingly sourcing pharmaceutical ingredients from India to reduce costs. At present, India's pharmaceutical exports are primarily to US, Germany, Russia, UK, and Nigeria.

US imports of medicinals increased 10.2% during 2007 to US$71.83 billion, as compared with a growth of 16.3% in 2006. During 2008, US imports increased 11.4% to US$80 billion. The major suppliers to the US market by value were Ireland, UK, and Germany. Ireland continued to be the largest supplier of medicinals to the US because of its favourable tax policy toward high-technology industries such as medicinal chemicals, the availability of skilled workers, and relatively lower production costs. While US imports from India increased 49% to US$2,011 million in 2008, India's share increased from 1.9% in 2007 to 2.5% in 2008. During 2008, US imports from low cost importers in developing countries have increased at a higher rate.

US Imports of Pharmaceuticals

	Value (US$ million)				Growth		Market Share (%)		
	2003	2006	2007	2008	2008	2006-08	2003	2007	2008
Ireland	16,200	17,096	18,520	18,975	2.5%	4.7%	32.9%	25.8%	23.7%
UK	6,440	8,651	9,932	11,394	14.7%	22.1%	13.1%	13.8%	14.2%
Germany	4,350	6,538	8,107	9,229	13.8%	17.3%	8.8%	11.3%	11.5%
France	3,366	4,567	4,816	5,814	20.7%	7.8%	6.8%	6.7%	7.3%
Canada	1,940	3,605	4,937	4,861	-1.5%	24.7%	3.9%	6.9%	6.1%
Switzerland	1,899	2,872	2,823	4,024	42.6%	20.1%	3.9%	3.9%	5.0%
Israel	828	2,601	2,691	3,847	42.9%	34.1%	1.7%	3.7%	4.8%
Belgium	1,168	2,320	2,281	3,272	43.4%	35.9%	2.4%	3.2%	4.1%
Italy	1,171	1,948	1,901	2,520	32.6%	7.9%	2.4%	2.6%	3.1%
Singapore	1,632	2,922	3,562	2,422	-32.0%	14.1%	3.3%	5.0%	3.0%
Japan	3,138	2,307	2,465	2,317	-6.0%	-6.0%	6.4%	3.4%	2.9%
India	503	788	1,348	2,011	49.2%	55.2%	1.0%	1.9%	2.5%
Sweden	1,672	2,793	1,901	1,870	-1.7%	-4.6%	3.4%	2.6%	2.3%
China	425	696	876	1,501	71.3%	35.7%	0.9%	1.2%	1.9%
Denmark	708	1,271	1,173	1,207	3.0%	-6.7%	1.4%	1.6%	1.5%
Others	3,821	4,231	4,498	4,740	5.4%	5.9%	7.8%	6.3%	5.9%
Total	49,259	65,207	71,832	80,003	11.4%	12.6%	100%	100%	100%

Pharmaceutical imports of European Union (EU) increased 3.6% (yoy) in 10M2008 (January-October 2008) to Euro 135.44 billion. While intra-EU imports increased 1.8% (yoy) to Euro 101.79 billion, extra-EU imports increased 9.6% (yoy) to Euro 33.65 billion. Germany remained the largest exporter with a share of 17.2% in 10M2008. India's exports to EU increased 15.5% (yoy) in 10M2008 to Euro 544 million.

EU-27 Imports of Pharmaceuticals

	Value (Euro million)			Change		Market Share (%)		
	2007	2007 (10M)	2008 (10M)	2007	2008 (10M)	2005	2007	2008 (10M)
EU27 Intra	120,269	100,022	101,790	11.3%	1.8%	76.7%	76.9%	75.2%
Germany	28,680	23,786	23,289	20.3%	-2.1%	16.4%	18.3%	17.2%
Belgium	19,572	16,244	17,491	8.6%	7.7%	12.3%	12.5%	12.9%
Ireland	12,255	10,252	10,493	-6.5%	2.4%	11.0%	7.8%	7.7%
France	11,676	9,744	10,130	5.7%	4.0%	8.1%	7.5%	7.5%
UK	11,110	9,255	9,476	3.9%	2.4%	7.8%	7.1%	7.0%
Netherlands	11,119	9,335	9,457	26.7%	1.3%	6.2%	7.1%	7.0%
Italy	7,802	6,488	5,625	17.1%	-13.3%	4.3%	5.0%	4.2%
Spain	4,196	3,466	3,671	18.5%	5.9%	2.3%	2.7%	2.7%
Others	13,858	11,452	12,157	11.7%	6.2%	8.3%	8.9%	9.0%
EU27 Extra	36,152	30,692	33,648	2.8%	9.6%	23.3%	23.1%	24.8%
Switzerland	15,131	12,901	13,129	10.6%	1.8%	8.7%	9.7%	9.7%
US	14,251	12,130	11,661	-6.9%	-3.9%	10.3%	9.1%	8.6%
China	1,090	886	1,227	22.7%	38.5%	0.6%	0.7%	0.9%
Singapore	886	754	983	13.5%	30.4%	0.4%	0.6%	0.7%
Japan	1,127	969	917	-7.6%	-5.5%	1.0%	0.7%	0.7%
Canada	696	552	667	-6.5%	20.8%	0.5%	0.4%	0.5%
India	576	471	544	39.4%	15.5%	0.3%	0.4%	0.4%
Others	2,397	2,029	4,521	11.6%	122.8%	1.6%	1.5%	3.3%
Total	156,421	130,713	135,438	9.2%	3.6%	100%	100%	100%

The continuing growth of managed care organisations (MCOs) in the US has been a major factor in the competitive make-up of the healthcare marketplace and the increased sales of Indian companies in the US market. Approximately 180 million people in the US now participate in some version of managed care. The purchasing power of MCOs has been increasing in recent years due to their growing numbers of enrolled patients. At the same time, those organisations have been consolidating into fewer, even larger entities, thereby enhancing their purchasing strength. The growth of MCOs has increased pressure on drug prices. Due to their generally lower cost, generic medicines are often favoured over brand-name drugs1. The impact of MCOs on drug prices and volumes may increase as the result of their role in negotiating on behalf of Medicare beneficiaries in connection with the new Medicare Outpatient Prescription Drug Benefit, Medicare Part D, effective January 1, 20062, includes provisions to promote generics. Rising Medicaid (a joint US federal-state program that pays for medical assistance to over 55

1 In 2005, the average brand name prescription cost US$101.7 as compared with US$29.8 for an average generic prescription.

2 Prior to January 1, 2006, the traditional Medicare program (the federal health program for the elderly and disabled) did not provide coverage for outpatient prescription drugs. The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 established a voluntary Medicare outpatient prescription drug benefit (known as Part D) under which the 43 million Medicare beneficiaries can enroll in private drug plans, starting January 1, 2006. These plans vary in benefit design, covered drugs, and utilization management strategies.

million low-income individuals, and accounts for 19% of total US drug spending) costs have bolstered government support for using generic drugs to contain Medicaid prescription drug expenditures. To control drug costs, a 2005 survey of 36 states in the US found that around 92% of attempted to control Medicaid costs by requiring the use of generics. Forty-one State Medicaid programs have `mandatory generic substitution' policies, which require that generic drugs be dispensed whenever a generic version of the drug is available. Recent data suggests that on average, generics are dispensed 89% of the time when generic substitutes are available. On average, 54% of all drugs dispensed under Medicaid are generics. By comparison, generic usage is 48-52% for many private pharmacy benefit organisations and health plans.

The share of the Indian industry in global pharmaceutical exports of US$368 billion during 2007 is small at 1.2%. World pharmaceutical exports are dominated by EU, US, and Switzerland. With research focus traditionally been in the area of reverse engineering, very few Indian players have ventured in the area of innovative research in the recent years, thus they do not have a product portfolio comprising of patented products (therefore cannot compete with their international counterparts).

World Exports of Medicines and Pharmaceuticals Products

	US$ million				Growth		Share	
	2000	2005	2006	2007	2007	2003-07	2000	2007
Germany	13,754	38,189	44,931	55,686	23.9%	26.1%	12.67%	15.11%
Belgium	6,878	35,039	38,230	47,384	23.9%	16.7%	6.33%	12.86%
Switzerland	10,446	25,907	31,177	36,234	16.2%	17.9%	9.62%	9.83%
US	13,122	25,946	29,105	33,464	15.0%	15.7%	12.09%	9.08%
UK	10,767	22,490	25,633	29,168	13.8%	14.2%	9.92%	7.91%
France	10,461	22,963	25,186	28,449	13.0%	13.4%	9.64%	7.72%
Ireland	4,970	18,078	17,772	20,081	13.0%	6.3%	4.58%	5.45%
Netherlands	4,430	11,878	13,701	17,325	26.4%	18.9%	4.08%	4.70%
Italy	6,380	13,154	14,044	15,542	10.7%	11.6%	5.88%	4.22%
Sweden	3,918	7,240	8,740	8,780	0.5%	14.3%	3.61%	2.38%
Spain	2,106	6,755	7,629	8,340	9.3%	19.7%	1.94%	2.26%
Denmark	2,924	6,402	6,533	7,423	13.6%	14.0%	2.69%	2.01%
Singapore	1,011	2,944	5,265	6,289	19.5%	46.7%	0.93%	1.71%
Austria	1,853	4,516	5,339	6,279	17.6%	16.8%	1.71%	1.70%
Canada	1,228	3,485	4,675	6,181	32.2%	31.8%	1.13%	1.68%
China	1,788	3,778	4,486	6,003	33.8%	20.9%	1.65%	1.63%
India	1,140	2,713	3,362	4,393	30.7%	22.7%	1.05%	1.19%
Israel	429	2,068	3,164	3,509	10.9%	30.5%	0.39%	0.95%
Australia	1,166	2,463	2,600	3,263	25.5%	25.3%	1.07%	0.89%
Japan	2,732	3,327	3,193	3,188	-0.2%	2.5%	2.52%	0.86%
Total	108,572	274,034	311,949	368,537	18.1%	17.2%	100%	100%

India's competitive advantages arise from complex synthesis capabilities, increasingly good manufacturing practices (GMP) and low-cost production. This enables them to export drugs and formulations (including the ones covered by patent protection in the developed markets of the US and the Europe) to the countries with relatively weaker patent laws. In the developed markets, the presence of select Indian players is restricted to the generics market. The introduction of price ceilings on the domestic market seems to have had a positive impact on

India' exports of pharmaceuticals. These ceilings have tended to make exports more profitable, and thus provided an incentive for domestic pharmaceutical firms to engage in export activities. They also help boost innovation, because Indian companies that manufacture new medicines on the basis of indigenous technologies were exempted from price controls for five years. However, domestic innovativeness in India's pharmaceutical sector owes most to the Indian Patents Act of 1970. One stated objective of that Act was the development of an independent and self-reliant pharmaceutical industry. The Act facilitated the acquisition of foreign technology, as it protected production processes but not products (i.e. permitted reverse engineering). This enabled India to become one of the world's leading exporter of generic medicines, and for Indian companies to capture 65% of the domestic market in pharmaceutical products, compared to 25% in 1971.

However, India's export competitiveness continues to be hampered by shortage of advanced training programmes and scarcity of qualified personnel. Indian companies trying to improve their national and global competitiveness and enhance their in-house expertise and capabilities require access to a pool of highly trained personnel. Firms are finding that such a workforce of researchers trained in leading-edge biological methodology remains limited in India. This is in part due to the migration of a large number of talented Indian PhD students and research scientists out of India, where they seek training and where greater research funds are available.

Export prospects for India's pharmaceutical industry depend to a large extent on the effects of the new Patent (Third Amendment) Act 2005. After 2005, Indian companies will increasingly need to look beyond the domestic generics market to sustain their sales, since their traditional strategy of copying on-patent drugs will no longer be allowed. India had to change its patent legislation to comply with its obligations under the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). The new Act provides for the granting of product patents. However, it affects only newly invented medicines, whereas specific regulations apply to those medicines that were invented between 1995 and 2005. India was allowed to delay the patenting of pharmaceutical products until 2005, but had to establish a system (a so-called mailbox) for receiving and filing patent applications starting in 1995. The Indian patent office will decide whether these mailbox applications meet the patentability criteria laid down in the Act, and accept or reject them accordingly. If the application is accepted, Indian companies can continue producing such medicines after payment to the patent-holder of a reasonable royalty, provided that they made significant investment and were producing and marketing the concerned medicines prior to 2005. However, product patent regime, all over the world, thrives on frivolous claims for 'me-too' drugs of similar chemical entities. Under the mailbox provisions (for which India is accepting applications for product patents in the areas of pharmaceuticals and agro-chemicals since 1999, although not granted any patents since the amendment was made only in March 2005), there were reportedly 4,792 applications for product patents although during 1995-2004, only 297 new chemical entities have been bestowed with product patent status in the world. It is therefore clear that the rest of the applications for patents are only frivolous in nature.

Exports to countries with no manufacturing capacity of patented medicines produced in India through a compulsory licence will be possible based solely on the notification by the importing country, in accordance with the implementation of the Doha Declaration on the TRIPS

Agreement and Public Health. If the granting of such compulsory licences does not lead to protracted litigation processes between the patent-holder and the producers of generic medicines, India can continue supplying the developing world.

FINANCIAL PERFORMANCE

For the purpose of analysing industry performance, we have categorised listed players in the Indian pharmaceuticals according to ownership—multinationals (MNCs) and Indian companies. ICRA sample comprises 12 MNCs and 105 Indian companies, who reported a combined gross sales of Rs. 481 billion during FY2007. Overall, the financial indicators of the Indian pharmaceutical industry had come under some stress during FY2005 because of increase in competition and decline in profitability in certain markets. Besides, significant and long-gestation investments have impacted the industry's ROCE and credit coverage indicators. However, industry sales growth, margins and ROCE have improved during FY2006-08 because of higher domestic and export sales growth. The improvement in financial indicators has been driven by certain positive developments: increase in geographical diversification, increase in research orientation, and increase in long-gestation investments in manufacturing facilities and in skilled manpower. Moreover, Indian companies have of late made global acquisitions and also entered into alliances with MNCs to improve reach, particularly in the regulated markets.

Margins and Returns

FY	2004	2005	2006	2007	2008
MNCs					
Operating Margins	15.92%	20.47%	20.30%	22.06%	22.16%
Net Margin	12.44%	19.32%	20.10%	23.19%	26.16%
ROCE	37.92%	51.52%	51.15%	51.00%	50.82%
RONW	25.32%	36.99%	35.30%	36.36%	35.21%
Indian companies					
Operating Margins	16.72%	13.32%	15.85%	18.10%	17.02%
Net Margin	12.53%	9.73%	12.22%	14.84%	14.19%
ROCE	22.41%	15.33%	16.77%	19.93%	17.08%
RONW	24.54%	16.94%	21.23%	24.18%	18.54%
Total					
Operating Margins	16.61%	14.38%	16.44%	18.56%	17.65%
Net Margin	12.52%	11.14%	13.27%	15.81%	15.66%
ROCE	23.85%	18.51%	19.50%	22.28%	19.91%
RONW	24.65%	19.67%	23.08%	25.63%	20.54%

During 9MFY2009, the sample companies reported a 17.4% (yoy) increase in OI to Rs. 445.01 billion. While sales for MNCs increased 12.1% (yoy) mainly because of pricing pressures, sales growth for Indian companies was high at 18.1% (yoy). Overall OI (yoy) growth improved from 16.1% (yoy) in Q4FY2008 to 23.2% (yoy) but declined to 13% (yoy) in Q3FY2009. In the domestic market, with the implementation of a new pharma policy, sales and margins have been under pressure because of price controls on a wider range of drugs. Operating margins have declined because of pricing pressures in the generic exports business. With several large patents expiring during the year, significant new generic launches have been made in the regulated markets.

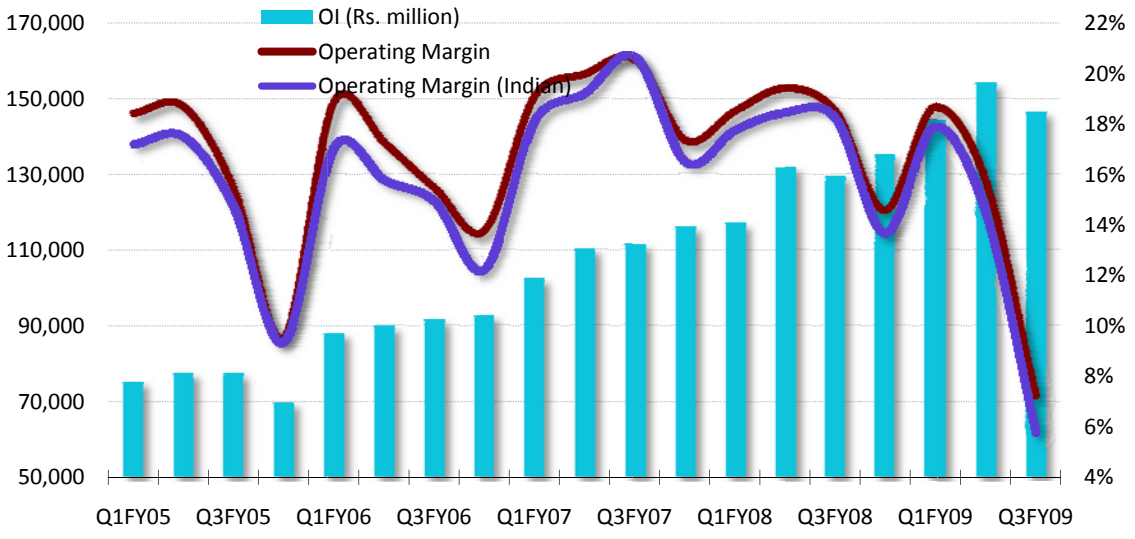
Financial Performance

Rs. Million, except percentages

	Rs. Million		Change (%)	% of OI	
9MFY	2009	2008		2009	2008
Net Sales/OI	445,005	378,957	17.4	100.0	100.0
Raw Material Cost	222,367	189,153	17.6	50.0	49.9
Employee Costs	39,824	33,202	19.9	8.9	8.8
Other Operating Costs	120,952	85,290	41.8	27.2	22.5
Cost of Sales	383,295	307,775	24.5	86.1	81.2
OPBDIT	61,710	71,182	-13.3	13.9	18.8
Interest	18,034	5,896	205.9	4.1	1.6
Depreciation	13,530	11,515	17.5	3.0	3.0
OPBT	30,146	53,771	-43.9	6.8	14.2
Other Income	15,429	25,738	-40.1	3.5	6.8
PBT	45,575	79,509	-42.7	10.2	21.0
Tax	5,473	14,385	-62.0	1.2	3.8
PAT	40,102	65,124	-38.4	9.0	17.2
Indian					
Net Sales	397,630	336,691	18.1	100.0	100.0
Operating Profit	50,542	61,199	-17.4	12.7	18.2
Net Profit	29,427	53,243	-44.7	7.4	15.8
MNCs					
Net Sales	47,375	42,266	12.1	100.0	100.0
Operating Profit	11,168	9,983	11.9	23.6	23.6
Net Profit	10,676	11,881	-10.1	22.5	28.1

On a quarterly basis, operating margins declined from 18.8% in Q1FY2009 to 16% in Q2FY2009, and to 7.2% in Q3FY2009.

Trends in OI and Operating Margins



CONCLUSION

India's pharmaceutical industry has evolved from almost non-existent to a world's leader in the production of high-quality, low-cost non-branded or generic drugs, accounting for nearly 20% of the world's production. India currently produces almost all its own drug needs and domestic companies control over 80% of the Indian market. It has made tremendous strides over the last two decades. Because of low barriers to entry and low capital requirements, there are tens of thousands of companies producing pharmaceuticals in India. The vast majority of them are small by Western standards with revenues of less than Rs. 200 million.

With the re-introduction of product patents in 2005 and the fiercely price competitive nature of the Indian pharmaceutical industry, many smaller, less competitive producers were forced to abandon the industry as it begins slowly shifting away from vanilla generic drugs to becoming a regional hub for R&D, drug discovery, contract manufacturing, and technology licensing. In this transition, many midlevel Indian producers will turn to contract manufacturing, outsourcing, contract research, contract clinical trials, or other tie-ins with MNCs. Since 2005, many MNCs began re-entering the Indian pharmaceutical market by setting up their own manufacturing and R&D facilities. This will gradually neutralize the cost advantages enjoyed by Indian pharmaceutical majors. These alliances and millions of dollars spent on establishing domestic and foreign-based manufacturing facilities, acquiring foreign drug manufacturing firms, as well as marketing and sales networks, will enable India's leading pharmaceutical producers to re-direct large sums of their cash flow to R&D and move up the value-added chain. These foreign acquisitions will enable Indian companies to gain a foothold in Western regulated markets, diversify their portfolios, acquire recognized brands, and gain R&D capabilities.

The US has some of the highest drug prices in the world and has attracted imports of generic drugs from India and a number of low-cost countries. However, severe price compression and growing competition from other low-cost countries is forcing Indian majors to offset their losses by shifting their attention to Western Europe. Nonetheless, Indian companies have made tremendous strides in the U.S. market and companies like Ranbaxy are major sources of generic drugs. Indian companies also enjoy comparative advantages in cost, strength in reverse engineering skills, and number of U.S. FDA approved plants located in India. Indian companies have spent millions of dollars filing ANDAs with the U.S. FDA to gain exclusive production rights for many drugs losing their patent protection in the US.