CHAPTER 2: PHARMACEUTICAL INDUSTRY

2.1 Overview of the Global Pharmaceutical Industry

The pharmaceutical industry is the building block of the healthcare system. Research based pharmaceutical companies contribute to the global health through the development of innovative medicines. The IMS Institute for Healthcare Informatics predicts that the pharmaceutical market will reach nearly USD 1,200 billion by 2016, an increase of nearly USD 250 billion from the USD 956 billion recorded in 2011. This growth is due to the market expansion and generics (IFPMA, 2012).

2.1.1 Early Period in the World Pharmaceutical Industry

The first known drug store was opened by Arabian Pharmacists in Baghdad in 754 CE, and was adopted into medieval Europe. The modern pharmaceutical industry has its origins in the coal tar industry that arose in German speaking lands in the mid-nineteenth century, and can be traced to two sources: apothecaries that moved into wholesale production of drugs such as morphine, quinine, and strychnine in the middle of the 19th century and dye and chemical companies that established research labs and discovered medical applications for their products starting in the 1880s. Merck, for example, began as a small apothecary shop in Darmstadt, Germany, in 1668, only beginning wholesale production of drugs in the 1840s. Likewise, Schering in Germany; Hoffmann-LaRoche in Switzerland; Burroughs Wellcome in England; Etienne Poulenc in France; and Abbott, Smith Kline, Parke-Davis, Eli Lilly, Squibb, and Upjohn in the U.S. all started as apothecaries and drug suppliers between the early 1830s and late 1890s. William Perkins, in the nineteenth century manufactured the first artificial dye, aniline purple which instigated German and Swiss companies to take up the manufacture of dyes seriously, thereby leading to the discovery of a number of chemical compounds which were therapeutically useful. Bayer in Germany developed Aspirin in 1899. In 1880, Burroughs Wellcome & Co. was established by two American trained pharmacists who introduced American style marketing and manufacturing methods, and created a research laboratory within the company, the first of its kind in the country. The discovery of penicillin in the 1920s heralded the era of mass production of drugs and can be considered as the harbinger of the development of global pharmaceutical companies.
2.1.2 The Pharmaceutical Golden Era: 1930-60

In 1942 Dr. Selman Waksman of Rutgers University discovered the anti-tuberculosis agent streptomycin, thereby opening the flood gates for new products post World War II. The development of penicillin by 11 US Pharmaceutical companies, under the oversight of War Production Board, gave US firms a leading position after World War II. Antibiotics that were produced were streptomycin (Merck), chlortetracycline (Lederle), chloramphenicol (Parke-Davis), erythromycin (Abbott and Lilly) and tetracycline (Pfizer). Success in these ventures, led the pharmaceutical companies to invest in synthetic chemistry. Rapid advance in analytical techniques and instrumentation aided in determining molecular structure and aided in the transition of wet chemistry to dry chemistry involving minute samples and molecular models.

In 1938 Food, Drugs and Cosmetic Act was enacted in the US. Approval of any new drug required preclinical and clinical trials failing which no new launch was approved by the Federal Authorities. The USFDA promoted the double-blind, clinically controlled trials as the gold standard for testing new medicines on patients. The decisions regarding the suitability of the drug was dependent upon, the characterization of safety and effectiveness of the drug in large populations. Thus the therapeutic revolution in drugs stimulated two fundamental changes in the manufacturing firms, major companies were transformed from a full line commodity house to a vertically integrated research and information intensive “specialty” manufacturer by the late 1950s, where the products were protected by patents, promoted by brand names and purchased only with a doctor’s prescription. The second change was that nationally based companies became transnationally organized, thus sales, production, research and marketing were carried out in different countries. By 1950s, corticosteroids, oral contraceptives, antihistamines, antidepressants, diuretics, semi synthetic penicillin and many more drugs were discovered and patented, thereby transforming the pharmaceutical industry from a commodity business to a highly research intensive, marketing oriented, business (Taggart, 1993).

2.2 Characteristics of the World Pharmaceutical Industry

The pharmaceutical industry is characterized by: High costs of drug discovery, patents and globalization in the recent times. The industry has large number of small companies and a small
number of large companies. The big pharmaceutical companies are concentrated in the highly industrialized, Organization for Economic Co-operation & Development (OECD) countries.

2.2.1 Patents

The patent protection for pharmaceutical industry is critical as the actual manufacturing process is easy to replicate and can be copied with very little investment. The TRIPS Agreement in 1994, allowed the developing countries to be brought under the blanket of patent protection. Countries that have joined the WTO have obliged to accept the protection whereas the least developed countries are not required to meet this obligation until 2016.

The World Trade Organization was established in 1994 in Marrakech after the Uruguay Round of Trade Negotiations. The predecessor to the WTO was the General Agreement on Tariffs and Trade (GATT). The Uruguay Round brought in the Agreement on Trade Related Aspects of Intellectual Property Rights, known as TRIPS. The objective of the TRIPS was to create an equitable system of international trade, wherein developed countries reduce import barriers and developing countries open the market for high value exports from developed nations. A unique aspect of the pharmaceutical industry is that the invention or the new molecule needs to be disclosed well before the product is brought to the market, to enable trials and share the information with the group. This leads to considerably short periods of patent exclusivity for the firm planning to launch the new product, thereby eroding its profits. According to UNCTC, the patent protection is of four types in the pharmaceutical industry:

- Patents on the composition of matter
- Patents granted for a specific product
- Process patents relating to the production process rather than the finished products
- Application or usage patents

2.2.2 Globalization

The International Monetary Fund (IMF), defines globalization as the growing economic interdependence of countries through increasing cross-border transactions in goods & services,
free flow of international capital, and rapid and widespread diffusion of technology. Narula & Dunning (1998) observed that globalization, alliance capitalism and R&D-intensive value adding activities are hallmarks of economic activity in advanced industrial countries. According to them globalization is an increasing interdependence and convergence in consumption patterns and technologies across countries, internationalization of production through networks, overlapping and merging of industrial sectors, increasing capital and knowledge intensity as well as a concurrent shortening of technology life cycles. They have observed an increase in alliances across all of the advanced industrialized economies and the nature of the alliances are strategic and alliances are no longer simply undertaken as a means of avoiding transaction and coordination costs of markets. One of the original motives for alliance formation was to acquire market access and/or overcome supply bottlenecks, i.e., to achieve vertical integration where such integration was not possible through hierarchies. They indicate that inter-firm alliances are increasingly being undertaken, through various modes, as a direct response to pressures brought about by contemporary technological developments and globalization.

Kesic (2008), has identified some factors that are responsible for pharmaceutical globalization in the last decade. They include: Lack of new products in the pipeline, need for huge investment in R&D & marketing, increased competitiveness, world reforms in healthcare, and increased focus on regulations. The success of the molecule would depend on the marketing and sales activities. Therefore the success of a pharmaceutical company largely depends upon, strong research and development combined with a compelling marketing and sales related activities. The large pharmaceutical companies invest on an average, 16% of their sales turnover into R&D, and 26% into marketing and sales related activities (Kesic, 2006). Originators invest heavily on R&D and produce new and inventive products which earn maximum profits during the patent period. The generics are engaged in producing cheap drugs by imitating the original one, thus their strategy is oriented towards producing products that are considerably less priced.

2.2.3 Drug Development Process and Medical Research

The actual drug manufacturing is the consequence of a complex and lengthy set of activities whose objective is new drug discovery. Every ethical drug manufacturing company is
constantly on the lookout for new molecules that would sustain the profitability when patented.
A new molecular entity is discovered, developed and marketed through the process called as
Drug Discovery. The new molecular entities discovered may be original or may be the
outcome of minor molecular modifications of existing drugs. Drug Discovery process involves
screening millions of chemical compounds with therapeutic properties. The objective is to find
potential molecules which can alleviate or prevent disease conditions (Ratti and Trist, 2001).

The process of developing a molecule for therapeutic applications involves a number of
complex steps including clearance from regulatory authorities. The phases are:

(i) Target selection, wherein a promising compound with therapeutic efficacy is
selected from a myriad of chemical entities
(ii) Preclinical phase involves the necessary testing on animals before it is tried on
humans. The toxicity of the drug is evaluated in this phase
(iii) Clinical phase:
   • Phase I - the compound is studied for the first time in healthy human volunteers
   • Phase II - proof of concept and evidence of efficacy and safety in patients
   • Phase III - the studies are conducted on a large population to generate data on safety
     and efficacy of the drug. The therapeutic product is then filed for license for
     marketing purpose
   • Phase IV- post marketing studies

DiMasi and Grabowski (2003), have estimated the research and development costs of 68
randomly selected new drugs of 10 pharmaceutical companies and arrived at a figure of USD
$403million. They indicate that the expenditures on pharmaceuticals have grown since the late
1990s, which was attributed to the lengthy and costly process of new drug development. They
have described that an overall clinical approval success rate is the probability that a compound
that enters the clinical testing pipeline will eventually be approved for marketing and attrition
rates describe the rate at which investigational drugs fall out of testing in the various clinical
phases. R&D costs for new drugs (including the costs of failures and time costs) have been
estimated to average in excess of $800 million (in year 2000 dollars) for development that led
to approvals in the 1990s, with a marked upward trend relative to earlier decades (DiMasi et al., 2003).

2.3 Leading Pharmaceutical Companies of the World

According to Kesic (2006), the leading ten world pharmaceutical companies command more than 42% of the market share of the global pharmaceutical market. The global pharmaceutical companies can be categorized as Originators and Generic firms. Originators include those companies who invest substantial amounts on R&D and bring out new block buster molecules. The generics include those firms that produce equivalents of the original block buster molecules. These manufacturing giant are able to achieve cost actualization with massive scale ups.

Table No 8: Leading World Pharmaceutical Companies in 2010 (Originators)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company name</th>
<th>Country</th>
<th>Sales ($Billion)</th>
<th>R&amp;D Investment (Million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Johnson &amp; Johnson</td>
<td>USA</td>
<td>6190</td>
<td>6986</td>
</tr>
<tr>
<td>2</td>
<td>Pfizer</td>
<td>USA</td>
<td>5001</td>
<td>7845</td>
</tr>
<tr>
<td>3</td>
<td>Roche</td>
<td>Switzerland</td>
<td>4735</td>
<td>9874</td>
</tr>
<tr>
<td>4</td>
<td>GlaxoSmithkline</td>
<td>UK</td>
<td>4583</td>
<td>6335</td>
</tr>
<tr>
<td>5</td>
<td>Novartis</td>
<td>Switzerland</td>
<td>4427</td>
<td>7469</td>
</tr>
<tr>
<td>6</td>
<td>Sanofi</td>
<td>France</td>
<td>4199</td>
<td>5729</td>
</tr>
<tr>
<td>7</td>
<td>AstraZeneca</td>
<td>UK</td>
<td>3281</td>
<td>4409</td>
</tr>
<tr>
<td>8</td>
<td>Abbott Laboratories</td>
<td>USA</td>
<td>3076</td>
<td>2744</td>
</tr>
<tr>
<td>9</td>
<td>Merck &amp;Co</td>
<td>USA</td>
<td>2743</td>
<td>5800</td>
</tr>
<tr>
<td>10</td>
<td>Bayer Healthcare</td>
<td>Germany</td>
<td>2230</td>
<td>2306</td>
</tr>
</tbody>
</table>


Table No 9: Leading World Pharmaceutical Companies in 2010 (Generics)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company name</th>
<th>Country</th>
<th>Sales ($Million)</th>
<th>World Market Share (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Teva Pharmaceutical</td>
<td>Israel</td>
<td>6,956</td>
<td>21.8</td>
</tr>
<tr>
<td>2</td>
<td>Mylan</td>
<td>USA</td>
<td>3,620</td>
<td>11.3</td>
</tr>
<tr>
<td>3</td>
<td>Sandoz</td>
<td>Germany</td>
<td>2,494</td>
<td>7.8</td>
</tr>
<tr>
<td>4</td>
<td>Watson Pharmaceuticals</td>
<td>USA</td>
<td>2,000</td>
<td>6.3</td>
</tr>
<tr>
<td>5</td>
<td>Greenstone</td>
<td>USA</td>
<td>1,700</td>
<td>5.4</td>
</tr>
<tr>
<td>6</td>
<td>Par Pharma</td>
<td>USA</td>
<td>1,319</td>
<td>4.1</td>
</tr>
<tr>
<td>7</td>
<td>Hospira</td>
<td>USA</td>
<td>1,061</td>
<td>3.3</td>
</tr>
<tr>
<td>8</td>
<td>Apotex</td>
<td>Canada</td>
<td>879</td>
<td>2.3</td>
</tr>
<tr>
<td>9</td>
<td>Mallinckrodt</td>
<td>USA</td>
<td>860</td>
<td>2.7</td>
</tr>
<tr>
<td>10</td>
<td>Dr. Reddy’s</td>
<td>Inda</td>
<td>834</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Increased competitiveness is pushing the pharmaceutical companies towards consolidation which leads to the formation of bigger pharmaceutical concerns across the globe. It is also evident that innovator companies invest substantial amounts of their profits into R&D.

2.4 Indian Pharmaceutical Scenario

Traditionally two systems of medicine were in vogue in India, the Ayurvedic and the Arabian medicine systems. The ayurvedic medicine uses a combination of herbs and minerals and has references in the ancient texts like Vedas. The Arabian medicinal systems are the outcome of innumerable invasions from the Arabic world. With the advent of the British rule, the western medicinal system, namely the Allopathic medicinal system was introduced into India. With the educational system, including the medical education being modeled on the British system, allopathic and modern medicine started taking roots in India and has evolved to be widely accepted over the last 250 years.

The exact date on which the Allopathic medicine entered India is not really documented, however it is assumed to be during the early part of the 19th century. Medicines imported by the British for their personal use marked the beginning of the usage of allopathic medicines in India. In 1901, the Bengal Chemical and Pharmaceutical Works was started with the objective of starting indigenous production of medicines in India. The company started with the production of Tetanus antitoxin, in 1930. Two MNCs namely ParkeDavis(1907) and Burroughs Welcome(1912), commenced trading operations for formulations. Indigenous production was sufficient to meet only 13 percent of the demand, thus a large portion of the domestic demand was still being supported through imports mainly from Germany and United Kingdom. Between 1904 and 1907 four research institutes were commissioned: Haffkine Institute, King Institute, Pasteur Institute and Central Research Institute. The domestic production of medicine received an impetus due to the steep demand during the First World War. Production of caffeine and quinine salts registered substantial growth, till the end of the war (Bhojwani, 2005).

By 1941, the Indian pharmaceutical industry took up the manufacture of new drugs like iodochloro-hydroxyquinolone as well as a number of alkaloids like ephedrine and codeine. Chemotherapeutic drugs, anti-leprotics, glandular extracts – liver extracts, colloidal solutions of
Calcium, Manganese, Silver and Iodine were being produced by the Indian Pharmaceutical industry during this period. By the end of the First World War, four global pharmaceutical majors- Glaxo, Boots, May&Baker, CibaGeigy had established their presence in India (Bhojwani, 2005).

Post the war a large number of pharmaceutical products entered obsolescence, thereby older antibiotics and chemotherapeutic agents were replaced by newer ones. This was indeed a set back to the Indian industry. They started the manufacture of formulations based on imported bulk drugs and the extraction of therapeutic agents from plant sources.

2.4.1 Evolution of the Indian Pharmaceutical Industry

Five decades ago, the pharmaceutical industry in India was at a rudimentary stage, with a high dependence on imported medicines from abroad. Manufacturing facilities in India were almost non existent due to the lack of manufacturing facilities as well as the archaic laws that were being followed post Indian independence. Medicines were priced very high and were beyond the reach of the common Indian.

Post independence the Government embarked upon planned expansion of Indian industry including the pharmaceutical industry. In 1947, the estimated value of production of pharmaceuticals was Rs.10crores, which rose to a whopping Rs.26540crores in 2002-03. The evolution of this industry is the result of number reasons. The new Indian government in 1947, emphasized on industrialization invested in pharmaceuticals among other industries. The government did not discourage foreign firms from competing in India, as there were no local substitutes for MNCs technology. The first concrete step taken towards self reliance in pharmaceuticals was the establishment of Hindustan Antibiotics Ltd (HAL) in 1954 and Indian Drugs and Pharmaceuticals Ltd (IDPL) in 1961. The IDPL played an important role in developing technical know-how to develop antibiotics and move towards self reliance. It was a soviet sponsored program which showed that it was possible to produce drugs in India, it helped develop human and physical capital and spurred the mushrooming of support institutes like pharmacy colleges and other business elements upstream and downstream (Sean Eric Smith, 2000).
The colonial patent law of 1911 secured the Indian market to British industry. A large majority of drugs were imported from abroad until the Patents Act 1970 brought a turnaround. The major growth of the Indian pharmaceutical industry can be attributed to the enactment of the Indian patents Act 1970, which came into force in 1972 and was a part of a wider set of policies of the government of India to develop ‘self reliant’ pharmaceutical industry. This Act provided for product patents for all inventions except for food, medicine, drugs and substances produced by chemical process. For the latter category only the process patent was accorded. The patent term was also reduced from 16 years to 5 years from the date of patent approval or 7 years from the date of application whichever is earlier. Consequently, Indian companies evolved to reverse engineer and copy the major drug and produce them at minimal costs. Although this act was ethically unacceptable to foreign MNCs, it provided the opportunity to develop India’s pharmaceutical industry throughout the 70s and 80s. The provision of compulsory licensing which provided for the opening of the patented drug for the generic replication by others if the drug was found to be unnecessarily high priced was made after three years from the date of approval of the patent (Nauriyal D K, 2006).

From 1970, local Indian firms reverse engineered bulk drugs, which they sold wholesale or processed into simple formulations, which further discouraged the MNCs to expose their IP. Thus by 1997, MNCs accounted for 30 percent of bulks and 20 percent of locally produced formulations. By 1970, the number of drug manufacturing units grew from 2257 (in 1970), to 5156 (in 1980) to 16,000 (in 1990) and to over 23000 (in 2005) with 349 units in the formal sector. In the 1980s the industry had grown at a rapid rate of 11 percent per annum. The average growth of the industry in the last few years has been about 12% compared with the growth of the fast moving consumer goods sector, which has grown approximately at 4.7% (Greene William, 2007).

The industry was producing only formulations in the pre-1970s, and started manufacturing more than 400 bulk drugs amounting to 6% of the international bulk drug market. More than 85% of the formulations produced in the market are sold in the domestic market. The essential drugs comprising antibiotics, antibacterial, antiparasitic and cardiovascular constitute a major portion of turnover of the industry.
The evolution of Indian pharmaceutical industry can be tracked over four stages:

The first stage 1950s and 60s witnessed a huge dependency on foreign multinationals to provide essential medicine to the Indian population. The domestic manufacturers were engaged in repacking the formulations produced by multinationals (Lalitha, 2002). Since the Patents Act of 1911 was in vogue, the indigenous firms were legally prevented from manufacturing any drugs introduced in the country. The domestic firms, as per the laws prevailing at that time were also forbidden from processing a patented drug into formulations or importing it.

The second stage of the industry took place in the 1970s with the enactment of the Indian Patent Act (IPA) 1970 and the New Drug Policy (NDP) 1978. This is a significant phase as this was the foundation for the development of the pharmaceutical industry in India. Critical aspect of this Act was reducing the scope of patenting to only process and not the product, for a short period of seven years, from the initial period of 16 years. The 1970 Patent Act provides protection for the processes of manufacturing drugs for 7 years from the date of filing the application, or 5 years from the date of grant of the patent. Under this Act, only one process that was used to manufacture the drug could be patented. The NDP 1978 increased the pressure on the foreign firms to manufacture bulk drugs locally from the basic stage. This period led to the birth of “Reverse Engineering” in India. Pharmaceutical units started producing essential drugs and drugs that were imported till then. By 1972, over 100 essential drugs covering a wide spectrum of therapeutic groups like antibiotics, sulpha drugs, anti leprotic drugs, analgesics, antipyretics, vitamins, tranquillisers, photochemical and various other pharmaceutical chemicals were produced in India from basic stages (Narayana, 1983:42).

This period also witnessed the introduction of two significant Acts: The Monopolies and Restrictive Trade Practices Act (MRTP) and the Foreign Exchange Regulation Act (FERA). These two Acts were aimed at reducing the concentration of economic power in the hands of a few units and controlling the flight of the foreign exchange from the country (Lalitha, 2002).

In the third stage of its evolution, domestic enterprises based on large scale reverse engineering and process innovation achieved near self sufficiency in the technology and production of bulk drugs belonging to several major therapeutic groups and have developed
modern manufacturing facilities for all dosage forms like tablets, capsules, liquids, orals and injectibles and so on.

The fourth stage in the 1990s witnessed dramatic changes in the policy regime governing the pharmaceutical industry. The licensing requirement for drugs was abolished, 100 per cent foreign investment was permitted under automatic route, and the scope of price control had been significantly reduced. All those drugs which were limited to the public sector were de-licensed, thus leading to an increase in drug production. This also enhanced the competition between domestic and foreign firms in the 1990s. The Government of India signed the TRIPS Agreement in 1994. Thus, started a new chapter in the history of Indian pharmaceutical sector where free imports, foreign investment and technological superiority would determine the trade patterns and industrial performance.

The Indian pharmaceutical industry has grown from a mere US$ 0.32 billion turnover in 1980 to approximately US$ 21.26 billion in 2009-10. The country now ranks 3rd in terms of volume of production (10% of global share) and 14th largest by value (Indian business.nic.in/industry). The Indian Pharmaceutical Industry currently represents US$ 6 billion of the $550 billion global pharmaceutical industry (KPMG 2007). It represents 8 percent of the global industry by volume and 13 percent by value, thereby taking the fourth place worldwide.

The Indian pharmaceutical industry can be divided into two sectors, the organized sector consisting of 250-300 companies and the unorganized sector with an estimated 20,000 firms. An expert committee set up by the government of India has clarified the number of active units on the basis of drug manufacturing licenses issued to 5877(Sampath 2005). Primary associations which represents most of India’s pharmaceutical companies: the Organization of Pharmaceutical Producers of India (OPPI), the Indian Pharmaceutical Alliance (IPA) and the Indian Drug Manufacturers' Association (IDMA).

According to the OPPI, India has a strong well established manufacturing base and a large number of well educated, English speaking workforce which contributes to the positioning of India as a likely hub to meet the current worldwide demands for reduced manufacturing costs, trained personnel and reduced R&D costs. 700,000 scientists and engineers graduate every year,
including 122,000 chemists and chemical engineers with 1500 PhDs, thus providing a high
intellectual capital per dollar worldwide.

2.4.2 The TRIPS Agreement

The Indian Government post independence was deliberating on the patent law, with the
ultimate objective of revival the domestic pharmaceutical industry. In 1972, after repeated
expert reports and deliberations in Parliament, the India Patents Act of 1970 came into force
(Mueller 2007, 22-25). The 1970 Act with the intent to encourage indigenous technological
skills and inventions imposed substantial limits on the patent rights of the western world
(Katherine et al, 2003). Critical aspects were:

a) Lack of patent protection for pharmaceutical products.

b) Firms were permitted to patent only a single process for making a pharmaceutical product, a
firm could not block competitors by patenting all possible processes for making a drug.

c) The term for pharmaceutical process patents shortened to five years from the grant of the
patent or seven years from application filing, whichever was less, compared to 14 years from
application filing for all other inventions.

d) The Act imposed very broad “compulsory licensing” provisions for pharmaceutical process
patents.

This legislation weakened the intellectual property protection in India thus making
pharmaceutical products unpatentable, thereby allowing inventions patented elsewhere to be
freely copied and marketed in India (Lanjouw, 1997). The reducing of the statutory term on
pharmaceutical process patents opened the floodgates for the domestic players to reverse
engineer and introduce cheaper generics into the Indian market. The number of patents
granted per year fell by three-quarters over the following decade, from 3,923 in 1970-71 (of
which 629 were to Indian applicants, 3,294 to foreign applicants) down to 1,019 in 1980-81
(349 Indian, 670 foreign), (Lanjouw 1997).
In the Uruguay round of negotiations, India opposed the TRIPS mandate on pharmaceutical product patents. One of the implications of India joining the WTO is the requirement to comply with all the provisions of the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPs). The Government of India introduced the Patents (Amendment) Ordinance on 8 January 1999 to meet part of the obligations under TRIPs.

2.4.3 Major Players in the Indian Pharmaceutical Industry

Many Indian companies have become global players, thanks to the convergent strategy adopted by them (Bower & Sulej, 2007), which involves three steps: Develop generic drug manufacturing competency through reverse engineering, obtain approvals and market the generic products in regulated countries like USA and Europe and finally develop in house drug discovery capabilities to produce new bio-molecules. Indian companies have already established their credibility in the first two aspects and now are concentrating their efforts towards R&D and Drug development. Dr Reddy’s, Ranbaxy and Cipla have achieved considerable success in this regard. Some of the major players in the Indian pharmaceutical industry are in the table below.

Table No. 10: Indian Pharmaceutical Industry – Major Players

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Revenue (2011) $Mio</th>
<th>Employees</th>
<th>Founded</th>
<th>Infrastructure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cipla</td>
<td>1348.5</td>
<td>16000</td>
<td>1935</td>
<td>Indore, Sikkim, Baddi, Goa, Mumbai, Bangalore, Patalganga, Kurkumbh</td>
</tr>
<tr>
<td>2</td>
<td>Ranbaxy</td>
<td>1327.56</td>
<td>14000</td>
<td>1961</td>
<td>Dewas, Mohali, Paonta Sahib, New Delhi, Goa</td>
</tr>
<tr>
<td>3</td>
<td>Dr. Reddy’s Lab</td>
<td>1178</td>
<td>14900</td>
<td>1984</td>
<td>6 FDA approved plants in India, FDA approved plants in Mexico, UK, USA</td>
</tr>
<tr>
<td>4</td>
<td>Lupin</td>
<td>929.8</td>
<td></td>
<td>1968</td>
<td>Mandideep, Tarapur, Goa</td>
</tr>
<tr>
<td>5</td>
<td>Aurobindo Pharma</td>
<td>865.19</td>
<td></td>
<td>1986</td>
<td>Hyderabad</td>
</tr>
</tbody>
</table>


2.4.4 Regulation in the Indian Pharmaceutical Industry

In India, the import, manufacture, distribution and sale of drugs and cosmetics are regulated by the Drugs and Cosmetics Act, 1940 (DCA), the Drugs and Cosmetics Rules, 1945 (DCR).
Drug (Prices Control) Order, 1995, Drugs (Magic Remedies) Objectionable Advertisement Act, 1954 and Pharmacy Act, 1948 are other regulations which have a bearing on the pharmaceutical business in India. The classification of the drugs in India is as: OTC drugs and Prescription drugs.

*Over the Counter Medicines (OTC):* ‘OTC Drugs’ means drugs legally allowed to be sold ‘Over The Counter’ by pharmacists, i.e., without the prescription of a Registered Medical Practitioner. The current market for OTC medicines in India is about $940 million and is growing at 20 percent a year, which is double the rate for prescription medicines.

*Prescription Drugs:* Prescription drugs are those medicines that are listed in the Schedule H and X of the Drugs and Cosmetics Rule. Drugs listed in Schedule G do not need prescription to purchase but require a warning stating, “Caution: It is dangerous to take this preparation except under medical supervision”. Drugs in the above three schedules are not advertised directly to the public under a voluntary commitment by the Pharmaceutical industry (OPPI, 2009).

*Marketing of Drugs in India:*

*The Ministry of Health and Family Welfare, Central Government* is the responsible body for all legislations and regulating the pharmaceutical business in India. The state government through its Food and Drug Administration (FDA) enforces the Directives of the Ministry of Health.

The office of the Drugs Controller General of India (DCGI) has the primary responsibility of approving new drugs, molecules and standards, vaccines and sera, new usage and claims, new method of administration, clinical research and trials, introductions of new unique formulations and granting import and export licenses.

The Drugs and Magic Remedies (Objectionable Advertisement) Act and Rule lists out the ailments for which advertising is not permitted in India. A voluntary code on OTC Advertising is being followed by all OPPI member companies. Additionally based on the DCGI code the Advertising Standards Council of India (ASCI) has brought out a code of advertising for pharmaceutical products.
Distribution:

Distribution in India is a challenge due to its huge geographical proportion. The drugs may be manufactured in any part of the country; however, for it to reach the retail pharmacy, a distribution system is essential. The manufacturer transports the drugs to depots for stocking before the sale is made. The depots can be company-run depots or outsourced to Clearing and Forwarding (C&F) agents on behalf of the company. The C&F agent is supervised by the company directly. The C&F raises invoice to stockists or distributors who have stocking points in a particular area/town. The stockist is responsible for the sale of goods to a retailer or wholesaler.

Price Control in Indian Drug Market:

The Drugs Price Control Order (DPCO) exercises price control on certain drugs in India. It takes the base from the Essential Commodities Act (ECA). It is the responsibility of the Ministry of Chemicals and Fertilizers, and is under the supervision of the National Pharmaceutical Pricing Authority (NPPA). As per the DPCO 1975, 347 drugs were under the price controlled category, which was brought down to 143 as per DPCO 1987. This number has been further brought down to 74 as per the DPCO 1995. In 1995, the DPCO introduces three criteria to assess whether a particular drug should fall in the price control market: turnover, monopoly, and competition. The government will continue to fix prices of those drugs whose annual turnover exceeds 44 million. A drug is said to enjoy monopoly when the retail sales fall in the 10 million to 40 million bracket and a single manufacturer has a market share of 90% and more. Ayurvedic medicines enjoy no price control.

Pricing:

The margins for the stockists and retailers are fixed by an agreement of Industry Associations and the All India Organization of Chemists and Druggists (AIOCD). The margin for the stockist/wholesaler is fixed at 10% on the Maximum Retail Price and 20% for Retailers. For drugs which fall under the price controlled category, the margins for the retailer is mandated at 16% as per the DPCO. The stockists retain 5-6% margin and pass on 3-4% margin to the sub-wholesaler or bulk retail buyer.
2.4.5 Indian Pharmaceutical Industry Post 1995 – a Transition

Rapid growth in the Indian pharmaceutical sector is attributable to three critical changes (Rai, 2008), setting up of public sector enterprises to boost the pharmaceutical production of drugs and increase Indian competency in pharmaceutical production, second The Drug Price Control Order (DPCO) and third The Indian Patents Act of 1970, which opened the flood gates for generics in India. There was a spurt in activities around the drug production, including support areas like pharmacy colleges and downstream businesses.

One of the important strategies adopted by the Indian pharmaceutical industry post liberalization was active internationalization (Chittoor et al. 2008). This includes external internationalization like overseas acquisitions and inward internationalization like import of technology, raw materials, capital goods and trained manpower.

Sampath (2005) indicated that, the Indian pharmaceutical sector consisted of more than 20,000 manufacturing units of which 5877 firms were actively involved in the production of bulk drugs and formulations. 300 companies account for over 95% of the total domestic market and the rest are small players. Based on the sales turnover the 300 firms can be categorized under 3 broad groups as indicated in the table below.

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Formulations firms</th>
<th>No. of API Production (No. of firms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>275</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>5700</td>
<td>5700</td>
<td></td>
</tr>
<tr>
<td>6000</td>
<td>6000</td>
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</tbody>
</table>


Group 1 comprises of large scale pharmaceutical firms that are subsidiaries of MNCs in India or wholly owned Indian firm. It includes firms like Ranbaxy, Cipla which spend considerable amount in R&D and are powered by the strategy to enter the global regulated market along
with semi regulated and domestic markets. Group 2 comprised of pure generic manufacturers who have limited competency on product development but are focused to cater to the needs of domestic and the semiregulated and unregulated markets. These firms are identified to have turnovers between Rupees 100-300 crore. Group 3 includes companies which perform contract research and manufacturing (CRAM) for bigger Indian companies, both local and MNCs. These companies have an annual turnover of less than Rupees 100 crore, whose strength is local network and connections. They do not have any R&D facilities and investments are made only towards upgradation of the manufacturing facilities.

Rai (2008) demonstrated that the dominant strategy of Group 1 firms are positive patenting, research on new chemical entity (NCE), innovation, biopharmaceutical research and developing New Drug Delivery Systems (NDDS). The Group 2 firms focus on non-infringing processes, innovations, positive patenting and specialty generics. Group 3 firms do not have any dominant competitive strategy.

Some of the criticisms that have been levied against the Indian pharmaceutical industry are: The focus on reverse engineering; Lack of expenditure on R&D; Inability to produce new drugs, which has resulted in an industry which is not invention based and aimed only at producing incremental modifications of existing drugs (Sampath, 2005).

Today the Indian pharmaceutical industry is on the threshold of exploring new opportunities and scaling global heights. Although a large spectrum of the Indian pharmaceutical firms are active as generic manufacturers, many firms are focusing on R&D for innovations like novel drug delivery systems (NDDS), novel combinations, original R&D, thereby aiding the transition of the Indian Pharmaceutical Industry to modern times.

Historically, Indian firms have begun their foray into the pharmaceutical industry by mastering the process of reverse engineering and developing low cost drugs to meet the domestic needs in India. Basic research, development of chemical entity was completely omitted. Large firms were in a position to move towards NDDS which is research based.

Indian firms are building knowledge base and conducting incremental innovation through R&D and moving towards the generation of New Chemical Entities (NCEs), Indian
outsourcing industry for contract manufacturing and contract research (Chaturvedi and Chataway, 2006). Additionally, many firms are outsourcing chemistry services to India primarily for organic synthesis and combinatorial chemistry to develop new chemical entities, which can be developed into new drugs. Indian contract manufacturing focuses on: contract manufacturing of patented drugs, specialized generics and old molecules (Nauriyal, 2006).

The biopharmaceutical sector is a promising area for Indian manufacturers with the focus being on the development of vaccines like Hepatitis B vaccine. Another area of promise is the biogenerics sector like insulin, erythropoietin for the world market.

Indian Pharmaceutical Industry’s capabilities include bioinformatics, organic chemistry syntheses, clinical research on bioavailability and bioequivalence. The areas of improvement are genomics, proteomics medicinal chemistry and animal trials (Lagnado, 2006). The new rule enacted by the government of India in Jan 2005, allows multinational companies to conduct trials of the same phase both in India and in other countries simultaneously. Thus with the genetically varied population, reduced costs of trials and companies have made India a clinical research hub (Nundy et al, 2005).