Chapter 1 - Introduction

There exists a lot of diversity in Indian pharmaceutical environment in various aspects. The pharmaceutical sector in Indian Health care industry should be adaptable and compatible with guidelines laid in National Drug policy (1986) which also lays special emphasis on availability of good quality generic drugs at affordable prices to common man. Such drugs cover the range of medicines required to treat widely prevalent diseases in Indian scenario. Many Indian firms including PSUs of state and central governments have started manufacturing such cheaper and good quality alternative drugs formulations, which are as of now available as patented innovator drug from private drug companies including MNCs at a very high cost. The Ministry of consumer affairs, Government of India has announced setting up of Jan Aushadhi Medical stores (JAS) at various kendriya Bhandars, on behalf of Department of Pharmaceuticals, Ministry of Chemicals and fertilizers, Government of India, (www.janaushadhi.gov.in/www.pharmaceuticals.gov.in, www.fcamin.mic.in) at many centres in Andhra Pradesh, Chandigarh, Delhi, Haryana, Odisha, Punjab, Rajasthan, Uttarakhand and West Bengal. These outlets sell same generic medicines at far lesser prices in place of branded medicines offered by private drug companies at higher prices. These include brands from multinationals also, for example difference in price of these formulations is illustrated in the table below:

**Table 1.1 Differences in price of formulations**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Branded medicine at available market price (INR)</th>
<th>JAS price (INR)</th>
</tr>
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<tbody>
<tr>
<td>Ciprofloxacin 500 mg. Pack of 10 tablets</td>
<td>97</td>
<td>21.5</td>
</tr>
<tr>
<td>Diclofenac 100 mg. Pack of 10 tablets</td>
<td>36.7</td>
<td>3.35</td>
</tr>
<tr>
<td>Cetrizine 10 mg. Pack of 10 tablets</td>
<td>20</td>
<td>2.75</td>
</tr>
<tr>
<td>Paracetamol 500 mg. Pack of 10 tablets</td>
<td>10</td>
<td>2.45</td>
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</tbody>
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So, the message that is being emphasized is “Quality medicines at affordable prices for all”. But this effort, of providing medicines of good quality at cheaper rates through
Kendriya Bhandars, has not yet achieved a generalized wide spread demand / supply across the country because such government sponsored drug sale and distribution centers are very few and far. The quantity, range and variety of available medicines are also inadequate. It may require voluminous effort on the part of government in this direction.

This also requires strong political will, better infra-structure, a well-established effective drug- distribution network, continuous R&D efforts and efficient and effective marketing management. At present Council of scientific & Industrial Research (CSIR), Government of India) has central drug Research Laboratory at Lucknow which is conducting research in new drug discoveries as well as production of cheaper and good quality drugs. There are a few recognized drug testing laboratories under government. All inexpensive drugs have to pass through stringent tests and get approval of drugs controller general of India (DCGI), before entry into the market.

Announcement by DCGI indicated that government will no longer allow popular drugs to be sold under the same name if their active ingredients are changed. In such cases, pharmaceutical companies have to change brand names (Ref: TOI dt.16.02.2011)-“New Ingredients in drugs? Can’t retail retain old name”). A scan of pharmaceutical sector in Indian market will reveal that there is over-loading of the market by the abundance of unnecessary drugs and various combinations of drugs. Scarce resources should not be spent on unnecessary medicines or on a more expensive medicine when a cheaper and equally effective alternative is available. This rational and ethical principle should be accepted by all the participants of pharmaceutical industry who are bound by legalities of good business and manufacturing practices.

It may be appreciated that India is rapidly growing to become a major and vibrant economic power, in spite of the wide disparities within its social milieu. There is increase, also in population of higher income group, who do not hesitate to afford branded costlier drugs in preference to cheaper alternatives (FICCI – Ernst & young study, 2010). India is now becoming a lucrative destination for global pharmaceutical giants. It is estimated that India may become a US$ 8 billion drug market by 2015 for
the MNCs. Domestic pharmaceutical market is expected to touch USD 21 billion by 2015, from 7.1 billion in 2007.

(Ref: http://www.moneyexpress.com/business/33701.txt.html)

Thus in India, pharmaceutical sector is a fast growing sector, second only to Information Technology sector with a 15% annual growth rate and exports worth Rs. 12000 crores. Even in period of “slow down” this sector is one of the biggest employers in India, with over 20000 manufacturing units. The management of pharmaceutical business includes marketing, quality assurance, R&D, finance, operations, wholesale and drug store management. The application of drug laws and/or intellectual property rights will be of necessary use for those in pharmaceutical business.

Recent developments in pharmaceutical sector in India reveal many mergers and acquisitions (M&A) taking place, resulting in shooting up of revenues of the business. The Indian companies are getting involved in this M&A space as there is growing domestic market for cheaper versions of patent drugs. (i.e. generic drugs) which also will be able to serve developed markets abroad. Unlike in past, the MNC pharmaceutical companies are clearly shifting their strategies:- from giving out manufacturing contracts to Indian companies to owning them. MNCs are attracted by the emerging markets in Indian scenario for generic drugs. This trend is noticed in the strategy of companies such as Pfizer, GSK, Abott and Sanofi. The pharmaceutical market has witnessed a strong double – digit growth ranging from 13.5% to 17% over the past four years (with the exception of the year 2008 when growth was relatively low at 10%). So for those MNCs facing sluggish sales in their home markets, even a market share of 2-3% in India could be attractive. (source: Mergers & Acquisitions in Pharmaceutical industry- News report TOI : 16.02.2011: “Pharma sector injects fresh life into M &A space”).

As the spending on health care increases with increase in personal incomes, market is all set to grow (and it may be double by 2015 AD!) On the other hand, this tendency of Indian pharmaceutical majors being bought by MNCs orients them away from Indian markets, and it may have adverse effect on drug pricing and affordability on the part of the average Indian consumer. In last four years, at least six big acquisitions of this kind took place including sell out of Ranbaxy Laboratories to Japanese Company, Daiichi
Sankyo, as shown in Table 1.2. Recently Daichi is taken over by Sun Pharmaceutical which is dealt in detail when discussed later on the firms.

### Table 1.2 Mergers and Acquisitions

<table>
<thead>
<tr>
<th>Year</th>
<th>Indian Company taken over</th>
<th>Foreign Buyer</th>
<th>Deal size $ Million</th>
</tr>
</thead>
<tbody>
<tr>
<td>June'08</td>
<td>Ranbaxy Lab</td>
<td>Daiichi Sankyo, Japan</td>
<td>4600</td>
</tr>
<tr>
<td>July'08</td>
<td>Shantha Biotech</td>
<td>Sanofi Aventis, France</td>
<td>783</td>
</tr>
<tr>
<td>Dec'09</td>
<td>Orchid Chem</td>
<td>Hospira, USA</td>
<td>400</td>
</tr>
<tr>
<td>Aug'06</td>
<td>Matrix Lab</td>
<td>Mylan Inc.</td>
<td>736</td>
</tr>
<tr>
<td>May'10</td>
<td>Piramal Healthcare</td>
<td>Abott, USA</td>
<td>3720</td>
</tr>
<tr>
<td>Dec'10</td>
<td>Paras Pharma</td>
<td>Reckitt Benckiser, USA</td>
<td>726</td>
</tr>
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The biosimilar opportunity is also big, that big pharmaceutical giants don’t want to miss it. Merck has established a subsidiary and Pfizer has tied up with Biocon. A biosimilar is an approximate copy of a patented biological drug. It is approximate copy because it is hard or impossible to make an exact copy of a biological at the moment. While generic drugs have made a big dent in the market, regulators had not allowed generics companies to make off-patent biological. They are relaxing their attitudes due to the high cost of patented biologicals. As in the generics, Indian companies are looking at a large global market in biosimilars. Big opportunity for Indian firms as several blockbusters goes off patent during year 2017 -2024. The size of the biosimilars market by 2020 is expected to be $11 Billion (source: Economic Times, 1st March 2012).

In view of above discussed scenario, it is quite obvious that costly drugs, which are ordinarily beyond the reach of average Indian consumer and which are manufactured by pharmaceutical companies including MNCs, are still reigning the market and enjoying their share in a tough competitive market. The drugs manufactured by pharmaceutical
companies including multinational corporations (MNCs) are costly drugs and these are ordinarily beyond reach of average Indian consumer. In 2010 the Planning Commission (a central government body), instituted a high level expert group to propose an overall framework for establishing universal health coverage (UHC) in India. The UHC will primarily grow generics market, with low prices moderating financial impact of increased volume, thereby eroding the margin for MNC generic players competing with low-cost locals. Nevertheless, keeping larger public good in mind, it will be in the best interest of even these companies to tailor down their costs to meet needs of consumer, without any compromise on quality. Keeping wide spectrum of prevalent diseases in India in view, analysis may be conducted to assess the firms in making available of the essential and vital drugs on basis of certain criteria such as:

1. Generic formulations of single drugs or generic formulations of scientifically acceptable and rational combinations.
2. Quantity versus demand and supply of specific formulations related to availability and affordability of drugs.
3. Market share of different brands of medicines of the same generic formulae manufactured by the different drug companies vis-à-vis their unit costs.
4. Assessment of these firms’s cost efficiency based on various inputs and outputs.
5. Does expenditure on R&D, actually yielding in new drug discovery in Indian context.
6. Are acquisitions by global companies targeted to control the generic and biosimilars markets?
7. Relooking on pricing strategies as marketing efforts by the firms supposedly improves the accessibility and affordability of drugs.

By such a study, it may be possible to understand clear picture of comparative assessment of the market place economics of drugs and of different firms at large to help the policy makers of government as well as business world of pharmaceutical and biotech sector, as to what inputs are required in this particular sector. This should help concerned agencies to plan their strategies to provide the essential medicines of acceptable quality standards in sufficient quantities at affordable price. The study may
generate healthy competition amongst various firms to provide drugs of high quality along with sustainable profits for the business. Business ethics as well as medical ethics and rationality are also equally very important while competing to get a good market share for any drug. Unethical practices result in poor economics. It may also be a fact that some MNCs may not want to introduce their latest drugs into the Indian pharmaceutical market. While the generics game continues, the consumer keeps paying more for patented drugs. (ref: www.rediff.com/money/2005/jan/html) So the new drug interventions that are the most suitable to use in our population have to be addressed and better ways needs to be identified to monitor, availability of these drugs as well as the drugs currently being in use. A realistic assessment of the cost effectiveness of these products in relation to their impact on health and socio-economic development is also desirable.

1.1 Indian pharmaceutical industry scenario

Indian pharmaceutical industry has emerged as a major player in the international stage as the fourth largest manufacturer of pharmaceutical drugs in the world and is widely respected for its high-quality low-cost generic drugs. Over the first two decades since independence, the 1950s and the ’60s, the domestic market in India was almost entirely import dependent and drug prices were among the highest in the world. Virtually all of the pharmaceutical drug patents in India were held by multinational companies. In order to ensure self-sufficiency in the supply of basic drugs and to end foreign domination of the industry in general, the Government of India introduced a number of important regulatory changes facilitating the entry of a large number of small firms. What contributed most to the phenomenal growth of the domestic industry was the Patents Act of 1970 which replaced product patents by process patents. Process patent allows an indigenous firm to manufacture through reverse engineering a generic substitute for an existing patented pharmaceutical product without paying a licensing fee so long as the production process for the generic substitute differed from the one used by the patent owner. Further, the Drug Price Control Order, also introduced in 1970, imposed a rigid price control on most of the drugs in the market with explicitly stipulated “maximum retail price” for the product. While these policies fostered competition, the industry
remained highly regulated through import restrictions, high tariff rates, and ceiling on foreign equity participation.

The protective trade policies, effectively nurtured the domestic industry into a sustainable stage of development. The consumers benefited from greater access to basic drugs at reasonable prices. The only drawback was that it permitted a large number of smaller firms, the so called unorganized sector of the industry to operate profitably in a highly knowledge-based industry by essentially copying the processes developed by others without having to develop their own Research and Development (R&D) capabilities.

**Post-2005 TRIPS scenario and Implications**

In most of the nations across the world, manufacturers of medicinal drugs, chemicals, processed food products and many articles such as mechanical appliances apply to the concerned governmental authorities for grant of “Patents”. A patent is a permission to have a sole and exclusive right granted by the authority over the production and marketing of, for example, say a medicinal drug. A drug manufacturer applies for the grant of patent after rigorous studies and testing of the drug for 10 to 15 years, so as to ensure its efficacy, safety and to satisfy prescribed quality assurance standards. If the patency rights are granted, then the manufacturer enjoys exclusive rights to produce market and sell the drug. The drug is question is said to be patented or in some sort means branded. This “patent protection” enables the owner to recover the costs incurred in research and development and to make profits. A particular period is prescribed for the “patent protection” to operate. When the number of years of patent protection elapses a “generic” drug is usually developed and sold by a competing company. The generic version of the drug is usually less expensive to develop and get approved. Often the owner of the patented or innovator drug introduces a generic version before the patent expires in order to get a head start in the market. The manufacturer may export his brand and enjoy his patency rights internationally as per the laws prevailing in the country of export.
Patent medicines have been criticized in the developing world especially in view of the financial constraints prevailing there and the lack of financial incentives to patents. Innovations in medicines have been discouraged. The “price discrimination” of medicines which is prevailing as an international policy, has been a hindrance for universal access to medicines for the needy and poor.

When India was under colonial rules by the British, there was hardly any encouragement for domestic pharmaceutical drug industry. The patent laws were foreign – favoring. The economy was largely agrarian. (Planning Commission, Government of India, 1st five year plan, Dec. 7, 1952). The prevailing healthcare system was such that most medicines manufactured abroad and imported into India were sold at some of the highest prices in the world. (Sudip Chaudhuri, 2005) Multinational companies mostly controlled the Indian drug industry. (Donald G. McNeil Jr., 2000). Life-saving essential drugs like penicillin and insulin were imported into India (Ist Five year plan, 1952). These were sold at prices which were definitely very high and unaffordable at that point of time. After Indian independence, there was realization of the need to provide medicines at lower costs to the Indian consumer. The policy changes had consumed quite some time, ultimately the independently drafted Patent law came out only in 1970s, after persistent demand by the Indian leaders for major changes of the then existing patent laws of British period in order to manufacture drugs which can be sold at affordable prices. The Indian patents Act, 1970, prohibited patents as products useful as medicines & food. It shortened the term of chemical process patents, and significantly expanded the availability of compulsory licensing. This paved the way for rapid growth of the generic drug industry in India. With respect to drugs, the basic concept of “generic” versus patented or “innovator”, the “brand name” versus “non-proprietary name” or “generic name” have been clarified since long. Non–proprietary name is the name of the active ingredient in the medicine that is decided by an expert committee and is understood internationally (WHO, 2013 a) (example: paracetamol / acetaminophen is a non-proprietary name or generic name while Crocin/ Metacin/ Tylenol are brand names). Generic drugs are usually intended to be interchangeable with an innovator product that is manufactured without license from the innovator company, and marketed after the expiry date of the
Bioequivalence is a Sinequanon to generic drugs. To ensure safety, efficacy and potency of a generic drug, good quality bio-equivalence studies come to help. Time and again the importance of generic prescribing has been emphasized, primarily to reduce the cost of drugs (Mukherjee R, 2013, MCI to doctors). The patent act (1970), allowed only “process patents” and not the “product patents”. The Indian pharmaceutical companies were allowed to use reverse engineering (i.e methods of organic chemistry) root to make and sell the generic drugs. The Government policy as well as the market environment overall, succeeded in lowering the market entry barriers. This exclusion of pharmaceutical products from patent protection, by allowing only process patents, has helped India develop a world class generic drug manufacturing industry, by the year 1972. (The Patents Act,1970). However, the process of making generic drugs remained patentable, with a very short patent term (manufactured to marketing, 5 to7 years) (P.Narayanan, 1998). Of course, the term of non-medicinal types, such as mechanical devices was 14 years from the date of patent. The act also included expansive compulsory licensing provisions, such that patented processes for manufacturing drugs were deemed automatically endorsed with the designation “licenses of rights”. The Indian government quite emphatically justified it’s broad limitations on the patent exclusivity in the 1970 act statement of “general principals” namely that “patents are granted to encourage inventions and to secure that the inventions are worked in India on a commercial scale and that they are not granted merely to enable the patentees to enjoy monopoly for the importation of the patented article”. (Janice M. Mueller, 2007)

As an eventual economic effect of the Indian patents act, 1970, there was a huge increase in the domestic generic drug manufacturing and a sharp decline in the prices of medicines sold in India. Any pharmaceutical product patented outside India could be freely copied in India, under the act, without infringing on the India process patent (which in any event lasted only 5 to 7 years). No violation of any foreign patent laws occurred as long as the copied drugs were made and sold only in India or exported to only such other countries which also did not recognize the pharmaceutical product patents.
This first indigenous patents regime was a deliberate choice of India to stimulate domestic manufacturing and reduced the price of medicines. In the wake of the patent act 1970, Indian pharmaceutical industry flourished as indigenous firms made huge gains in market share as against the multi-national pharmaceutical companies (Hamied Y.K, 2005). A number of multinationals left India or chose not to invest here, given the lack of patent protection (Imam.Ali, 2005). Scientist employed in the generic drug industry became skilled in process chemistry and reverse engineering (Chaudhari.S, 2005). There was a marked fall in drug prices in India. example: Price of Indian equivalent of Ranitidine (active ingredient in Glaxo’s Zantac anti-ulcer medicine), was over 160 times less than the price of Zantac in the US market (Keayla, B. K, 1998).

Virtually no research and development was undertaken in India in the pre – TRIPs era. (Bagchi, Amiya Kumar, 1984). Despite the patent act of 1970, India’s generic drug industry did not become an innovator of new molecules. Skilled scientists migrated to the west leading to “brain drain”. (Cohen Stephen Philip, 2001). Amongst the weaknesses of India’s domestic pharmaceutical sector, are said to be low investments in innovative R&D, lack of resources to compete with MNCs for new drug discovery research and to commercialize molecules on a worldwide basis. R&D investment of Indian companies as a percentage of total sales remained paltry as compared to the western pharmaceutical companies (Chandran et al, 2005).

TRIPS Agreement: The World trade organization (WTO) (WTO TRIPS Implementation, Agreement of TRIPS (Part I, II) WTO Annual report (2005)) was formed on the first of January, 1995, under Marrakech agreement, replacing the earlier GATT (General agreement on Tariffs and trades) which itself started functioning since 8th July, 1948. WTO organizes, supervises and liberalizes international trade and helps regulate the trade, negotiates issues related to trade and formalizes agreements and participates in dispute resolution process among the member countries. WTO also aims at enforcing the participating countries to adhere to agreements.

The trade–related aspects of intellectual property rights (TRIPS) (TRIPS Art I (3)) is an international agreement administered by the WTO, that sets down minimum standards for many forms of intellectual property regulations as applied to nationals of other WTO
members. It was negotiated at the end of the Uruguay round of the general agreement on Tariffs and trade (GATT) in 1994.

The TRIPS agreement introduced intellectual property law into the international trading system for the first time and remains the most comprehensive international agreement on intellectual property to date. In 2001, developing countries, being concerned of the insistence by developed countries and overly narrow reading of TRIPS, initiated a round of talks that resulted in the Doha declaration. The doha declaration is a WTO statement that clarifies the scope of TRIPS. For example: TRIPS should be interpreted in the light of the goal “to promote access to medicines for all”. After the Uruguay round, the GATT (replaced now by Marrakech agreement), became the basis for establishment of the WTO. Ratification of TRIPS is made compulsory requirement of all WTO member countries. Any country seeking to obtain easy access to the numerous international markets opened by WTO, must exact the strict international laws mandated by TRIPS.

For this reason, TRIPS is the most important multinational instrument for the globalization of intellectual property laws. Furthermore, unlike other agreements on intellectual property, TRIPS has a powerful enforcement mechanism. States can be disciplined through the WTOs dispute settlement mechanism. Amongst the several requirements of TRIPS is that the member states have to provide strong protection for intellectual property rights. For example, under TRIPS,

- Copyrights must be granted automatically
- Patents must be granted for “inventions” in all “fields of technology” (provided all patentability requirements are met), and must be enforceable for at least 20 years (Article 33).
- Legitimate interest of third parties has to be taken into account by the patent rights. (Art. 30)
- In each states intellectual property laws may not offer any benefits to local citizens which are not available to citizens of other TRIPS signatories, under the principle of national treatment (with certain limited exceptions, Art. 3 & 5
- TRIPS, also has a “most favored nation” clause.
Has TRIPS affected access to medicines? The most conflict has been over AIDS drugs in Africa, despite the role that patents have played in maintaining higher drug costs for public health program in Africa, this controversy has not lead to a revision of TRIPS. Instead, an interpretive statement, the Doha declaration, was issued in Nov, 2001 (mentioned above), which indicated that TRIPS should not prevent states from dealing with public health crisis. After, Doha, Pharmaceutical Researcher and Manufacturers of America (PhRMA), the US and to a lesser extent other developed countries began working to minimize the effect of the declaration.

A 2003, agreement loosened the domestic market requirement, and allows developing countries; to export to other countries where there is a national health problem as long as the drug exported are not part of a commercial or industrial policy. Drugs exported under such a regime may be packaged or colored differently in order to prevent them from prejudicing of markets, in the developed world.

In 2003, the Bush administration in USA, also altered its position, concluding that generic treatments might in fact be a component of effective strategy to combat HIV. Bush created the PEPFAR program which received $ 15 billion from 2003-07 and was re-authored in 2008 for $ 48 billion for the next five years. Despite wavering on the issue of compulsory licensing PEPFAR began to distribute generic drugs in 2004 – 05.

**Implementations of TRIPS in developing countries including India:**
India has been a WTO member since 1st of January, 1995, and a member of GATT since 8th July, 1948. India’s entry into the global economy at the end of 20th century, compelled the nation to once again award patents to drugs. Liberalization of the economy and the related structural reforms in 1990 led to increased growth rate, which in turn helped technical advancements to take place due to research and development (R&D). During the third globalization period (approximately from 1986 to the present), India had to eventually enter the WTO, as an active member with it accession to the Paris convention for the protection of intellectual property and the patent cooperation treaty (WIPO, Treaties Database—Contracting Parties—Paris Convention—India—Details, 1998). This has compelled our nation for significantly strengthening the patent
laws, in order to comply with the TRIPS agreement. India had to accept the TRIPS agreement in order to avoid any restrictions on its exports (Nadia Natasha Seeratan, (2001)). In order to gain the economic and political benefits of participation in the WTO’s trading system, India had no choice but to bring its patent laws into conformity with the WTO’s intellectual property rules as set forth in TRIPS. (WTO, Apr. 15, 1994, Marrakesh Agreement). All through this period India was clamoring for protectionism and shying away from intellectual property (IP) rights. Now, this country henceforth would have to apply internationally accepted criteria for granting patents, and the term of its patents would have to extend 20 years beyond filing. Until after trips compliance, several Indian Pharmaceutical companies were beginning to prove their metal in the International market for a few years. They were however not investing much in R&D for want of adequate government support. In the past, the Indian government made extensive use of the price control mechanism to control prices of bulk drugs and selected formulations (Cynthia M. Ho, 2011). The drug prices in India were among the lowest in the world, for almost 80% of the medicines. The outlook for the global generic pharmaceutical industry, including India appeared positive. There was a strong global generic market opportunity for India, with an estimated $ 60 – 70 billion worth of branded products expected to go off patent by 2006-2010. There were about 20000 pharmaceutical manufacturers in the country. The Indian pharmaceutical industry was poised to become the preferred global supplier for the manufacturing of bulk drugs and dosage forms. The interest of common consumer was being served fairly well. It is in this context, consequence of strict TRIPS compliance by India has to be viewed, just as for other developing countries.

The obligations under TRIPS apply equally to all member countries. However, extra time has been allowed for the developing countries to implement the applicable changes in their national laws in two tiers according to their level of development. TRIPS was extended to 2013, and until 1st January, 2016 for pharmaceutical patents, with the possibility of further extension. It has been argued that the TRIPS criteria requiring all countries to create strict intellectual property systems will be detrimental to poorer countries (www.ipjustice.org). A 2005 report by the WHO found that many developing
countries have not incorporated TRIPS flexibilities (e.g. compulsory licensing parallel importation, limits on data protection, use of broad market research and other exceptions on patentability, etc.) into their legislation to the extent authored under Doha (Musungu, Sisule F.; Oh, Cecilia, 2005). Banerjee and Nayak (Banerjee and Nayak, 2014), show that TRIPS has a positive effect on R&D expenditure of Indian firms.

Criticism: A growing level of criticism to TRIPS has been received from developing countries, academics and NGOs since the act came into force. Some of this criticism is against WTO as a whole. TRIPS is also regarded as a bad policy by many advocates of trade liberalization. The common bases for such criticisms are the wealth concentration effects of TRIPS, (moving money from people in developing countries to copyright owners and patent owners in developed countries) and its imposition on artificial scarcity on the citizens of the countries that would otherwise have had weaker Intellectual Property Laws.

India, though an emerging superpower is mired in immense domestic poverty and public health crises. The patent regime changes due to obligatory compliance to TRIPS criteria, came with lots of controversies. The extent of implementation of TRIPS is still uncertain. It is far too early to empirically establish, for example, whether India’s adoption of stronger patent laws will catalyze a significant shift from generic drug manufacturing to indigenous pharmaceutical innovation. What is clear, however, is that the implications of India’s tumultuous patent system transformation will be felt not only nationally but also around the globe (India’s Choice, 2005). From the perspective of the millions suffering from life threat diseases, who benefited in the low-cost-products of India’s thriving generic drug industry, the introduction of a pharmaceutical product patent regime (due to TRIPS compliance) in India is viewed as an International health care tragedy (Hamied. Y.K, 2005). This may be an extreme view. The true impact of the changes will turn on implementation. There appears to be the need to protect public from social costs of stronger patent protection and to provide incentives of domestic R&D in medical and health-care systems. This transformation of the nation’s patent regime is also viewed as entirely consistent with a burgeoning domestic pharmaceutical and
biotechnology industry that is beginning to invent rather than merely reverse engineer. The pharmaceutical industry is a “sunrise sector” for India (Kamal Nath, 2004). The government seeks to exploit the drug manufacturing skills well-honed in the generic drug industry to form a solid base for innovation in development of new drugs. Only a handful of pharmaceutical product patents have been generated since Jan 1, 2005 (Janice M. Mueller, 2007). So, it is too early to draw any conclusions about the impact of patent protection. The costs for developing a new drug in India are far below that of the same in U.S.A. Estimates are that it will cost only $100-200 million to develop a new drug in India, as compared to the U.S cost of $ 500-900 million. India signed the Uruguay round agreements (along with 116 other nations) as April 15, 1994 and became a member of W.T.O with effect from January 1st 1995 (Janice M. Mueller, 2007). Thus India became obligated to amend its domestic patent laws. Ultimately India enacted the patent (Amendment Act) 1999 and formally implemented the mailbox procedure for patent applications claiming pharmaceutical and agro-chemical products and made it retroactive to January 1, 1995 (Janice M. Mueller, 2007). Subsequently, the Patents(Amendment) Act, 2002 which was promulgated with effect from June, 25, 2002 (The Patents (Amendment) Act, 2002) brought some important changes, most significant was the extension of the patent term to 20 years from the date of filing the application. Prior to this amendment, Indian process patents for drugs lasted only for five years from sealing or 7 years from the date of patent (The Patents Act, No. 39 of 1970,). Another notable aspect of the 2002 amendment was formal recognition of India’s patent act of nations accession to the leading International Intellectual treaties, both administered by UN affiliated World Intellectual Property Organization (WIPO). The Patents (Amendment) Act 2002, implemented a myriad other changes intended to bring India’s Patent Laws into accord with the TRIPS agreement, including of new definition of “Invention” and “Inventive step”, “New exclusion” from patentable subject matter (Keayla, B. K. 1998), a new burden of proof of provision for cases of process patent infringement (The economist, 2004) and a revised compulsory licensing framework (Fareed Zakaria, 2006). Thus, during the TRIPS transition period, the Indian Patent act was amended on a couple of occasions until the latest amendment of the Patent Act, in 2005.
India’s accession to the WTO, which brought obligations to implement the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS), changed the conditions by re-introduction of product patent regime.

The era of protected development virtually ended with the amendment of the Patents Act in 2005 reintroducing product patents in place of process patents. Under the provisions of this Amended Act, it was no longer legal to manufacture generic substitutes for products patented in 1995 or later. Also, as part of the liberalization policy following the economic reforms, restrictions on import of bulk drugs were removed and the scope of price control was limited to fewer drugs with the expectation that the liberalized market environment would allow firms to function freely in response to market forces by entering into technological collaboration with foreign firms, exploiting economies of scale due to market expansion, and introducing new products and processes.

Implications

- The strengthening of IPRs regime may further limit the access of technology
- Local enterprises may be under pressure to close down or form alliances with larger firms, resulting in a concentration of the industry and dependence on imports may go up.
- Drug prices are probably going up upon introduction of product patents

**Indian Patent (Amendments) Act, 2005**

The Indian patents (Amendments) Act, 2005 came into force with effect from 1st Jan, 2005. This act was the last step towards achieving complete TRIPS compliance (Shamnad Basheer, 2005). After becoming a signatory of GATT, India revised the intellectual property protection from a softer “process patent” regime to a stronger “product patent” regime in 2005, in a phased manner starting from 1999. The domestic generic drug industry which has been internationally renowned this far, has come under treat because of this introduction of product patents for pharmaceutical inventions in place of process patents. This has triggered widespread protests both nationally and
internationally, to an extent never before witnessed in the annals of intellectual property law making in India. This latest act of amendment of the patent law is an attempt to balance the competing interest of a variety of stake holders, including domestic generic medicine producers, the domestic research and development committee, foreign multinational pharmaceutical companies, civil society group concerned with access to medicines and intellectual property lawyers.

In practical terms, with effect from 1\textsuperscript{st} Jan, 2005, (the day from which the patents (amendment) act 2005 came into force), any new patent application file in the patent office of the Indian Government and claiming a pharmaceutical product would need to be substantially examined for patentability in addition to the approximately 9000 mail box application pending during the TRIPS transition period. The government of the day had made last minute amendment on 10 out of 12 points (as demanded by the political partners of the Government) (Janice M. Mueller, 2007). Among the other changes, these amendments excluded embedded software from the ambit of the product regime and curved the evergreen patents by clarifying the concept of patentability, in unmistakable terms. The amendments also encompassed pre–grant opposition, a procedure within the patent office allowing the third party challenges to pending application. After the final touches and the official enactment of the act in April 2005, the patent (amendment) Act, 2005 became effective from Ist Jan, 2005. (The Patents (Amendment) Act, 2005).

Any analysis of India’s patent system must pass through a mosaic lens as a product of a multitude of powerful influences viz, the political compulsion because of a multi-party democracy, the unique structure of the pharmaceutical sector, the nation’s formidable demography, precarious condition of the country’s health care system and the governments in position of price control of essential drugs. In India, multinational companies held only 23 % share of the pharmaceutical market in 2004, as compared to the domestic companies. In fact Japan and India are the only two countries where multinationals do not dominate (Chaudhari,S, 2005). The Pharmaceutical Researcher and Manufacturers of America (PhRMA) organization took the position that India’s pre TRIPS patent law “was designed to punish importers of patented technology into India and to coerce local production” (Chaudhari.S, 2005).
Today, with the strengthened patent regime in India, multinationals are reconsidering and seeing India as a “Rising star”. The US based PhRMA declared that patent protection will provide the Indian scientists with incentives to discover and develop new life saving drugs. A good many of the leading multinational Pharmaceuticals firms now have their subsidiaries in India. (Janice M. Mueller, 2007). (Abbott Lab, Astra Zeneca, Burrough welcome, Novartis, E-Merck, Glaxo, Hoechst Mane Roussel, Sanofi Aventis, Smith Klime Beecham and Wyeth Ltd. Etc). The MNCs capitalize on Indians Labor costs and skilled work force. For example, Gen Electric built Medicity near New Delhi (Gurgaon) providing multi-specialty and holistic healthcare since 2007 (Saritha Rai, 2005). The research based MNCs led the call for stronger patent protection in India. Two leading trade groups for manufacture of branded drugs; viz the Indian Pharmaceutical Association (IPA) and the Organization of Pharmaceutical Producers in India (OPPI), strongly supported the TRIPS reforms (www.ipapharma.org/, http://www.indiaoppi.com/). OPPI took the position that if there is an assured climate of world class patent protection there can be productive collaboration between Indian and foreign companies with fresh investments, focus on R&D and clinical trials. As far as the domestic pharmaceutical companies are concerned, very few of these firms engage in R&D. Hundreds of other smaller firms subsist exclusively on reverse –engineering drugs that are still under patent outside of India as well as those off-patent. Thus, the wholly India owned domestic pharma sector is itself highly fragmented. However two of the top Indian pharmaceutical measures, in terms of sale viz, Ranbaxy Laboratories Limited and Dr. Reddy’s Labs limited (DRL) have been in partnerships and collaborations with MNCs and developed significant independent R&D capabilities. Indian major pharmaceutical companies are attempting to increase their share of US generic market, by aggressively challenging the validity of MNC – owned pharmaceutical patents in US courts. Ranbaxy and Dr. Reddy’s labs are particularly active in attacking US patents through filing of Abbreviated New Drug Applications (ANDA) with paragraph IV verifications (Fareed Zakaria, 2006) in the United States Food and Drug Administration (USFDA) (Ragavan, S, 2006). Even as more and more block buster drugs go off patent and thus may be freely copied, number of generic manufacturers competing for the US market is expanding. Indian generic drug
manufacturers (e.g Wockhardt limited, Nicholas Piramal India Limited, Sun Pharma industries limited, Lupin Limited and Cadilla Healthcare limited) compete today not only against US generic firms (such as Watson Barr, and Mylan), but also other generic firms based in Israel (e.g Teva), China, Italy and a number of other countries. Nicholas Piramal prefers to partner US firms and join them in collaborative R&D, rather than confront them in court (Janice M. Mueller, 2007), unlike Ranbaxy and DRL which challenge US pharmaceutical product patents.

The smaller numbers of firms produce formulations that are the processing of bulk drugs into finished dosage forms such as tablets and capsules. The export market is the mainstay for the smaller firms, but most exports only to markets characterized as “unregulated”. Such markets have little or no requirements for registration and quality inspection, and include country such as Vietnam, Syria, Jordan, Brazil, China, Korea, Taiwan and Egypt. Of the total exports of the bulk drugs from India in 2001-2002, and estimated 62 % were to unregulated markets. The remaining 38 % of exports were to regulated markets with higher entry barriers including the US, and other north American countries, Western Europe, Japan, Australia, New Zealand.

The recent Patent law reform has been vehemently opposed by many Indian drug firms. For example, Dr. Yusuf Hamied, the chairman of leading generic manufacturer, Cipla declared the enactment of the patent act 1970 to be “The dawn of a Golden Age” for the Indian Pharmaceutical Industry (Hamied. Y.K, 2005), while contrasting the 2005 introduction of pharmaceutical product patent protection in India as “One of the greatest predictable tragedies the World has witnessed”. IDMA (Indian Drug Manufacturers Association), a leading trading group for the nation’s generic drug manufacturers, warned that the strengthened patent regime would have “adverse implications” for the drug industry and the consumers in India. As recently observed in Sub-Saharan African countries, the impact of the strong patent protection could indeed be very grave, if the national patent law fails to provide for an effective compulsory licensing system (www.idma-assn.org).
Other Indian drug manufacturers, with significant R&D functions in addition to generic manufacturing took a more favorable stance towards, patent protection. For instance, “Ranbaxy has quoted: (The Patent (Amendment) Act, 2005) provides an incentive for organizations to be innovative and promises a plethora of opportunities for forward thinking organizations that believe in R&D”. Ranbaxy seeks patent not only in India but worldwide, (Janice M. Mueller, 2007) filing a total of 185 patent applications during 2005, (Ranbaxy Laboratories Limited Annual Report-2005).

The Intellectual Property Rights (IPR) commission of UK succinctly summarized as follows:

“In developing countries with strong generic industries, the outlook (for stronger patent protection) is also uncertain. On the one hand, manufacturers of mainly generic drugs are likely to be adversely affected by the introduction of patent protection, and also consumers and governments who will need to pay more for drugs that receive patent protection. On the other hand producers who are developing a research capability, or who may be able to obtain licenses from MNCs, may perceive benefits from patent protection. These conflicting impacts explain why the introduction of patent protection in India is so controversial.” (Commision on Intellectual Property Rights, 2002).

The Indian generic drug market is not going to vanish any time soon (Chandran et al). The new provisions of this amended patent law of 2005, guarantees that generic manufacturers can continue to copy any pharmaceutical products already available on Indian market prior to 1\textsuperscript{st} January, 2005. With respect to those products for which a mailbox applications matures into a granted patent on or after January 1, 2005, payment of a royalty to the patent will be required, but on going production by the generic firm cannot be restrained. The buying power of the Indian consumer and the market penetration are less than the more developed markets outside India. But still the Indian Pharmaceutical industry is worth about US $ 25 billion (2010) (Janice M. Mueller, 2007). India’s population of 1.1 billion (2010) includes rapidly growing middle class of about 300 million. (Fareed Zakaria, 2006). Ernst & Young Capital reports that about one-third that is 100 million of this group “can afford quality private healthcare” (Janice M.
Mueller, 2007). This wealthiest 10 % or so of the Indian population is no doubt the target population for companies such as Hoffman – La – Roche, which is pricing its new patented Hepatitis C Therapy, Pegasys, in India at about $ 10,000 per patient per year (Datta, P.T. Jyothi, 2006). [Now it is reported that pharma major Gilead to give licenses to 7 Indian firms to produce Sofosbuvir, the wonder medicine for Hepatitis C in India in its generic form. Gilead will be selling Sofosbuvir at $ 300 per bottle (one month treatment at one pill per day), i.e at about 1% of US price (TOI, 16 Sep, 2014)]

However, the remainder of India’s population of 800 million lives within less than $ 2a day (Fareed Zakaria,2006) There is hardly any social security network for citizens unlike in developed countries. Healthcare system is in “perpetual crisis” (Hamied .Y.K, 2005). The per capita expenditure as healthcare is about $ 28 a year (Approx) (2005) with $ 3 a year per capita on medicines. Less than 4% of India’s population carries health insurance coverage. In such a situation any changes in the demand structure could have a significant impact on the poor (Janice M. Mueller, 2007). The lack of a well-established medical insurance industry in India may perversely benefit patients in one respect which is that a breadth of Therapeutic alternatives available in the Indian Market. The wide variety of alternatives available for many drugs operates as a lever to keep prices in check, and should continue to function even after the introduction of pharmaceutical product patent protection. Drug prices are market driven. In India, all major therapeutic areas have multiple drug choices. So any new drug cannot command a premium just because it has a patent, because of low coverage by medical insurance, most drug purchases are paid out of pocket . If an Indian doctors gives a prescription to his patients for a branded generic drug priced above what the patient can afford, the pharmacist will likely to suggest an unbranded generic cheaper alternative.It was too soon to quantitatively assess the impact of drug pricing after 18 months of operation of the Act of 2005 (June , 2006).

At least for the time being, the introduction of pharmaceutical product patent protection in India will have a relatively minor impact on drug prices. The Indian government takes the position that “The fear that prices of medicines will spiral is unfounded” noting that 97 % of all drugs made in India are off patent, and so will remain unaffected by the new
regime. (Kamal Nath, 2004). “Another estimate is that in short term, prices will be impacted for at most about 15% of medicines sold in Indian market (Chandran et al). Compulsory licensing and Government-set ceiling on drug prices are the available safety valves. Patent protection may have a more substantial and negative impact on the public in the long term, only when a new generation drug will be invented and patented. At risk are new generations of much expensive AIDS drugs needed worldwide as resistant builds to medicines” (Editorial, The New York Times, 2005).

Almost three fourth of the Indian patent applications are still foreign owned. Traditionally there has been a negative view of patents as a “westernized” system required by the TRIPS agreement. So, there is a question of acceptability of the concept. This is an evolutionary stage of India’s patent regime which many view as a journey, not a destination.

Drug price controls: It is still unknown whether the newly patented pharmaceutical products will be considered for controls by DPCO (Drug price control organization), but governmental authorities mentioned price controls as one of the several tools at their disposal for protecting the Indian public from unreasonably high prices.

Some highlights of the amendment act of 2005:

- Product patents for pharmaceutical inventions, as already discussed.
- Software patentability. The earlier position under patent act, 1970 that a computer program per se is not patentable but now, prevails after the 2005 act.
- A “New invention” as defined under the 2005 act provides for ‘absolute’ novelty. In order to qualify as “new invention”, the said invention should not have been anticipated by publication in any document or used in the country elsewhere in the world. (Patents Act, 1970, as amended by Patents (Amendment) Act, 2005).
- A “New exclusion” under section 3(D) of the Patents Act, 1970, excluded a “New use for a known substance”, from the ambit of an invention. The 2005 act expanded on this exception by providing that “the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance would not be patentable.” It then states that salts,
esters, ethers, polymorphs, metabolite, etc shall be considered as same substance unless they “differ significantly in properties with regard to efficacy”.

- The “Inventive Step” test which means a feature of an invention that involves technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to the person skilled in the art. While the fundamental yard stick for measuring an ‘Inventive step’ remains that which is “not obvious to a person skilled in the art”, a requirement that the invention involve a ‘technical advance’ or have an ‘economic advance’ or have an ‘economic significance’ of some sort has been added. These changes in the law can lead to loose interpretation. (Pillai, M., 2005).

- The “New Use Exclusion” section 3D of the patents act 1970 excluded a “New Use” for a known substance from the ambit of ‘Invention’. The 2005 act has expanded on this exception by providing that the mere discovery of the new form of unknown substance which does not result in the enhancement of the known efficacy of that substance would not be patentable. It then states that salts, esters, ethers, polymorph, metabolites etc. shall be considered as the same substance unless they differs significantly in properties with regard to efficacy. As regards “Efficacy” the 2005 act also defines a “generic” medicinal product as:
  
  - Medicinal product which has the same qualitative and quantitative composition in active substances and same pharmaceutical forms as the reference medical product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bio availability studies. The different salts, esters, ethers, isomer, mixtures of isomer, complexes, or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and / or efficacy. In such cases additional information providing proof of safety and / or efficacy of the various salts, esters, or derivatives of the authorized active substance must be supplied by the applicant. The various immediate – release oral pharmaceutical forms shall be considered to be one and the same
pharmaceutical form. Bio availability studies need not be required of the applicant if he can demonstrate that the generic medicinal product needs the relevant criteria as defined in the appropriate detailed guidelines. (Directive, 2004). The term “Efficacy” would be construed in a drug regulatory sense. Firms generally file patent applications at the initial stage of discovery of the drug, while only at the later stage clinical studies on the drug (phase –III) takes place in order to gather information pertaining to the therapeutic efficacy of the drug. The requirement of information on “Efficacy” at the stage of filing a patent application is therefore an onerous one. (Shamnad Basheer, 2005). If on the other hand, the term “Efficacy” word to be construed in liberal sense to include a general hint of an added advantage in using the new form, It is possible that a good number of formulation would qualify as new substance upon showing an increased efficacy.

- Pre Grant / Post grant Opposition: While the patent act, 1970 is endowed with a fairly robust pre grant opposition mechanism, the 2005 act has introduced post grant opposition mechanism for the first time. Within a year of the patent being granted, a “person interested” can challenge the issued patent on the ground that are identical at the pre grant opposition stage (Patents Act, 1970, as amended by Patents (Amendment) Act, 2005). The combination of a pre grant opposition mechanism, a post grant opposition mechanism and a revocation mechanism makes the regime a very effective one for filtering out frivolous claims (Patents Act, 1970).

- Compulsory Licensing: This is one area where substantive and procedural changes have been made. India amended the patent act in the year 1999, to provide that the application claiming the pharmaceutical inventions would be accepted and put away in a mail box to be examined in 2005. These applications are commonly referred to as “mail box applications”. This amendment was in pursuance of a TRIPS obligation aimed at preserving the novelty of pharmaceutical inventions in those developing and least developed country
(LDC) members that did not grant product patents for Pharmaceutical innovations in 1995. (Samnaad Basheer, 2005). By virtue with this “Mail box” facility application would be judged ‘novelty’ on the basis of the filing date and not with reference to 2005, the year in which product patents were first incorporated into the patent regime. The mail box applicant who is granted patent would be issued an automatic compulsory license, if he is manufacturer of a generic drug and made a “significant investment” and was producing and marketing a drug covered by the mail box application prior to 2005.

**Figure 1.1 Three modes of compulsory Licensing**

- Compulsory Licenses for exports: The act provides for compulsory licenses to enable exports of pharmaceutical products to those countries with no manufacturing capacity of their own. Unfortunately, this suffered from an handicap – the provision required that the exporter obtain a compulsory license from the importing country as well. In the process the provision failed to cater to those situations where there was no patent in such importing country and no requirement for obtaining a compulsory license there. The 2005 act therefore seeks to rectify this by adding that an exporter can resort to sec 92A, where the importing country ‘has by notification’ or otherwise allowed importation of patented pharmaceutical products from India. (Patent act, 1970).

- Broad Implication of 2005 act:
  - Access to Medicines: The 2005 act has a number of safe guards built in to ensure that the production of existing generic version of drugs is not jeopardized. It also has provisions to ensure affordable access to new drugs. Whether such provisions will be interpreted in a manner conducive to public health needs, remains to be seen. Measures such as compulsory licensing, pre grant and post grant opposition mechanisms, retrospective damages provision, patentability threshold are all in built in the law.
  - Price control/ competition regime: Fears that price of patented pharmaceutical inventions may spiral also fail to take into account price control mechanisms and the newly instituted completion regime in India. In view of the 2005 act and its expected impact on prices, the government is considering strengthening the price control regime to increase competition and to ensure affordable medicines to the general medicine. To this end, a new drug pricing (Regulation and Management )Act is being considered (Samnaad Basheer,2005). The National Pharmaceutical Pricing Authority (NPPA) is established to check exorbitant drug price rise (Mukherjee,R, 2007).
  - Triggering an innovation culture in India: It is argued by MNCs of Pharmaceutical industries that a product patent regime is essential for
encouraging R&D in new drugs and catapulting the domestic industry into the innovative drugs sphere. Basic reverse engineering skills (Organic chemistry skills) are, however different from skills required for new drug discoveries. (Medicinal chemistry skills). Besides the cost involved for a researching upon and introducing a new drug into the market is colossal (Samnaad Basheer, 2007). It therefore remains to be seen whether incentives through patenting regime will achieve the desired results, and whether Indian companies will be able to compete with the global MNCs? Until recently the emphasis has been “mainly on building a system of production and not on a system of innovation (Padmashree Gehl Sampath, 2005). However off late some Indian firm has been engaging in incremental modification of pharmaceutical products in foreign countries. Innovations such as new drug delivery systems and formulations that are created to withstand tropical temperatures are of immense value. (see Sampath). Global MNCs could outsource some of their drug manufacturing and clinical trials to India and enter into appropriate partnerships with Indian companies. (Manojit Saha, 2005).

- Implications of Patents (amendment) Act, 2005 on TRIPS: The 2005 act is purportedly India’s final step towards TRIPS compliance. Yet, the TRIPS compatibility with some of its provisions may be in dispute. The DOHA declaration paragraph 4 reads as follows: “We agree that the TRIPS agreement does not and should not prevent members from taking measures to protect public health. Accordingly while reiterating our commitment to TRIPS agreement, we affirm that the agreement can and should be interpreted and implemented in a manner supportive of WTO member’s right. To protect public health and in particular, to promote access to medicines for all”.

Article 27 of TRIPS states that “all patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced”. The non-grant of retrospective rights to mail
box applications, coupled with making them automatically susceptible to compulsory licensing provisions, and may violate Article 27. Mailbox applicants could argue that when compared with other fields of technology, they have been discriminated. Whether this disadvantageous treatment of mail box applicants is an “unjustifiable imposition” will depend upon assessment of public health concerns and affordable access to medicines in India and the casual link between such concerns and the provisions that are allegedly in contravention of TRIPS. Article 27.1 is to be interpreted in the context of DOHA declaration paragraph 4, quoted above.

Pannu, Dinesh kumar, and Jamal A (2010), have specifically analyzed the impact of R&D and innovation on the relative efficiency and productivity change and firm performance in Indian pharmaceutical industry using DEA and economic models between 1998 and 2007, which covers the post – TRIPS (1995) and post Indian patent act (amendment) 2005 period. The authors have found a positive impact of innovation represented by R&D investment and patents on productivity (sales), market share, exports and ability to attract contract manufacturing among Indian companies.

Whether the patent (amendment) act, 2005 will serve the Indian national interest in the long run, remains to be seen. The act is the final step taken as a compromise, after lots of deliberations due to obligations on the country to comply with the TRIPS agreement. The government of the day had to dexterously maneuver around competing interest. The hasty legislation could have resulted in some lack of clarity. The provisions, however as off today, leave sufficient scope for the continued production of some generics. In so far as new drugs are concerned, the costs are likely to increase and in the absence of a nationwide healthcare system, the common man may have to bear the brunt of the new regime. However, there are some provisions in this regime that could be interpreted in a manner as to keep the cost down for the furtherance of public health concerns.

The Indian Patent (Amendments) Act, 2005 seeks to complete India’s full scale compliance with the TRIPS Agreement. The Act has the effect of invalidating Section 5 of the Indian Patent Act, which granted only process patents for food, medicines and other drug substances. As a result, reverse engineering possibilities available to the
pharmaceutical industry will only be limited to those drugs that are off-patent. The Act also introduces Section 92 (A) on compulsory licensing, in keeping with 30 August 2003 Decision of the WTO. Section 92 (A) of the Act deals with compulsory licensing of pharmaceuticals for export purposes. This is meant to facilitate the Indian industry to continue supplying cheaper generic versions of patented drugs to those LDCs that do not have adequate domestic manufacturing capabilities. The Patent (Amendments) Act of 2005 was preceded by an earlier 2004 Patent (Amendments) Ordinance that was different in several aspects from the Amendments Act of 2005 that has now been enacted. For example, the 2004 Ordinance provided for exclusive marketing rights (hereafter, EMRs) that were to be effective under the same terms under which they were granted, and also laid out the power of the government to sell or distribute the article for which the EMR was granted and to direct that the EMR-based product be sold at a regulated price (Section 24 D). The Patent (Amendments) Act, 2005 has now omitted Section 24 of the original Patent Act.

A large number of strategic options have been suggested (and promoted) as the way ahead for Indian firms, both by the government of India and also by agencies within India that are actively involved in industry analysis and growth. These include: focusing on original R&D activities, such as vaccines, and genetics research in addition to incremental product and process innovation; focusing on newer opportunities in the generics market, such as biogenerics / biosimilars, expanding into other areas such as clinical trials and herbal remedies/botanical medicines; specializing activities in order to benefit from outsourcing venues for contract research and manufacturing (CRAM), using collaborative ventures in both R&D and marketing to their advantage; among several others.

1.2 Firms strategies

It is cited below on the firm’s strategies adopted by different firms during the period.
### Figure 1.2 Emerging firm strategies: a categorization

<table>
<thead>
<tr>
<th>Firm group</th>
<th>Drivers</th>
<th>R&amp;D Strategies</th>
</tr>
</thead>
</table>
| Group 1    | • Entry and establishment in regulated markets  
• Realization that gains of entry are higher than initial costs to overcome barriers to entry  
• Need to strengthen product portfolios to insure against greater global competition | • Greater investment into R&D through revenues earned by product sales in regulated markets  
• Higher innovation in generics, new products and processes and bulk drugs. |
| Group 2    | • Taking advantage of business opportunities created by the shift in focus of group 1 companies to regulated markets  
• Need to strengthen competitive advantages, to make use of CRAM opportunities | • Active supply of offpatent generics to the semi-regulated and unregulated markets, by setting up manufacturing plants outside India or strengthening supplier partnerships  
• Focus on establishing themselves as niche players for contract research by choosing specific areas that give them competitive advantage: e.g., clinical research, domestic marketing.  
• Moving up the industry’s value chain gradually. |
| Group 3    | • Survival in the light of Schedule M of the Drugs and Cosmetics Act and India’s full fledged TRIPS compliance | • Upgrading facilities to Schedule M standards in order to continue manufacturing for group 1 and 2 companies. |

Main competitive strategies adopted by Indian firms

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialty generics</td>
<td>Several development initiatives at both Cipla and DRL are actively focusing on the development of specialty generics.</td>
</tr>
<tr>
<td>No infringing processes</td>
<td>Ranbaxy’s non-infringing process on Cefuroxime Axetil enabled Ranbaxy to be its sole seller for almost one and a half years in the US market. Matrix Laboratories has developed its own non-infringing process on Citalopram and is the sole exporter of the API to Europe presently.</td>
</tr>
<tr>
<td>Novel drug delivery systems</td>
<td>Ranbaxy has licensed its NDDS on ciprofloxacin to Bayer AG that is under consideration in the USA right now. It is also actively involved in developing NDDS in several other therapeutic areas such as gastric retention.</td>
</tr>
<tr>
<td>New chemical entities</td>
<td>Ranbaxy licensed out its NCE RBx 2258 for the treatment of cancer to Schwarz Pharma AG. This NCE has now been dropped from clinical trials. Dr. Reddy’s had licensed out its molecule for the treatment of Diabetes (Balaglitazone) to Novo Nordisk in 1997, for carrying out toxicology studies that form part of Phase II clinical trials. This molecule also had to be dropped from clinical trials due to toxicity issues.</td>
</tr>
</tbody>
</table>

Main collaborative strategies adopted by Indian firms

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-licensing arrangements</td>
<td>Nicholas Parimal and Roche agreement on launching Roche’s products dealing with cancer, epilepsy and AIDS in the local market (CII, 1999, p. 23). Agreement between Ranbaxy and K. S. Biomedix Ltd accords Ranbaxy exclusive marketing rights for TransMID, a biopharmaceutical product used in the treatment of brain cancer in India with an option to expand this to China and other South East Asian countries (IBEF and Ernst and Young, 2004b, p. 26). Agreement between Zydus Cadilla and Fermenta Biotech Ltd (A subsidiary of Duphar Interfran Ltd) that gives Zydus process technologies to manufacture Lisinopril and Benazepril exclusively within India.</td>
</tr>
<tr>
<td>Collaborative R&amp;D</td>
<td>Glaxo SmithKline and Ranbaxy have a collaborative R&amp;D arrangement for the development of new drugs in the areas of infective diseases and diabetes. Cipla has established an R&amp;D deal with a smaller biotechnology firm, Avestagen Laboratories to produce the biogeneric drug for Arthritis, N-Bril. Ranbaxy and Avestagen Laboratories have collaboration for the production of NCEs using biotechnological techniques. Avestagen has collaboration with Astrazeneca Research Facility to help develop their TB Dots products.</td>
</tr>
<tr>
<td>Contract research</td>
<td>Biocon’s subsidiary Syngene performs a large range of contract R&amp;D activities for pharmaceutical firms world-wide Avestagen Laboratories, also a biotechnology firm, performs R&amp;D for European pharmaceutical companies.</td>
</tr>
</tbody>
</table>

Source: IBEF and Ernst and Young, 2004b.
Major pharmaceutical companies in the Indian health sector with their comparative market size falls under below mentioned categories:-

- Global firms / MNCs
- Indian companies
  - Private sector
  - Public sector

Some of the top global firms are Pfizer, GlaxoSmithKline, Sanofi-Aventis, AstraZeneca, Novartis, Merck, Johnson & Johnson, Roche, Wyeth, and Abbott Laboratories.

1.3 **Mechanism of Drug Price Control in India**

The Indian pharmaceutical market has some special features. The most prominent feature is the fact that a very large proportion of drugs consumed in India are procured through retail sales. Retail sales of pharmaceuticals were US$ 6.2 billion while institutional sales were estimated around US$ 1.1 billion in 2006, i.e. 85% of drugs were sold through retail outlets. Institutional sales which account for 15% of the market include consumption through the public sector as well as through private hospitals and other institutions (Dr. Amit Sengupta, 2010). This is very different from what is seen in developed country markets, where a bulk of drug consumption is through supplies from large institutional mechanisms (hospitals, health insurance, etc., both in the public and private sector). Given this, the major issues related to drug prices are related to those that impact on retail prices. Since 1970, the Government has endeavoured to regulate the prices of some drugs through successive Drug Price Control Orders (DPCO). It must be understood that DPCO regulates the prices of only a fraction of the drugs in the market, and those drugs whose prices are controlled are notified in the relevant DPCO. In the case of all other drugs, the prices are not controlled and companies are at a liberty to charge whatever they wish. Over the last three decades, successive Drug Policies have specified different norms to exercise control on drug prices. The changing norms have included the following major areas:
i) The number of drugs under Price Control – From 342 in the DPCO of 1979 the drugs under price control have come down to 74 drugs in the DPCO of 1995 (which is still under operation)

ii) Criteria used to determine the drugs to be kept under price control – in the DPCO of 1979 the criteria for choosing which drugs should be under price control was based on how essential the drug was. Later DPCOs, instead, rely on market criteria, that is criteria that look at whether there is enough competition in the market.

**Drug Policy Formulation in India**

Drug policies in India are formulated by the Ministry of Chemicals and Fertilizers. In addition, in 1997, the National Pharmaceutical Pricing Authority (NPPA) was instituted as an independent body to take decisions on pricing. The Ministry of Health and Family Welfare looks into the issues of quality, manufacturing, sales and distribution of drugs. These two functions are performed in isolation and there is minimal co-ordination between the two major areas of policy making in the pharmaceutical sector. As a consequence the drug policy focuses only in the areas of production and pricing. With the exception of 1978, the drug policies have not incorporated a focus on health. According to guidelines formulated by the WHO (How to Develop and Implement a National Drug Policy. Geneva: WHO, 2001): a national drug policy is a commitment to a goal and a guide for action. It expresses and prioritizes medium- to long-term goals set by the government for the pharmaceutical sector, and identifies the main strategies for attaining them. It provides a framework within which the activities of the pharmaceutical sector can be coordinated. It covers both public and private sectors and involves all the main actors in the pharmaceutical field. In the broadest sense, a national drug policy should promote equity and sustainability of the pharmaceutical sector. The present practice in of drug policy making in India is thus at gross variance of accepted norms. Thus, what is known as a national drug policy in India does not conform to WHO’s broad definition of a drug policy. With its limited focus on production and pricing the objectives of access, quality and rational use, are only partially addressed through drug price control. The lack of involvement of the Ministry of Health and Family Welfare in
formulation of drug price control is evident from the fact that the criteria of selecting drugs to be kept in the price controlled category have been consistently market-driven, with no attempt since 1986 to link these up with health needs. Even after the national essential drugs list was formulated in 1996, there has been no attempt to link price control with it. At best, the essential drug list is used by the public health system to shortlist drugs to be procured within their often-constrained budget. (ref. Dr. Amit Sengupta, 2010)

**Drug Policy of 2002**

The Pharmaceutical Policy, 2002 by its own admission was formulated against the backdrop of policies of economic liberalization and the Government’s commitment to strengthen patent laws, i.e. becoming TRIPS compliant by January 2005. The Policy proposed a further relaxation in the criteria for selection of drugs to come under price control. For a bulk drug to come under price control it required to have a moving annual turnover of over Rs. 25 crore and the formulator’s share of 50% more of the market. If a bulk drug has an annual turnover of less than Rs 25 crore, it would come under price control if it has a minimum turnover of Rs 10 crore and the market share of any one formulator is 90% or more. Clearly, the criteria do not take into account the possibility of the existence of oligopoly, i.e. existence of a few firms and formation of cartels. It also does not consider situations where drugs may have high value and low volume, which may nonetheless be life-saving, such as drugs for cancer. High volume and low-value drugs may also escape the price net under this criterion. As in earlier policies, the 2002 Policy too does not attempt to link the proposed exemptions with health needs. It provides exemptions for new drugs, new processes and new delivery systems developed through indigenous R&D, patented in India and not produced in any other part of the world. These exemptions are based on the assumption that patents are perfect indicators of R&D. It is well established that not everything that is granted a patent is an innovation. With implementation of product patent regimes in January 2005, price regulation has assumed greater importance. The Policy was completely silent on this aspect. The Pharmaceutical Policy, 2002, thus, further deviated from path of promoting health objectives. The 2002 Policy was challenged in the Supreme Court of India and
was never put into operation. Thus, the Policy of 1994 and the DPCO 1995 remain in operation till date. If a new DPCO were to have been formulated based on the 2002 Policy, it is estimated that 20-25 drugs would have remained under price control.

1.4 Drug development process

"Emerging" infectious diseases can be defined as infections that have newly appeared in a population or have existed but are rapidly increasing in incidence or geographic range. Drug development is a long, expensive, and failure-prone process. It requires cutting-edge scientific skills, and collaboration across multiple disciplines within the pharmaceutical industry and among educational institutions, research laboratories, government regulators and healthcare professionals.

It takes 8-12 years on an average for a new drug to be developed for human use, and only 10 of around 10,000 substances identified as potential drugs will make it to the human testing stage. What’s more, only about one in 10,000 substances identified as potential drugs on preliminary screening will eventually be marketable. Potential new medicines are patented as soon as they are discovered, and the discoverer usually has less than 10 years of exclusive marketing rights remaining by the time regulators approve a medicine for marketing.

Drug development goes through three basic stages: discovery, full development and clinical trials.

Figure 1.3 Stages of Drug development
Drug discovery: The process begins with a new idea directed at chemically modifying a disease process. It involves developing a drug that will react with a new molecular target within the human body. The idea is usually generated from a thorough knowledge and understanding of disease processes and a continuing involvement with research in specific therapeutic area of interest (DiMasi J. A. and Grabowski H. G, 2007).

Full development: Drugs that are shown to work the best in Phase 2 studies have the least side effects, are expected to be the most economically viable, and are mass tested on thousands of patients. This phase of drug development is called Phase 3 or full development. New medicines are very expensive in the early years of sales to pay for the cost of drug development, publicize the benefits of the new therapeutic option, and provide returns to shareholders of the company.

Clinical research: Human trials are carried out when pre-clinical data demonstrates that it may be useful in treating a disease, and reasonably safe for initial testing in humans, among other things. A clinical trial has to be properly designed and planned to provide reliable efficacy and safety data. It also has to be approved regulatory authorities and by an Ethics Committee that permits the trial to be conducted at a particular institute.

The cost of developing a new drug is estimated to be around US$231 million in 1990. It has subsequently risen to over US$300 million in 1993 (Rs.950 crore) and 700-800 million in 21st century (Rajesh Jain, 2006). These figures give an idea about the failure /success rate in R&D and the cost of success per drug.

Thus research and development in pharmaceutical industry is a highly risky and expensive investment.

Small Molecule Drugs & Biomolecular Drugs (Biologics)

Most traditional pharmaceutical drugs are relatively simple molecules that have been found primarily through trial and error to treat the symptoms of a disease or illness. Biopharmaceuticals are large biological molecules such as proteins and these usually target underlying mechanisms and pathways of a malady (but not always, as is the case with using insulin to treat type 1 diabetes mellitus, as that treatment merely address symptoms of disease, not the underlying cause which is autoimmunity). They can deal with targets in humans that may not be accessible with traditional medicines (Dimasi,
2001). A patient typically is dosed with a small molecule via a tablet while a large molecule is typically injected.

Small molecules are manufactured by chemistry but larger molecules are created by living cells such as those found in the human body: for example, bacteria cells, yeast cells, animal or plant cells.

Modern biotechnology is often associated with the use of genetically altered microorganisms such as *E.coli* or yeast for production of substances like synthetic insulin or antibiotics. It can also refer to transgenic animals or transgenic plants, such as Bt corn. Genetically altered mammalian cells, such as Chinese Hamster Ovary cells (CHO), are also used to manufacture certain pharmaceuticals. Another promising new biotechnology application is the development of plant-made pharmaceuticals.

Biotechnology is also commonly associated with landmark breakthroughs in new medical therapies to treat hepatitis B, hepatitis C, cancers, arthritis, haemophilia, bone fractures, multiple sclerosis, and cardiovascular disorders.

Modern biotechnology can be used to manufacture existing medicines relatively easily and cheaply. The first genetically engineered products were medicines designed to treat human diseases. To cite one example, in 1978 Genentech developed synthetic humanized insulin by joining its gene with a plasmid vector inserted into the bacterium *Escherichia coli*. Insulin, widely used for the treatment of diabetes, was previously extracted from the pancreas of abattoir animals (cattle and/or pigs).

Modern biotechnology has evolved, making it possible to produce more easily and relatively cheaply human growth hormone, clotting factors for hemophiliacs, fertility drugs, erythropoietin and other drugs. Most drugs today are based on about 500 molecular targets. Genomic knowledge of the genes involved in diseases, disease pathways, and drug-response sites are expected to lead to the discovery of thousands more new targets.

Biotechnology creates a broad range of therapies, including vaccines, cell or gene therapies, therapeutic protein hormones, cytokines and tissue growth factors, and monoclonal antibodies. The bio/pharmaceutical industry embraces the discovery and development of both small molecule drugs (also referred to as New Chemical Entities or NCEs) and biomolecular drugs, also called biologics (also referred to as New Biological
Entities or NBEs). Small Molecule and biomolecular drugs can take on different names over the lifetime of drug discovery and development and marketing. (Source: www.fdli.org/pubs/journal/toc/vol54_2.html). Biosimilars are also referred to as Follow-on Biologics. By 1997 worldwide sales of biologics were over $7 billion dollars. The global sales of biologics have continued to rise – monoclonal antibodies alone in 2006 totaled $4.7 billion dollars. A popular misconception is that in early days most of new biologics were discovered and developed within biotech companies.

In recent years most of the large pharma have gained an expertise in biologics through entry into field, and also through acquisitions and are now bio/pharmaceutical companies, Prior to the ‘80s there were sufficiently few biomolecular drugs that the very term “pharmaceutical” or “drug” was taken to mean small molecule. With the exception of insulin, the few biomolecules approved for human use were administered by a trained health practitioner and were often considered “therapies”. With technological advances in the discovery and development of biologics most therapy areas (80%) are now amenable to either a small molecule or biologic strategy.