

India's Pharmaceutical Sector in 2008

Emerging Strategies and Global and Local Implications for Access to Medicines

By

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ABBREVIATIONS

ACT	Artemisinin Combination Therapy
AIDS	Acquired Immunodeficiency Syndrome
ANDA	Abbreviated New Drug Application
API	Active Pharmaceutical Ingredient
AR-LUM	Artemether Lumefantrine
ART	Antiretroviral Therapy
ARVs	Antiretrovirals
Cap Ex	Capital Expenditure
CHAI	Clinton HIV and AIDS Initiative
CNS	Central Nervous System
CVS	Cardiovascular System
CSIR	Centre for Scientific and Industrial Research
DFID	Department for International Development, UK
DMF	Drug Master File
EIU	Economist Intelligence Unit
FDA	Food and Drug Administration of the USA
FDC	Fixed Dose Combination
FY	Fiscal Year
GPRM	Global Price Reporting Mechanism
HIV	Human Immunodeficiency Virus
IBEF	India Brand Equity Foundation
IDMA	Indian Drug Manufacturers Association
IPA	Indian Pharmaceutical Alliance
MNCs	Multinational Companies
MDR TB	Multi-drug Resistant Tuberculosis
NDDS	New Drug Discovery Systems
NPPA	National Pharmaceutical Pricing Authority
PEPFAR	President's Emergency Plan for AIDS Relief
OI	Opportunistic Infections
OPPI	Organisation of Pharmaceutical Producers of India
R&D	Research and Development
TRIPS	Agreement on Trade Related Aspects of Intellectual Property Rights
UNITAID	International Drug Purchase Facility
USD	United States Dollar
WHO	World Health Organisation

EXECUTIVE SUMMARY

The main objective of this study is to investigate the present legal and economic framework in India and the emerging response of the local pharmaceutical sector since 2005, in order to analyse its implications for access to medicines, both local and global. The main research questions dealt with in detail are:

- (a) What are the developments since India's compliance with the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) in 2005 in the legal and economic framework that have implications for firms' behaviour and global access to medicines? How do the issues raised by (a) the Mashelkar report (and its aftermath), (b) the Novartis case, and (c) the Reddy Committee Report on data protection impact upon the creation of a conducive regulatory framework for sectoral innovation?
- (b) How do emerging disease trends within India (especially the growing importance of non-communicable diseases) and in other developing countries affect issues of availability and pricing of medicines in these segments?
- (c) To what extent can India continue to be a global producer of cheaper generic versions of drugs that are important from a public health perspective despite its TRIPS-compliant patent regime?
- (d) What forms of policy interventions remain significant to enable the sector to expand as a global player, while retaining its role as a major producer of cheaper drugs?

The study conducted a firm-level survey of the 75 largest firms in the Indian pharmaceutical sector in order to answer these questions. The ranking was derived using total revenues of all firms in the sector for the year 2007. Semi-structured questionnaires were administered to all the 75 firms, of which 49 were retrieved. Additionally, interviews were conducted with top-level management (CEOs and directors of R&D) of the firms as well as industry insiders and procurement agencies worldwide, in order to substantiate the information collected through the firm-level survey. The study finds that the Indian pharmaceutical sector is growing despite India's full-scale TRIPS compliance in 2005. Indian firms still supply to 70% of the market and nine out of the top ten companies are local companies. The analysis of present activities of the local firms and their strengths points towards three main drivers of growth.

Firstly, trends in global health innovation that relate to *expansion of the global generics sector and increased pressure on 'big pharma' to cut costs* are catalysing the quick integration of Indian firms into the global market. This architectural re-structuring of global pharmaceutical innovation is caused as much by newer technologies that have modularized innovation in the health sciences, as by global regulatory processes and the needs of consumers worldwide to access drugs at reasonable costs. In such an environment, the expanding R&D activities and economies of scale in manufacturing of Indian firms are important assets. Local firms have been quick to fill in the emerging opportunities as a result of these changes and also have captured niches where they can influence global innovation processes in their favour. They pursue a simultaneous collaborator-competitor strategy in local and global markets. They compete with the international firms for generic drugs and launch patent disputes to protect their interests, but at the same time, collaborate with them on various R&D fronts. Varying business models seem to be emerging, depending on what the firms perceive to be their intrinsic strengths and how they can capitalize on it. As opposed to their extreme focus on regulated markets, firms diversify their portfolios between regulated and unregulated

markets to capture economies of scale depending on their product portfolios and areas of interest.

Only 6% of the 49 firms that participated in the survey conducted all of their research on local disease conditions, and a large majority of the firms (75%) conducted less than 25% of their R&D on local disease conditions. Despite this, several firms view the opportunities in developing and least developed country markets as their stronghold. Since 2005, several domestic firms have attempted to set up subsidiaries or independent companies in other least developed countries in order to be able to operate in legal regimes that are not TRIPS-compliant. Sun Pharmaceuticals recently set up a company in Bangladesh, Cipla has embarked upon a recent initiative with the Ministry of Health in Uganda to set up a plant for the manufacture of antiretroviral and anti-malarial drugs in the country. The alliance between Cipla and Ministry of Uganda is the first of its kind, between an Indian firm and an African government, aimed at building local capacity to produce drugs of critical relevance to the country's health care system. Several other Indian firms are seeking to branch out into African countries through joint ventures and alliances – Strides Acrolabss, for example, now has a joint venture with Aspen Pharmacare, South Africa. Indian firms have also begun to use their technological capabilities to create products for specific low-income markets thereby disrupting existing modes of pharmaceutical innovation, a case in point being the fixed dose combinations (FDCs) for antiretroviral drugs.

A second factor in favour of the Indian firms is the *rapid expansion of the local pharmaceutical market and health care within India*. Rising personal incomes, changing disease profiles (with a larger share of global diseases within the country) and the increased privatisation of health care (with a rise in specialised clinics, hospitals and treatment centres) are creating new market opportunities in second and third tier Indian cities and towns. Although the local market is crowded, has too many small and medium firms, and has had lower profit margins than what can be gained by entering regulated markets abroad up until now, the increase in local purchasing power along with the changing disease profile of Indians both amount to a lucrative market. The advantage of an expanding domestic market for a wide range of diseases, including global diseases, offers Indian firms a secure base to invest.

Thirdly, *the policy stance of the Indian government in favour of public health and the local industry* has lent a much-needed assurance to firms regarding the legitimacy of their generics production activities. Undoubtedly, the increased demand for drugs- both lifestyle-related and others - will be the driving force of all growth in the pharmaceutical sector over the coming years in India. The best and the most logical entry into the Indian market for multinational companies is to launch newly patented products locally, but this cannot proceed smoothly in the absence of a policy framework that clearly gives the patent holder firms the right to enforce their patents within the country. The multinationals rely to a large extent on a TRIPS-compliant regulatory framework, legal certainty in the way the patent regime is interpreted, and better physical infrastructure support to expand their activities in the Indian economy through the launch of their patented products. The Indian firms, on the other hand, need a regulatory framework that is sympathetic to their needs to extract synergies between their on-going generics activities and emerging R&D opportunities worldwide.

The review of the trends in India's TRIPS-compliant regulatory regime conducted in this study shows that the Indian policy on implementation of the TRIPS Agreement

post-2005 has been an effort to (a) maintain the *availability of drugs* (for local consumption and exports) *at low prices* and to (b) *minimize the impact* of the patent regime on the domestic industry. The Patent (Amendments) Act of 2005 contains some key provisions that lean in favour of public health. All pre-1995 patents do not qualify for protection in India and all products with patent priority dates between 1995 and 2005 can continue to be manufactured by generic firms despite grant of a patent in India, if the generic manufacturers already had a market approved version of the patented drug, in return for payment of a “reasonable” royalties to the respective patent holder firms. The term “reasonable royalty” is not defined in the Act and therefore subject to interpretation. Section 3 (d) of the Act that deals with the definition of patentability specifies that patents will not be granted automatically for different forms of the same molecules, such as salts, esters, polymorphs and decisions will be taken case-by-case to establish novelty in an effort to prevent ever-greening of molecules. This and several other provisions are in place in the regime to ensure a mitigated impact of the TRIPS-compliant patent regime on local pharmaceutical firms. Indian firms need time to manoeuvre themselves into the global pharmaceutical scenario for innovative R&D, and their strengths need to be harnessed to extract rents from generics and contract research and manufacturing activities: most of the policy developments in India fall into this line of vision.

The decision of the Indian high court on the Novartis case, as well as newer ongoing disputes, such as the one related to Roche’s Ertolonib (brand name Tarseva) analysed in the study show the on-going efforts in India to interpret the patent regime in the interests of public health. However, it also raises an important issue of legal certainty that the Indian regime needs to establish. Patents once granted need to be enforced, and in the absence of clarity on this issue, the Indian policy framework may promote a potentially precarious trend.

The analysis of the role of Indian firms in access to medicines worldwide shows that Indian firms remain the most important suppliers of first as well as second-line antiretroviral drugs, despite product patent protection. Whereas the market for first line ARVs is heavily commoditised with several generic manufacturers for each of the products, the second-line ARVs, especially Lopinavir/ Ritonavir and Atazanavir have limited supply and Indian firms are playing a very important role in ensuring competition in the market. Several local Indian firms have invested in the production of second-line drugs Lopinavir/ Ritnonavir and Atazanavir. According to the Global Price Reporting Mechanism (GPRM) database, generic competition amongst first line suppliers have brought down the median price of the most commonly prescribed fixed dose combination in first-line regimen (d4T 30 mg + 3TC 150 mg + NVP 200 mg) by 40% from US\$ 153 (2004) to US\$ 92 (2007) in low-income countries and from US\$ 154 (2004) to US\$ 91 (2007) in middle- income countries. The legal validity of the patents on these drugs in India is still in the open, but given the present trends, it seems that patents on second-line ARVs will not be granted in India on public health grounds. Indian firms are also the sole manufacturers of several fixed dose combinations for HIV/AIDS, especially paediatric fixed dose combinations.

Indian firms are also important suppliers of Malaria drugs, and have the potential of producing generic versions of drugs to treat opportunistic infections that are presently not available in resource-poor settings due to the high prices of patent holder firms. These include Valgancyclovir and Valacyclovir. There is an on-going patent dispute on the grant of patent to Roche for Valgancyclovir (Valcyte) and two Indian producers are presently producing the drug. Some international procurement agencies are in the

process of helping to organise the supply of the drug to resource poor environments where they are presently not in use due to their high prices.

The conclusions and policy recommendations that arise from the analysis are presented here under three separate headings: those of concern to the pharmaceutical sector, those related to the regulatory environment and those that are directed towards enhancing access to medicines.

On the pharmaceutical sector

There is an emergence of a new industrial structure due to the gradual integration of the Indian firms with the global pharmaceutical industry, increased modularization of pharmaceutical innovation globally and outsourcing possibilities. Indian firms have seized opportunities arising from pressures in the global innovation environment, but they have also been innovative in building their own niches. To a large extent, their model has been and continues to be one where they seek to disrupt global patterns of innovation through the introduction of products that are cheaper, affordable and in some cases, as in the case of the HIV/AIDS drugs, targeted towards the masses. In such cases, the economies of scale results in benefits that only focusing on high-value added products would not. Maintaining this diversified product portfolio is enabled by the strong domestic base at home that offers an opportunity to manufacture drugs for a wide range of diseases, including global diseases.

However, this mainstreaming of Indian firms into the global industry implies also a greater sensitivity to changes in global regulatory structures that seek to favour multinational firms and make it difficult for new entrants to establish themselves globally. The recent Ranbaxy-Daichii Sankyo deal serves as a reminder of the turbulent market in which the firms presently operate: the difficulties of integrating and making a place in global innovation are as numerous as the opportunities they pose. Global realities of pharmaceutical innovation are such that even established firms in developed countries tend to rely more and more on government sponsored 'translational' public sector research to create marketable products and venture capital institutions are coming under increased strain. Indian firms, seeking to compete globally in this changing scenario, will require much more strategic policy support by the government.

This strategic governmental support should be aimed both at encouraging firms to disrupt patterns of global innovation in the pharmaceutical sector to create products for the poor the world over, making medicines more accessible; and to help them focus their efforts on accumulating greater technological capabilities while maintaining their strength as low-cost innovators of high-value pharmaceutical products. This will include the following.

1. The role of the Centre for Science and Industrial Research as a pro-active, industry-oriented public sector institute needs to be revived apart from efforts to strategically allocate public sector resources to support the firms.
2. A wider range of initiatives for enhanced collaboration between various actors in the pharmaceutical innovation system needs to be put in place.
3. There is a need to re-think the relationship between price control and drug availability and affordability that takes into account two important features of the market:
 - a. The amount of competition in the market and the mark-ups in

- pharmaceutical products (due to unregulated intermediary stages) before it reaches the consumers;
- b. The importance of encouraging practices amongst Indian firms that allow for price discriminations between regulated and unregulated markets. Their products are intrinsically cheaper at the present, but this might become an issue in the future with rising costs of conducting R&D in India.
4. There is a need to enhance incentives for firms to invest into anti-retroviral drugs and drugs for Malaria and Tuberculosis. There have been no new entrants in the ARV market over the past three years, except Emcure and Cadila and the markets for Malaria and Tuberculosis remain largely stagnant. There is a need to envision newer incentives that focus on how to promote R&D in India for these diseases in addition to the production of generic versions.
- The newly created Department of Pharmaceuticals could play a critical role in enabling support structures of relevance to the sector's performance and growth.

On the Regulatory Framework

The way the Indian patent regime is being implemented calls for legal clarity. There is a need for greater clarity on what is patentable in India, when (and for which categories) can local companies apply for compulsory licenses, and under what conditions can patents granted within India be over-ridden by Indian firms. There is also a need to establish clearly how patents will be granted and what procedures will be followed for pre and post grant oppositions. In the absence of this, extended legal battles between local firms, MNCs and civil rights groups are costly and difficult to sustain. India also needs to establish that it can not only grant but also enforce patents on pharmaceutical products in cases where the applications are consistent with the requirements of the Indian Patent Act. The Tarseva case (on Roche's Ertolonib) for example, leaves one wondering about the sanctity of the patents granted in India. It is clear that the patent's absence would be a major boon for public health. However, this decision needs to be made at the *ex-ante* stage as to whether at all such products should be granted patents in India.

That said, the spate of patent disputes shows how Indian legislators and courts are seriously engaged in finding ways to promote access to medicines despite their obligations under the TRIPS Agreement. This commitment is extremely valuable, and should be fostered further through technical advice on how to achieve legal certainty in interpretations of the Indian patent regime that balance the country's obligations under the TRIPS commitments and public health objectives.

There is a need for enhanced coordination (and not linkage) between the Patent Office and the Drug Controller of India, which is in-charge of granting market approval to all new drugs. There is also a need for more transparency in the workings of the patent offices in the country. The Office of India's Controller General of Patents, New Delhi is now conducting an investigation on whether the grant of a patent on Valgancyclovir (Valcyte) violated Indian patent rules. These forms of institutional costs can be avoided by creating patent databases that allow for better functioning of the Patent Offices around the country, and also help clarify the status of patent grants to those interested in industry. Pre- and Post-opposition procedures also need to be clarified, the Valcyte case again being a case in point.

It is still not clear why India needs a data exclusivity regime as suggested by the Reddy Committee Report after the transition phase. Although the regime suggested by the Reddy Committee is in the interest of public health, the question that looms large is whether and if this regime will be implemented in its entirety eventually? As this study shows, leaving out one or two stipulations of the report will have far-reaching repercussions on public health.

On enhancing access to medicines

This study shows that Indian firms continue to play a critical role as suppliers of drugs for public health post 2005, especially HIV/AIDS, Malaria, TB and other opportunistic infections. Given the fact that their presence has already brought about some price reductions in Lopivavir/ Ritonavir similar to what was observed in the case of first-line ARVs, and their potential to further enhance competition in existing and future drug categories for these diseases, much more effort is required to expand the role as well as interest more firms in focusing on product portfolios that include these drugs. The lack of capacity (both regulatory and technological) in Bangladesh and the lack of political willingness to grant compulsory licenses on drugs of importance to public health in China reinforce the findings of this study on the role played by Indian firms. Given the importance of capabilities and economies of scale to engage in such activities, scarce international resources seem better spent to facilitate Indian firms to enhance their activities, rather than focus on building capacity in sectors in other least developed countries. These efforts should include a re-think on international procurement guidelines for ARVs in order to focus them on price-quality rather than the cheapest price, in order to prevent the scope for any predatory pricing practices amongst the generic producers. There is a need to preserve maximum dynamic competition in this segment in the interest of global public health. Most of the ARV producing firms interviewed for this study expressed difficulties of working with tenders that merely focused on price to supply newer ARV drugs that required greater technological inputs and increased formulation capabilities.

Specifically on the domestic regulatory strategies to enhance access to medicines within India, there is not much correlation between local production and marketing possibilities for various therapeutic categories of products and government's access to medicine strategies. Especially, there seems to be a very clear disjuncture between the government's plan to bring over 300 categories of drugs under price control and the extent of competition witnessed in the market for key therapeutic categories. Mistaken policy making in this regard may be detrimental to the interests of the sector at this point of time.

1.0 Introduction

India's product patent regime has brought the local pharmaceutical sector into the global system in a way that its protected regulatory structures had never allowed before. India continues to be a very significant global producer of generics drugs and local Indian firms are actively involved in expanding through foreign acquisitions, setting up global subsidiaries and hiving off separate R&D companies, all of which point to the emergence of new industrial structures. The emergence of this new industrial dynamism is strongly influenced by changes in global regulatory structures for pharmaceutical innovation, influx of newer technologies and strategies of global players that go much beyond outsourcing. Understanding the drivers of change will be important for the design of meaningful interventions to enable the local sector to perform in the face of global competition and in the interests of global public health.

The purpose of this study is to investigate the present legal and economic framework in India and the emerging response of the local pharmaceutical sector since 2005, in order to analyse its implications for access to medicines, both local and global. The main research questions that this study deals with are:¹

- (e) What are the developments since India's compliance with the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) in 2005 in the legal and economic framework that have implications for firms' behaviour and global access to medicines? How do the issues raised by (a) the Mashelkar report (and its aftermath), (b) the Novartis case, and (c) the Reddy Committee Report on data protection impact upon the creation of a conducive regulatory framework for sectoral innovation?
- (f) How do emerging disease trends within India (especially the growing importance of non-communicable diseases) and in other developing countries affect issues of availability and pricing of medicines in these segments?
- (g) To what extent can India continue to be a global producer of cheaper generic versions of drugs that are important from a public health perspective despite its TRIPS-compliant patent regime?
- (h) What forms of policy interventions remain significant to enable the sector to expand as a global player, while retaining its role as a major producer of cheaper drugs?

This study was conducted in three main stages. The first stage consisted of the preparation of a background report based on secondary sources and the expert perception of scholars and scientists in the field, on the basis of which a list of the top hundred firms in the Indian pharmaceutical sector was derived. A range of semi-structured interviews with experts and industry insiders were conducted as the second step in order to help clarify the structure and content of the study framework and to refine and provide content validation to the survey questionnaire. In the second stage, semi-structured questionnaires were administered to 75 firms within the list of the top hundred firms derived by ranking them according to their total revenue according to company annual reports. Of these, 49 were retrieved and these form the basis of the statistical analysis conducted in this study. The ranking of the top 100 firms on the basis of their total revenues is listed in annex 4 of this study. The third stage consisted of detailed field interviews with top-level management of firms that participated in the survey (CEOs and directors of R&D and marketing) and experts working in national,

¹ Taken from the TORs of this study.

regional and international organizations. The list of people interviewed is contained in annex 2.

The scope of this study is to *analyse the impact of emerging strategies of Indian firms and the new developments in the policy framework on global and local access to medicines*. The analysis particularly focused on the issue of pricing and availability of second line ARVs, in addition to other emerging segments. The survey targets a period of five years, from 2003 to 2007, and builds further upon a similar survey carried out by the author in 2005² that looked at the sector trends and emerging firm-level strategies from 2000-2005, and a study conducted by Grace (2005)³ for the DFID that looked at access to medicines in India and China.

2.0 The Indian Pharmaceutical Sector: Sector Growth and Main Drivers

The Indian pharmaceutical sector was estimated to be worth US\$12bn in 2006/07 according to the Department of Chemicals and Petrochemicals. Although there are some differences in industry forecasts – the Economist Intelligence Unit predicts it to be worth US\$ 20 billion a year by 2021,⁴ a Mckinsey analysis (2007) concludes this to be possible already by 2015⁵ and the Indian National Pharmaceutical Policy of 2006 sets this as a feasible target for 2010 – there is no doubt that the sector is thriving despite India's full-scale compliance with the TRIPS Agreement in 2005. In 2005/06 the Indian pharmaceutical industry's share of the global market stood at 1.5% (ranked 13th) in terms of value but at 8% (ranked fourth) in terms of volume.⁶ The domestic sector meets 70% of all local demands for drugs despite the increased presence of multinational companies since 2005,⁷ and 95% of all products sold in the market continue to be generic drugs.⁸

Although there are around 10,000 registered local companies,⁹ the organised sector is relatively small and comprises around 300 large and medium-sized firms, which account for 70% of the entire market. Nine out of the top ten companies as of 2007 are local companies (annual reports, see list of top 100 firms analysed in Annex 1) and they hold approximately 30% of the entire market.¹⁰

Box 1.0 Market Figures at a Glance¹¹

² Padmashree Gehl Sampath, "Economic Aspects of Medicines After 2005: Product Patent Protection and Emerging Firm Strategies in the Indian Pharmaceutical Industry, A study for the CIPIH, WHO, 2005.

³ Grace, C., "Update on China and India and Access to Medicines", Briefing paper for DFID, London: DFID Health Resource Centre, November 2005.

⁴ Industry Forecast: Health Care and Pharmaceuticals India, Economist Intelligence Unit, 2007, p. 9 (*hereafter referred to in this study as Economist Intelligence Unit Forecast, 2007*).

⁵ KPMG, The Indian Pharmaceutical Industry: Collaboration for Growth, 2006 (*hereafter referred to in this study as KPMG, 2006*).

⁶ India Brand Equity Foundation (IBEF), India: Pharmaceuticals, A report by Ernst and Young for IBEF, 2006.

⁷ This is a decrease of only 5% of the position held by the Indian companies in the fiscal year 2003, where they had a market share of 75%. See IBEF, India: Pharmaceuticals, Report prepared by the India Brand Equity Foundation and Ernst and Young, 2004, p. 8.

⁸ Economist Intelligence Unit Forecast, 2007.

⁹ Economist Intelligence Unit Forecast, 2007.

¹⁰ KPMG, 2006.

¹¹ Economist Intelligence Unit Forecast, 2007; Guatam Kumra, Palash Mitra and Chandrika Pasricha, Indian Pharma 2015: Unlocking the Potential of the Indian Pharmaceuticals Market, Mckinsey and Company, 2007 (*hereafter, Mckinsey, 2007*); Bain and Co, The Indian Opportunity in Pharmaceuticals and Manufacturing,

- In 2007, the local sector met 70% of the domestic demand for vaccines, APIs, intermediaries and fixed formulations.
- In 2006/07 around two-thirds of production was for domestic consumption and the rest was exported.
- This represented a 30% increase from 2005/06 figures and accounted for 2.5% of all exports.
- Generics and active pharmaceutical ingredients are the main exports to over 150 countries worldwide.
- The USA remains the main export market, with the EU becoming increasingly important.
- The pharmaceutical sector is the most R&D intensive sector in the country presently. In 2006, the sector's R&D investments exceeded all other major sectors, such as automobiles and software.
- Nine of the top ten firms continue to be local firms since 2004.

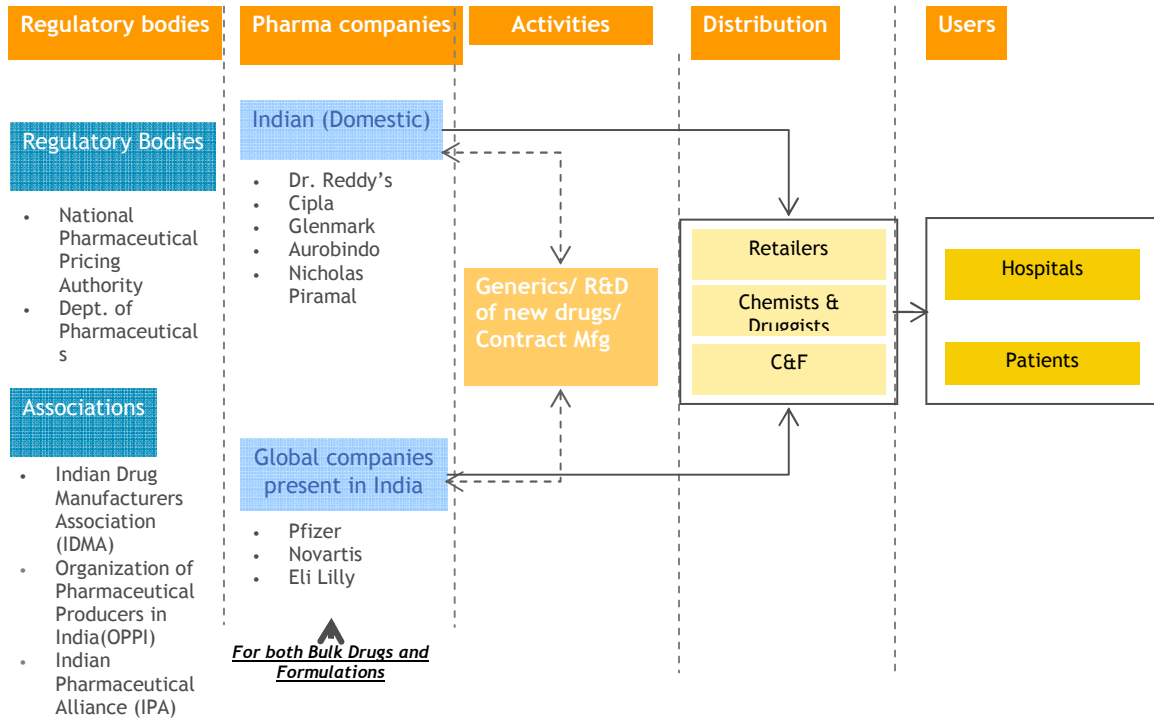
Figure 1 below shows the main actors in the sector, the activities and the distribution channels. The firms are engaged in both formulations (finished dosages) and active pharmaceutical ingredients (APIs, also called bulk drugs) that need to be mixed with excipients to create the final drugs). According to the Department of Commerce figures, formulations constitute around 80% of India's total pharmaceutical production and APIs make up for the remaining 20%.¹² Until June 2008, the pharmaceutical sector was under the mandate of the Department of Chemicals and Petrochemicals, located in the Ministry of Chemicals and Fertilizers. Recently, a new Department of Pharmaceuticals has been created.

The formulation of policies for the sector is split between the Ministry of Chemicals and Fertilizers, the Ministry of Commerce and Industry (and the Department of Intellectual Property Protection), the Ministry of Health and Family Welfare and the Ministry of Science and Technology (Department of Science and Technology and the Department of Biotechnology).

Presented at the Annual Meeting of the World Economic Forum 2008 (*hereafter referred to as Bain and Co, 2008*).

¹² Also see the Economist Intelligence Unit Forecast 2007 and Mckinsey, 2007.

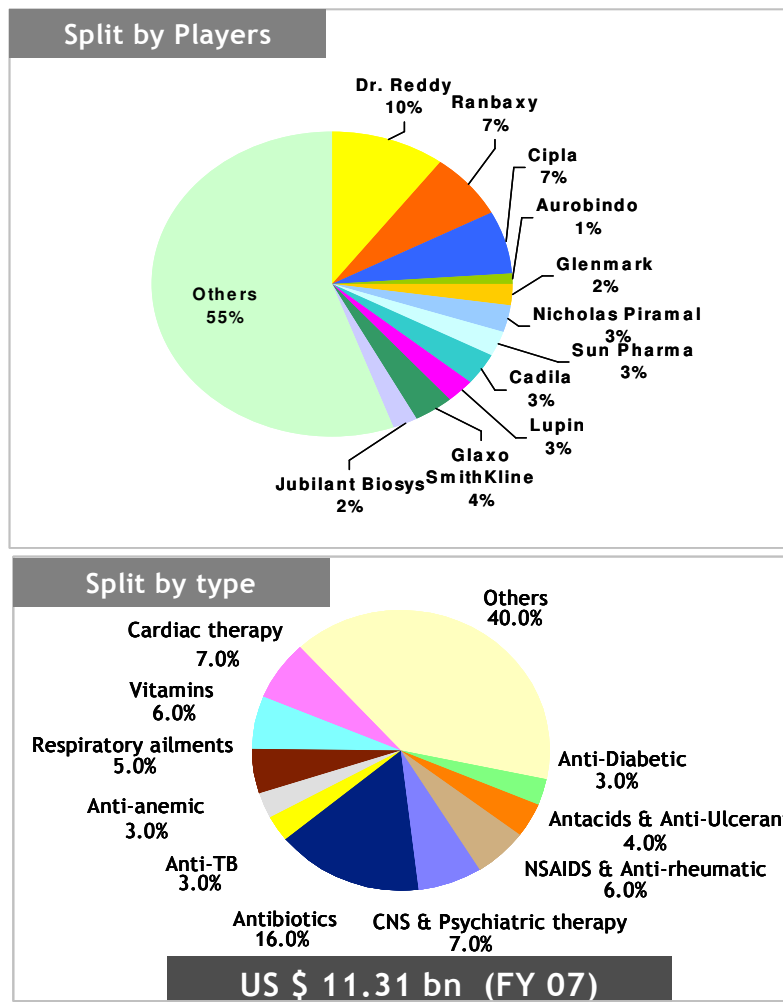
Figure 1: Organisation of the Indian Pharmaceutical Sector



Source: author.

Furthermore, the National Pharmaceutical Pricing Authority (NPPA) is an independent agency under the Department of Pharmaceuticals (it was earlier under the Department of Chemicals and Petrochemicals) in charge of fixing/revising prices of selected pharmaceutical products in the country (both APIs and pharmaceuticals), enforcing the provisions of the Drugs (Price Control) Order and monitoring the prices of controlled and decontrolled drugs in the country. India has implemented several versions of the Drug Price Control Order since 1964, and the Drug Price Control Order of 1995 brought down the coverage of price control to only 74 drugs. Presently there is a new price control policy (of 2006) under consideration, upon enactment of which, over 300 different drugs could be brought under price control. The sector is organised under three main industrial associations: the Organisation of Pharmaceutical Producers of India (OPPI), the Indian Pharmaceutical Alliance (IPA) that comprises 15 of the top Indian firms and the Indian Drug Manufacturers Association (IDMA) that is a much larger organisation with medium and small scale firms in addition to the large firms.

Figures 2 and 3: The Indian Pharmaceutical Sector: Market Shares and Main Therapeutic Segments¹³

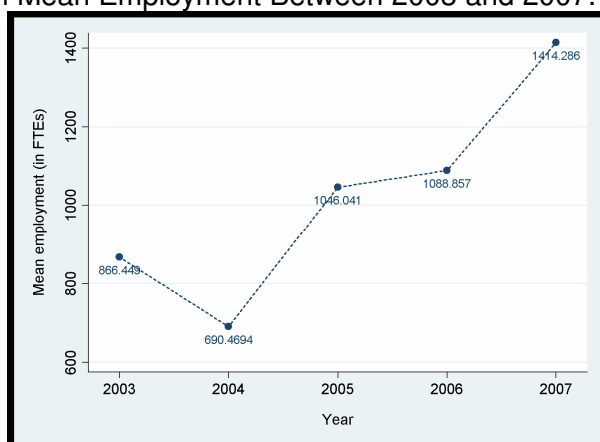


Dr. Reddy's Laboratories is the largest player in the Indian pharmaceutical sector with a market share of 10%, followed closely by Ranbaxy, Cipla, Aurobindo and the rest of the firms in the top ten category (figures 2 and 3). The drugs are distributed mainly through retail outlets and physicians maintain a large amount of influence on the introduction of new drugs/ substitution of existing drugs through other brand generics. Drug companies employ large marketing forces to penetrate local markets through institutional sales and private sales. Figures 2 and 3 show the market structure as well as therapeutic categories for the formulations market. The API market, not represented in the figures, is far more fragmented.

The industry continues to expand and figure 4 plots the increase in mean full time equivalent employees between 2003 and 2007 for the 49 firms surveyed. Employment rose from 866, 419 employees in 2003, to 1,414,286 employees (which is almost the double) in 2007.

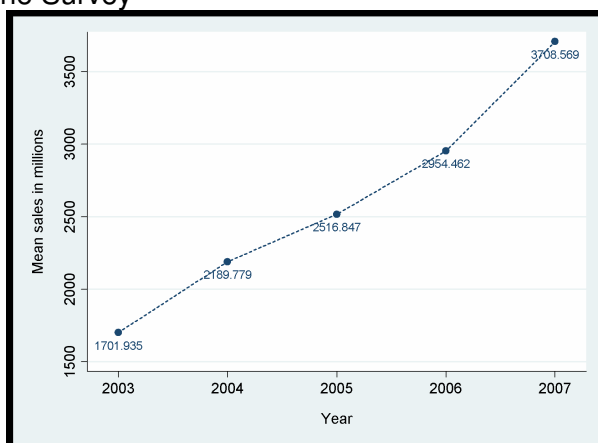
¹³ Source: Author. All figures used for the figure 2 are for fiscal year 2007, except for Ranbaxy, GlaxoSmithKline, Wockhardt, whose figures are for current year 2006.

Figure 4: Rise in Mean Employment Between 2003 and 2007: Results of the Survey



Source: Author's field survey, 2008.

Figure 5: Rise in Mean Sales for the 49 Firms Between 2003 and 2007: Results of the Survey



Source: Author's field survey, 2008

The main strategies and activities of the firms fall into three broad categories: generics production, R&D and frontier innovation and contract research and manufacturing, although there is a substantial overlap between these three activities in the way Indian firms operate in the current context.

2.1. Generics Production

Pharmaceutical production costs are estimated to be 30-50 percent lower in India than in Western countries,¹⁴ attributable to the expertise Indian firms have accumulated in reverse engineering processes for APIs, scale economies of production, and lower personnel and capital construction costs.¹⁵ According to the Department of Commerce and Industry figures for 2006/2007, India exported pharmaceutical products worth US

¹⁴ KPMG, 2006.

¹⁵ Bain and Co, 2008, p. 2.

\$3.1 billion thus recording a 30% increase over 2005/2006.¹⁶ Of the 20% of the APIs produced in the country for 2007, between 55-60% were exported and the sector exported almost two thirds of its total formulations production.

Box 2.0: Present Strengths in Generics Production¹⁷

- Expertise in reverse engineering processes for APIs
- Scale economies and production efficiency due to local API production capabilities
- Lower personnel and capital construction costs
- Expertise and investments in emerging areas, such as biogenerics
- Competitive pricing strategies, especially for formulations, where India has a head start of three to five years for finished formulations over China
- Large pools of English speaking scientific talent

Cost competitiveness of Indian generics continues to be the driving force of the expansion of the sector. In a study that compared prices of generic drugs between nine European countries and India in 2005, Indian and Scandinavian generic producers emerged to be the cheapest suppliers of drugs.¹⁸ Amongst the fifteen molecules that the study compared, Indian suppliers were 63% cheaper than other suppliers in the generics market in Belgium, and the study found Germany, France and the Netherlands as countries with the highest prices of generic drugs of the ten countries that were compared in the study.

The line separating generics and R&D is a fluid one in the Indian context because firms have tended to invest historically in R&D activities related to the production of generics. In the years leading up to India complying with the TRIPS Agreement, the dominant business model was one where firms focused on retaining generic product pipelines, albeit extending into more demanding and innovative generic categories, such as novel drug delivery systems.¹⁹ Now several pharmaceutical firms have established separate R&D companies making the division between generics “R&D” and new drug discovery more explicit. Broadly speaking, R&D investments in the sector can be split up into generics-related R&D and proprietary R&D for drug discovery research. The generics R&D is geared towards creating drug master files (DMFs) that are required to get approval in the US market for the sale of active pharmaceutical ingredients and to submit Abbreviated New Drug Applications (ANDAs) that are a pre-requisite to receive market approval for generic drugs. Indian generic firms are specialized in developing non-infringing processes for the manufacture of generic products. Production of non-infringing processes helps firms to produce generic versions of a product where the patent on the new chemical entity (NCE) has expired but the product may have process

¹⁶ Department of Commerce and Industry figures and the Economist Intelligence Unit Forecast, 2007. Prior to this, sector growth has been relatively steady at approximately 22.5% annually over the past few years (National Pharmaceutical Policy, 2006 and KPMG, 2006, p. 6).

¹⁷ Field interviews, Bain and Co, 2008 and KPMG, 2006.

¹⁸ Steven Simoens, “International Comparison of Generic Medicine Prices”, Current Medical Research and Opinion, 2007, at: http://www.redorbit.com/news/health/1195638/international_comparison_of_generic_medicine_prices/index.html, accessed on 5 April 2008.

¹⁹ See footnote 2 above.

and formulation patents that are still valid.²⁰ Firms such as Unichem Pharmaceuticals, Matrix Pharmaceuticals and Divi's Laboratories are good examples of firms in this category. Matrix Laboratories' non-infringing process on *Citalopram* (an anti-depressant) ensured the company a sole exporter status of the API to Western Europe in 2004.²¹ Matrix Laboratories has also subsequently developed non-infringing processes for the production of APIs for anti-retroviral drugs. Other categories of R&D includes those related to new drug discovery systems (NDDS) and specialty generics as well as biogenerics that are far more complex to manufacture, like injectables, biologics and oncology therapeutics.²²

Since India's product patent protection regime, local firms are no longer able to produce generic versions of drugs patented elsewhere in the world. There have been several estimates of the costs imposed by this restriction on the sector. However, recent estimates of off-patented products in the Indian market (including drugs whose patents have expired and those which are not patentable in India) are as high as 95%.²³ If this is true then there is still a lot of opportunity for the Indian firms to thrive in the generics market both in India and in other least developed countries that are exempt from implementing the TRIPS Agreement until 2016, by offering substitutes to products patented elsewhere.²⁴ However, in practice, the firms' abilities to cater to the demand for cheaper generics in other developing and least developed countries are determined by their choice of therapeutic product categories. The survey shows that the most popular product categories are those related to the central nervous system (CNS) and the cardiovascular system (CVS), followed closely by oncology and respiratory ailments. Almost all firms interviewed cited the desire to focus on these products due to the guaranteed long-term markets (since they are chronic ailments) and possibility to sell in regulated markets (which is synonymous with higher pricing abilities and increased profits). The surveyed firms were also asked to quantify the amount of their total research that is focused on local disease conditions. The responses to this question are shown in figure 6. Only 6% of the 49 firms that participated in the survey conducted all of their research on local disease conditions, 18% of the firms admitted to conducting up to half of their R&D on local conditions, and a large majority of the firms (75%) conducted only 25% or less of their R&D on local disease conditions.

²⁰ Sudip Chaudhuri, "Is Product Patent Protection Necessary in Developing Countries for Innovation? R&D by the Indian Pharmaceutical Companies After TRIPS", Working Paper Series of the Indian Institute of Management, Calcutta, No. 614, September 2007.

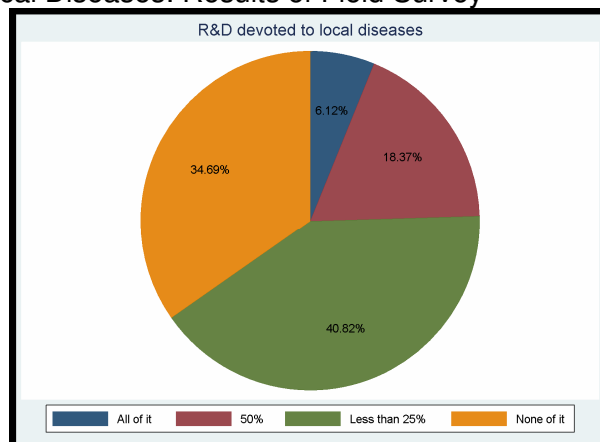
²¹ See footnote 18 above.

²² Bain and Co, 2008.

²³ Economist Intelligence Unit Forecast, 2007.

²⁴ This may not amount to many countries in reality, since most least developed countries are TRIPS-compliant as a result of several bilateral free trade agreements (see Chapter 4, Least Developed Countries Report of UNCTAD, Geneva, 2007)

Figure 6: R&D on Local Diseases: Results of Field Survey



Source: Author's field survey, 2008.

Markets: The USA remains the biggest export market for Indian firms. India has approximately 100 FDA-approved plants; the largest number outside the US and approximately twice the amount that China presently has.²⁵ Indian drug firms sold finished drugs and pharmaceutical ingredients worth US\$800m in the US in 2006 and accounted for over 20% of all generic drugs approved for marketing by the FDA in 2006, compared with less than 7% in 2002.²⁶ Recent estimates expect 250 Indian generics products to be launched in the US market by 2008, as opposed to 93 in 2003.²⁷

Up until the end of the 1980s, Indian firms focused extensively on the “rest of the world” markets where there was little or no patent protection coupled with lax registration requirements. The accumulation of enhanced technologies and production capabilities was accompanied by a gradual shift of focus to the highly lucrative US generics market. In recent years, companies’ performances reflect the gains from scale economies and diversification in key markets. Firms like Ranbaxy and Dr. Reddy’s Laboratories that set the trend of focusing on regulated markets initially showed that winning a 180 days exclusivity to sell their generics first in the US markets was a very lucrative option to generate revenues, once the initial barriers to market entry were surpassed.²⁸ Most field interviews with firms shows that even when firms do not target the first-to-file 180 days exclusivity afforded to generic drugs in the US market, their gradual expansion in the US market brings in large benefits due to the price competitiveness of Indian generics and the opportunities created by the US\$ 100 billion worth of drugs going off-patent between 2006-2008.²⁹

Ranbaxy was the second largest company in the Indian market until the recent sale of a 50% stake to the Japanese firm Daiichi Sankyo (in June 2008). As a result of

²⁵ Bain and co, 2008, p. 2.

²⁶ Economist Intelligence Unit Forecast, 2007, p. 11.

²⁷ KPMG, 2006, p. 9.

²⁸ In the USA, when an abbreviated new drug application is submitted for marketing a generic drug, the generic company is required to submit a certification regarding the patents for the drug in a so-called “orange book”. One of the ways to do so is to make a Para IV application. When a generic company wins a Para IV application, it is granted a 180 days exclusivity to market the drug in the US market.

²⁹ Approximately USD 100 billion worth of drugs will lose patent status in the USA by 2008, and products that went off-patent in 2006 itself generated USD 21 billion in sales. See Hans Loeffgren, “The Global Biopharma Industry and the Rise of Indian Drug Multinationals: Implications for Australian Generics Policy”, Australian and New Zealand Health Policy, June 2007.

this deal Daiichi is now the fifteenth largest pharmaceutical firm worldwide (and the second largest in the Japanese market after Takeda Pharma) and Ranbaxy gets to retain its name and its management until 2009. Prior to this, Ranbaxy was ranked within the top ten global generics firms and had a good foothold in European markets through a series of acquisitions. Other big firms like Dr Reddy's, Sun Pharma, Cipla and Ranbaxy focus on product portfolios that cater to all the regulated markets and are certified suppliers of generic medicines in the EU. However, the EU market is generally viewed as more problematic by the firms due to the costs involved in dealing with the varied regulatory approval processes (which are different for each of the twenty seven member countries), linguistic difficulties, complex pricing dynamics, greater generic competition and lack of experience of Indian firms to operate in the EU (field interviews). Despite this, the emerging picture is one where firms diversify their exports between the US, EU and other markets in Asia and Africa, albeit to different extents *depending on their product portfolios*.³⁰ Figure 7 below plots the revenues from exports for the top 10 firms from 2002 to 2007.³¹

Figure 7: Revenues From Exports for the Top 10 Firms, 2002-2007

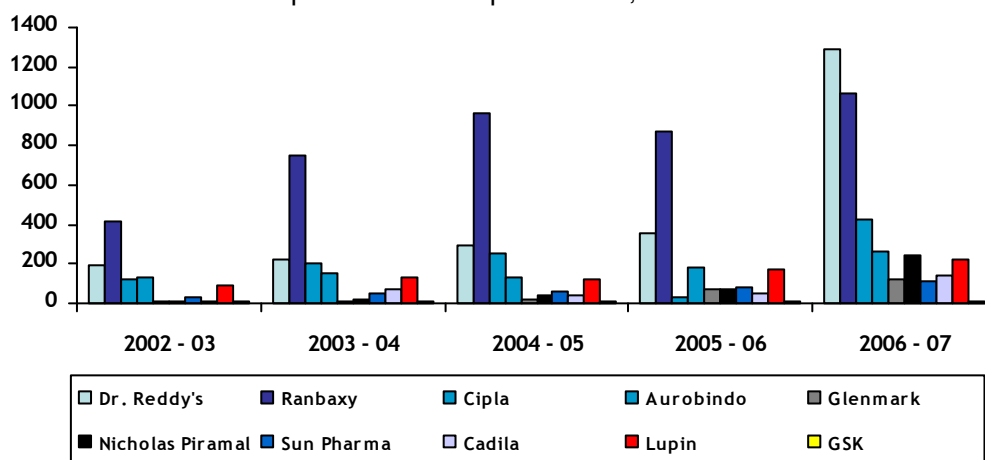


Table 1 below indicates the percentage growth in exports between 2003 and 2007 for the top 10 firms.

Table 1: Percentage Growth in Exports, 2003-2007³²

Company	2002-03	2003-04	2004-05	2005-06	2006-07
Dr. Reddy's	-1%	7%	-7%	31%	138%
Ranbaxy	32%	-0.5%	-5%	-16%	-3%
Cipla	15%	44%	30%	44%	18%

³⁰ This is somewhat contrary to the expectations and initial strategies of firms just a couple of years ago. In a similar firm level survey of the top 100 firms in 2005, most of the large Indian firms were very keen on focusing exclusively on the regulated markets, since the profit margins of success in these markets were very huge (Gehl Sampath, 2005, see footnote 2 above). Three years on, there seems to a consensus on the importance of diversification so long as their product portfolios are in demand in other unregulated markets, in order to insulate from shocks of focusing extensively on regulated markets.

³¹ Compiled by author using annual reports of the top ten pharmaceutical firms. Figures on the Y-Axis represent Rs. Millions.

³² Compiled by author using the annual reports of the top ten firms, except Nicholas Piramal, Cadila and Lupin.

Aurobindo	16%	14%	-14%	47%	34%
Glenmark	32%	58%		9%	116%
Sun Pharma	5%	46%	35%	33%	32%
GSK	-41%	-17%	-4%	10%	37%

Hitherto purely generics firms have expanded into more R&D intensive domains by acquiring R&D based firms abroad, thus combining their cost competitiveness with innovative activities to explore upcoming markets such as biogenerics, which are predicted to be worth US\$30bn by 2015 within just the USA.³³ In 2003-04, biopharmaceuticals accounted for 60 percent of India's total biotechnology market, which was worth an estimated \$709 million.³⁴ Several firms like Ranbaxy, Dr. Reddy's, Biocon and Wockhardt focus extensively on health biotechnology and biogenerics.³⁵ Wockhardt already had 55 biopharmaceutical registrations pending with 26 approvals in 18 different countries in 2005.³⁶

The firms and their strategies remain heterogeneous. Several top firms remain purely generic entities – Aurobindo, for example, the fourth largest firm in the market is a purely generic company. The company, which was formerly only producing APIs is now a producer of both APIs and formulations (although the formulations are sold only in export markets). Aurobindo has a large R&D department, which employs 700 people but they are all engaged in generics R&D (Field interviews). Similarly Cipla is a predominantly generics company. Other firms like Dr. Reddy's, Glenmark and Sun all pursue mixed strategies of generics and drug discovery through varied models, and these are discussed in the next section.

2.2. R&D Capabilities

Industry statistics show that large Indian firms invest approximately around 10% of their total sales into R&D since early 2000s. In 2005 when India complied with the TRIPS Agreement, the top five companies increased their R&D spending by 47% on the whole, which amounted to US\$ 192.3 million (as compared to USD 131 million for 2004).³⁷ Table 2 shows the R&D spending of the top five firms in the Indian pharmaceutical sector (excluding Cipla). A large share of this R&D still goes to developing novel delivery systems, non-infringing processes, and similar activities that feed into the generics business, thus building upon synergies between the need to be competitive in the present, with the aspiration to build greater innovative capabilities to integrate into the global structure.

Table 2: R&D Spending as a Percentage of Total Revenues of the Top 5 Firms From 2003 to 2006 (Excluding Cipla)³⁸

Company	2003	2004	2005	2006
Dr. Reddy's	7.6%	9.5%	12.9%	9.6%
Ranbaxy	4.5%	5.3%	6.2%	9.4%
Aurobindo	1.2%	2.0%	3.1%	3.6%
Glenmark	4.4%	6.5%	5.3%	4.4%

³³ Economist Intelligence Unit Forecast, 2007.

³⁴ KPMG, 2006.

³⁵ Field interviews; Economist Intelligence Unit Forecast, 2007; Hans Loeffgren (2007), footnote 29 above.

³⁶ KPMG, 2006.

³⁷ KPMG, 2006, p. 21.

³⁸ Compiled by author using company annual reports.

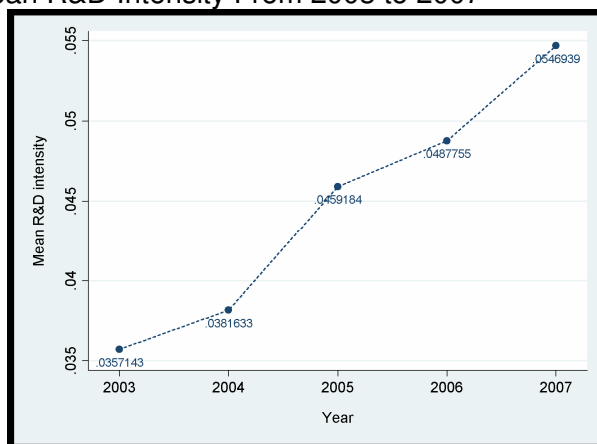
Sun Pharma	3.4%	5.0%	5.9%	6.3%
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It is important to note the considerable differences in R&D spending between the top firms: Dr. Reddy's spent 12% of its net sales on R&D in 2005 and almost 10% in 2006, whereas other companies like Nicholas Piramal, Aurobindo and Cipla still spend less than 5 percent of their net sales on R&D activities, and the combined R&D expenditures of the top five companies in India is still less than 3 percent of Pfizer (KPMG, 2006, p. 21). The importance that firms' place on R&D investments seems to be linked to their strategies on (field interviews):

- (a) Their product portfolios;
- (b) Export orientation; and,
- (c) Presence (or absence) of a vision to emerge as an R&D-based company.

For example, Ranbaxy exports between 65 to 70% of its total production, whereas Nicholas Piramal only exports around 10-15% of its total production.³⁹ There are several firms that rank within the top ten in the sector that focus largely on drug discovery such as Dr. Reddy's Laboratories, Sun Pharmaceuticals and Glenmark. This explains their increased emphasis on R&D spending. Leaving the top firms aside, if one would take a sector-wide approach considering all of the 10,000 odd firms, the R&D investments are negligible as one goes down the ranking, if not non-existent. For the 49 firms that participated in the survey, figure 8 shows the rise in mean R&D intensity from 2003 to 2007, from 3.5% of total sales to 5.5%.

Figure 8: Rise in Mean R&D Intensity From 2003 to 2007⁴⁰



Source: Author's field survey, 2008

In recent times, several major companies have hived off their R&D operations into newer entities. Ranbaxy, Sun Pharmaceuticals and Biocon have launched separate R&D companies of their own. Similarly, Wellquest, a clinical research arm of the Nicholas Piramal Group, launched a research centre in Hyderabad in mid-2007.⁴¹ The centre has an investment of Rs100m (USD 2.5 million) and will focus on clinical trials, generic-drug testing and the development of drug delivery systems. There are several other leading Indian generics companies setting up separate R&D companies, including Cadila Pharma and Lupin.

³⁹ Pers. Comm, Dilip Shah, President, IPA.

⁴⁰ R&D intensity is calculated as R&D as a percentage of total sales.

⁴¹ Economist Intelligence Unit Forecast, 2007, p. 11.

Three major factors explain the growing separation of R&D and generics activities in the pharmaceutical sector (field interviews). Generic products and proprietary R&D both have their own product cycles: generics are less risky than proprietary R&D, take only about 2-4 years and result almost always in a new product. Proprietary R&D, on the other hand, is capital intensive, can take up to fifteen years and a marketable product is not a certain outcome. Indian investors are used to a generics mode of investment: short-term (2 years on average) with assured returns and marketable products. Firms operating within this model find it increasingly difficult to raise finances for their proprietary R&D activities; hence separating the operations and potential investors makes it easier for them to operate. Secondly, huge R&D investments reduce the market capitalization of the big firms, which in turn affects their aspirations to acquire more firms abroad. Finally, Indian firms are collaborators and competitors for the global pharma at the same time. While they challenge big pharma patents in India under the local regime and abroad (to win the Para IV 180-days exclusivity in the US market) to protect their generics business, they also collaborate with the multinational companies on several drug discovery fronts, including phase III and IV clinical trials (which very few Indian firms can finance and conduct in-house). Most firms expressed the view that separating proprietary R&D from generics work helped to build trust with big pharma partners for collaborations on product development.

Box 3.0 Drug Discovery Prospects in the Indian Pharma Sector: Sun and Glenmark⁴²

Glenmark presently has eight molecules in clinical trails and its therapeutic areas of focus are inflammation, metabolic disorders (diabetes and obesity) and dermatology. Oglemilast, an asthma drug is in phase 2-B and the company has partnered with Forest, US for a deal that guarantees it 190 million dollars in upfront payment with back-to-back royalties on global sales of the product. Another molecule, GRC 8200 for Diabetes treatment is also in phase 2 B, for which Glenmark has partnered with Merck KGAA. The 250 million USD deal for GRC 8200 contains a 31 million dollar upfront payment and also stipulates back-to-back royalties along with milestone payments. GRC 6211 against Osteoarthritis, also in phase 2, is being jointly developed with Eli Lilly. As part of a 350 million USD deal for GRC 6211, Glenmark has received an upfront payment of 45 million, and the deal also segments the USA, Europe and Japanese markets to Eli Lilly.

Sun Pharmaceutical's lead product is an anti-allergic presently in phase 2 clinical trails. Although its product development is fully funded by Sun, the drug is being developed in collaboration with a clinical research organization since Sun does not have the requisite in-house capabilities. There are three other molecules lined up in pre-clinical stage; a soft steroid for asthma, a neurological drug and a muscle relaxant. In the last three years, the company has conducted five acquisitions, including three American companies, one in Hungary and one in India. The acquisition of an Israeli company based in the USA was underway in April 2008 when the field interviews with Sun Pharmaceuticals were conducted for this study.

Examples of acquisitions and expansions to enter new markets: Indian firms made 18 international acquisitions between January 2004 and October 2005, including Matrix Labs' acquisition of Belgium's Docpharma for \$263 million in June 2005; Dr Reddy's acquisition of Roche's API business for \$59.6 million; Ranbaxy's acquisition of a 40% stake in Japan's Nihon Pharmaceutical Industry; and Sun Pharma's completion of its purchase of ICN Hungary for an undisclosed sum.⁴³ In 2006, Ranbaxy acquired a South African generics company, Be-Tabs, apart from Ethimed (Belgium), Therapia (Romania) and Mundogen (Spain).⁴⁴ In 2006, Dr Reddy's bought out Germany's fourth-largest generics company, Betapharm Arzneimittel, from UK-based 3i for \$573.6 million, which was the biggest acquisition seen in the sector until then. In March 2007, Ranbaxy and Cipla pulled out of bidding for the generic-drug unit of a Merck.⁴⁵

Examples of acquisitions and expansions to enter newer segments: This includes Nicholas Piramal's acquisition of Avecia Custom Drug Synthesis of the UK for \$16.7 million in 2005 and Jubilant Organosys acquired Hollister-Stier Laboratories (US) in May 2007.⁴⁶ Wockhardt acquired the Wallis Laboratory (1997) and CP Pharmaceuticals (2003) based in the UK, and Esparma, Germany in 2004 for its biopharmaceutical work.

India's TRIPS compliance has been accompanied by some increase in R&D investments by the large MNCs. Merck inaugurated its first wholly owned subsidiary, MSD India Private Ltd in July 2005 after being absent in the Indian market for 20 years

⁴² Source: Personal communication with Glen Saldanha, CEO, Glenmark, 2 April 2008; Uday Baldohta, Vice President, Sun Pharmaceuticals, 2 April 2008.

⁴³ See also KPMG, 2006 for a discussion.

⁴⁴ Economist Intelligence Unit Forecast, 2007, p. 11.

⁴⁵ Same as above, at p. 12.

⁴⁶ Same as above, at p. 12.

in 2006.⁴⁷ The Indian interpretations of the patenting provisions under TRIPS are also encouraging foreign firms to either buy out Indian firms or to set up wholly new production units within the country thus helping the local sector to expand further. The most recent acquisition of a 50% stake in Ranbaxy by Daiichi Sankyo is one such move. The generic firm Actavis (Iceland) bought out the API division of Sanmar Pharmaceuticals Ltd (Chennai) in a bid to get into generic production in India in 2007.⁴⁸ Similarly, a Malaysian generics firm, Hovid, plans to establish a manufacturing plant in India in order to be able to produce generic versions of drugs it cannot produce in Malaysia due to Malaysia's more stringent patent regime.⁴⁹

2.3. Contract Research and Manufacturing

Indian firms have developed capabilities in various stages of the drug discovery and development process and conduct contract research and manufacturing for foreign firms. Apart from the low costs of the pharmaceutical production process, the overall R&D costs are about one-eighth and clinical trial expenses around one-tenth of Western levels,⁵⁰ which add to the profitability of contracting-out activities to Indian firms, in a global pharmaceutical environment that is hard-pressed to cut costs. Local firms conduct contract research and manufacturing (also called CRAM) for foreign firms in areas ranging from clinical trials to drug discovery to non-infringing process development to simply manufacturing APIs and formulations. These factors have accelerated the growth of the local contract research and manufacturing sector, which was estimated at \$895 million for fiscal year 2006.

Some recent, interesting forms of contract research include basic molecular research, gene mapping, drug discovery and managing clinical trials, discovery chemistry for domestic and global pharmaceutical companies.⁵¹ There are over fifty clinical research organizations in the country,⁵² the more cited ones being Kendle, Quintiles, Siro Clinpharm and iGate. India rates second on the list of the most attractive low cost global locations to run clinical trials outside the US. According to McKinsey (2007), India and China will account for almost forty percent of global pharmaceutical off shoring in the coming years. Pfizer has approximately twenty ongoing clinical trials in India, GSK has 7, and Eli Lilly has seventeen trials, in addition to other firms like AstraZeneca and Novartis.⁵³

Several large Indian firms have entered into contract research agreements for product development with the big pharma to gain R&D expertise in exchange for cheaper production possibilities. Ranbaxy and GSK have reached an agreement in 2007

⁴⁷ KPMG, 2006, p. 17.

⁴⁸ Deepti Ramesh, "Actavis to Buy Indian API Business", Chemical Week, February 14-21, 2007, p. 23.

⁴⁹ David Ho, Hovid's managing director believes that Hovid will be able to produce many more drugs in India due to its flexible interpretations of the TRIPS Agreement. See Deepti Ramesh, "Malaysian Firm to Establish Plant in India", Chemical Week, February 14-21, 2007, p. 23.

⁵⁰ KPMG, 2006.

⁵¹ Some of the firms have been really innovative in discovering and exploring new niche activities. For example, Avaant Pharmaceuticals' main focus is to secure drug development licenses for compounds that were discovered by global pharmaceutical firms, but subsequently ignored either due to research difficulties, change in R&D focus or management changes in the company. Avaant presently has licenses for drug development from several big companies, like Bayer (Krishnan, G. S., "Avaant Pharmaceuticals-The Contrarian", Cover Story, Businessworld, 13-19 June 2006).

⁵² Directory of Clinical Research Companies in India – November 2005, Cygnus India.

⁵³ KPMG, 2006.

where Ranbaxy will help develop some of GSK's products in return for tacit R&D skills and experience in handling complex pharmaceutical innovation processes (Field interviews). API production for large or international firms and marketing agreements are other popular kinds of cooperation. Matrix laboratories has been very successful as a contract manufacturer of cheaper non-infringing processes of API development for many years now (field interviews). Table 3 below contains an illustrative list of contract research agreements by major Indian firms.

Table 3: Some Major Contract Research Agreements⁵⁴

Company	Client	Drug
Cadila Healthcare	Altana	Two intermediates for pantaprazole
Dishman	Solvay	6 projects, including supply of starting material and intermediates for eprosartan
Dishman	Astra Zeneca	Intermediate for esomeprazole
Dishman	Merck & Co.	Intermediate for losartan
Dishman	GlaxoSmithKline	Three intermediates
Hikal	Degussa	Manufacturing intermediates and API's to Degussa on a project basis
Lupin	Cyanamid	Intermediates
Matrix	Wyeth	Supply of acyclovir
Nicholas Piramal	GlaxoSmithKline	MOU for drug intermediates; no fixed tenure
Nicholas Piramal	Astra Zeneca	Intermediates
Nicholas Piramal	Pfizer	Intermediates and APIs
Nicholas Piramal	AMO	Five year contract of ophthalmic products
Nicholas Piramal	Allegran	APIs for levobunolol and brimonidine
IPCA	Astra Zeneca	Contract manufacturing of APIs
Strides Acrolabs	Mayne	Injectables Manufacturing

Example of acquisitions to expand contract research: Jubilant Organosys acquired Target Research Associates plus 64 percent of Trinity Laboratories and its wholly - owned subsidiary Trigen Labs, in the USA in 2005. Bilcare Ltd acquired preclinical Inc., its first manufacturing facility in the United States in 2005.

3.0 Understanding the Emerging Industrial Dynamics

Three factors seem to be driving the growth of the Indian pharmaceutical sector presently. Its integration into the global industry is favourably advanced by trends in global health innovation that relate to *expansion of the global generics sector and increased pressure on 'big pharma' to cut costs*. There is a gradual blurring of the innovator and generics categories at the global level due to the complex innovation environment in which firms operate. Pharmaceutical innovation is becoming more modularized, with specific competencies for each stage that are often not available in-house, or do not make sense to conduct in-house due to cheaper outsourcing possibilities. This has meant increased out-sourcing at various stages of the drug discovery and development process.

⁵⁴ Compiled by author.

This architectural re-structuring of global pharmaceutical innovation caused by newer technologies, global regulatory processes as well as the needs of consumers worldwide to access drugs at reasonable costs, has opened up possibilities to modularize innovation stages.⁵⁵ Apart from the USD 100 billion worth of drugs that are expected to come off patent by 2008,⁵⁶ large pharmaceutical firms, such as Merck and Pfizer are in cost-cutting modes, making pharmaceutical off-shoring a real and important option globally.⁵⁷ It is estimated that the pressures on big pharma will lead to a surge in the contract research and manufacturing market, which is projected to grow at the rate of 10.8 percent annually to reach US\$168 billion by 2009.⁵⁸ Indian pharmaceutical firms are operating within this changing global landscape, and their expanding R&D activities and economies of scale in manufacturing are important assets. The superior competitive strategy at the generics level calls for evolved innovative prowess, and does not leave much space for the so-called pure generics company as opposed to the innovative big pharma.

Indian firms have been quick to fill in the emerging opportunities as a result of these changes and also influence the innovation process in their favour. They pursue a simultaneous collaborator-competitor strategy in local and global markets where they compete with the international firms for generics and launch patent disputes to protect their interests, but at the same time, collaborate with them on various R&D fronts. Varying business models seem to be emerging, depending on what the firms perceive to be their intrinsic strengths and how they can capitalize on it. As opposed to their extreme focus on regulated markets, firms diversify their portfolios between regulated and unregulated markets to capture economies of scale depending on their product portfolios and areas of interest. Several firms view the opportunities in developing and least developed country markets as their stronghold. Firms have also attempted to set up subsidiaries or independent companies in other least developed countries in order to be able to operate in legal regimes that are not TRIPS-compliant and to reap the scope for legal flexibilities in these countries. Sun Pharmaceuticals recently set up a company in Bangladesh; Cipla has embarked upon a recent initiative with the Ministry of Health in Uganda to set up a plant for the manufacture of antiretroviral and anti-malarial drugs in the country. This is the first alliance between an Indian firm and an African government, aimed at building local capacity to produce drugs of critical relevance to the country's health care system. Hetero Pharmaceuticals has acquired several firms in Latin America, and several other Indian firms are seeking to branch out into African countries through joint ventures and alliances – Strides Acrolabs, for example, now has a joint venture with Aspen Pharmacare, South Africa (field interviews). Indian firms have also begun to use their technological capabilities to create products for specific low-income markets thereby disrupting existing modes of pharmaceutical innovation, a case in point being the fixed dose combinations for antiretroviral drugs, discussed in section 5.1 of this study.

⁵⁵ See Ming Zeng and Peter J. Williamson, *Dragons at your Door: How Chinese Cost Innovation is Disrupting Global Competition*, Harvard Business Press (2007), for an analysis of this phenomenon in China.

⁵⁶ See Loefgren 2007, footnote 29 above.

⁵⁷ Merck intends to cut 25% of its manufacturing workforce and achieve a 30% reduction in product costs. It also intends to sell off or close five of its existing plants to create a network that combines its own manufacturing with the capabilities of external suppliers. Similarly, Pfizer plans to effect a ~25% cut in its manufacturing plants as part of its \$4bn cost-savings plan until 2008 and plans to close 23 of its 93 plants.

⁵⁸ Frost and Sullivan (2006), *Frost and Sullivan Study on Contract Research and Manufacturing, Health Care Practice Frost and Sullivan*. Downloadable at: www.icis.com/ICISCONNECT/files/folders/155/download.aspx, accessed on 7 March 2008.

A second factor in favour of the Indian firms is the *rapid expansion of the local pharmaceutical market and health care within India*. Rising personal incomes,⁵⁹ changing disease profiles (with a larger share of global diseases within the country) and the increased privatisation of health care (with a rise in specialised clinics, hospitals and treatment centres) are creating new market opportunities in second and third tier Indian cities and towns.⁶⁰ Although the local market is crowded, has too many small and medium firms, and has had lower profit margins than what can be gained by entering regulated markets abroad up until now, the increase in local purchasing power along with the changing disease profile of Indians both amount to a lucrative market. The advantage of an expanding domestic market for a wide range of diseases, including global diseases, offers Indian firms a secure base to invest. Several firms are expressly focusing on mass therapies to be delivered through the improving infrastructure and distribution channels into rural India (field interviews).

Thirdly, *the policy stance of the Indian government in favour of public health and the local industry* has lent a much-needed assurance to firms regarding the legitimacy of their generics production activities (field interviews). Undoubtedly, the increased demand for drugs- both lifestyle-related and others - will be the driving force of all growth in the pharmaceutical sector over the coming years in India. The best and the most logical entry into the market for the MNCs is to launch new patented products in India, but this cannot proceed smoothly in the absence of a policy framework that clearly gives the patent holder firms the right to enforce their patents within the country. The MNCs rely to a large extent on a TRIPS-compliant regulatory framework, legal certainty in the way the patent regime is interpreted, and better physical infrastructure support to expand their activities in the Indian economy through the launch of their patented products. The Indian firms, on the other hand, need a regulatory framework that is sympathetic to their needs to extract synergies between their on-going generics activities and emerging R&D opportunities worldwide.

Indian policy since its compliance with the TRIPS Agreement in 2005 has focused very much on public health and the needs of the local firms. Indian policy makers have been keen on extracting and retaining flexibilities permitted within the TRIPS framework, in order to promote public health and the local firms. Despite the fact that most local firms interviewed cited the policy developments to be purely in the interest of public health, they also admitted that they were favourable to them. However, given the present legal stance of the government, it remains to be seen whether the MNCs will go ahead to introduce patented drugs in the Indian market to the extent that is being anticipated. It is worthy to note here that the introduction of drugs by MNCs in India is the basis for many of the industry forecasts: Mckinsey (2007) for example, estimates that India will be ranked 10th with respect to value and its market will be worth \$US 20 billion by 2015.⁶¹ The base-case estimate made in the study for a US\$2 billion market size assumes that during 2010 to 2015, 35 to 40 new molecules will be launched globally every year, and 75% of these will be introduced in the Indian market within a year of global launch (see

⁵⁹ The EIU forecasts that healthcare spending (in rupee terms) will rise by 9% between 2008-2013. Indian government has also committed to enhance its healthcare expenditure to 6% and more in the coming years.

⁶⁰ The Economist Intelligence Unit forecasts a growth in consumption of pharmaceuticals to slow slightly in 2008-12 to an annual average of 4% in local-currency terms, from 6.2% in 2002-06, and the healthcare spending is predicted to have an average annual growth of about 9% in rupee terms between 2008-2013 (See Economist Intelligence Unit Report, 2007, p. 8-10).

⁶¹ See Mckinsey Report, 2007, p. 13-14.

p. 14). This is why the study also stresses on the government's need to take a pro-patent stance. The multinational firms interviewed for this study also expressed the need for India to take a pro-TRIPS stance, and implement patents that have been granted without legal ambiguity (field interviews). But then again, a country's pro-patent stance does not guarantee the introduction of patented drugs and products.⁶²

4.0 Indian Policy Framework and Access to Medicines Issues

The pharmaceutical sector has been a focal sector in India since the 1960s, and the government has put in several incentives in place to enable sectoral competitiveness, with changing emphasis over time. This has included investment in the creation of skilled manpower of relevance to the sector, establishment of public sector institutions such as the Centre for Scientific and Industrial Research (CSIR) and the Central Drug Research Institute (CDRI), investment in biotechnology parks, establishment of export processing zones and easing the emergence of venture capital institutions. Indian firms also receive several other benefits for exports that enables them to price their products competitively in export markets. For example, firms located in export processing zones are entitled to customs benefits, tax benefits for export (which could extend up to fifteen years) and also Capital Expenditure (Cap Ex) benefits.

Table 4 below contains the responses of the surveyed firms on the policies that matter most for new process and product development in the sector. The table shows that skilled manpower and venture capital that contribute positively and significantly to both types of innovations, and local infrastructure service that contributes positively and significantly to new product development.

⁶² A study that analysed the interrelationship between the two concluded that there were many factors other than patent regimes that influenced the decision of companies on whether or not to introduce drugs in developing country markets and often, the time lag between the introduction of a drug in the USA or a EU country and developing countries was as big as ten years. See Jean O. Lanjouw, "Patents, Price Controls and Access to New Drugs: How Policy Affects Global Market Entry", A Study Commissioned by the CIPIH, Geneva: World Health Organization, 2005.

Table 4: Institutions for New Product and Process Development: Results of Survey

Variable	New product development			New process development		
	No	Yes	p-value	No	Yes	p-value
	Institutions					
Govt. incentives	0.250	0.320	0.588	0.308	0.261	0.717
Skilled manpower	0.583	0.960	0.002**	0.654	0.913	0.030*
Collaboration with local R&D universities	0.333	0.400	0.628	0.346	0.391	0.744
Collaboration with local R&D institutes	0.417	0.440	0.869	0.462	0.391	0.620
Intellectual property	0.500	0.640	0.322	0.538	0.609	0.620
Local infrastructures	0.458	0.760	0.030*	0.615	0.609	0.962
Venture capital	0.208	0.560	0.012*	0.231	0.565	0.016*
SMI schemes	0.208	0.320	0.376	0.231	0.304	0.560
Govt.-firm tech. transfer	0.375	0.200	0.175	0.308	0.261	0.717
Staff transfer	0.542	0.600	0.680	0.538	0.609	0.620

Source: Field survey by author, 2008.

Controlling the data collected in the survey for the characteristics of innovator versus non-innovator firms in the sample shows that firms that are involved in new product and new process development receive more frequently government assistance than those that are not, once again underscoring the governmental focus on new process and product R&D in the sector. The R&D intensity is on average significantly larger for process innovators than for process non-innovators (i.e., product innovators), and product innovators export slightly significantly more often than product non-innovators.

The government also plans to introduce several new schemes of relevance to the local pharmaceutical sector.⁶³ This includes schemes that allow companies participating in R&D to set higher margins for their drugs, soft loans of three percent for companies who collaborate with governmental research facilities, R&D grants for firms who engage in clinical trials for drugs to treat neglected diseases. There are on-going efforts to revise other rules and regulations related to pharmaceutical research that seem outdated in the present context. For example, in order to encourage domestic R&D and capabilities, Indian regulations granted tax incentives to firms to engage in R&D within the country. This was a necessary incentive in earlier times where the government's motive was to encourage local R&D to enable the local sector to grow. However, in today's context, most MNCs are performing R&D in India (and benefiting from this incentive) and most Indian companies are contracting out phase III and IV clinical trials to companies abroad. The government therefore plans to introduce a new scheme that will serve as a fiscal incentive (in terms of tax deduction) for Indian firms that are conducting R&D outside India, recognizing the new realities of the sector.

The table also shows a slight rise, but not a significant contribution of collaborations with local institutes and universities to new product and process development efforts by firms. This reinforces the results carried out by a similar survey by the author in 2005⁶⁴ and calls for policies that can foster better collaboration between the various organisations involved in pharmaceutical innovation to enhance competitiveness. The Centre for Science and Industrial Research (CSIR) played a

⁶³ Field interviews with officials of the Department of Chemicals and Petrochemicals, Government of India.

⁶⁴ See Gehl Sampath, 2005, footnote 2 above.

central role in transferring technologies to local pharmaceutical firms when they were in their nascent stages in the 1970s and the 1980s, and along with several other public research institutes helped the pharmaceutical sector to develop its reverse engineering expertises. However, some recent reviews of the CSIR reveal that of the 984 technologies developed by 23 laboratories, 607 technologies were yet to be transferred to the private sector over the past decade. 247 technologies developed before 1996-97 were not transferred to the enterprise sector as of 2003. Analysing the reasons for non-transfer of 246 developed technologies showed that 77 technologies were not found fit for transfer, while 87 required further improvements/developments. In 82 cases including 34 developed prior to 1999-2000, the negotiations for transfer were under way, but results were unclear.⁶⁵

With the benefit of hindsight, it seems that public sector research was slow to change and focus on product development or other emerging needs of the industry as a result of organisational mandates and institutional inertia that is common to innovation environments in developing countries. As the firms moved further on from manufacturing to innovation territories, public sector organisations remained more inertia-driven. Some organisations managed to change and have newer visions of how they could support the private sector, whereas several others remained stagnant. The CSIR, for example, became quite active in promoting innovation largely perceived in terms of replication of the experience of the western countries for building innovation capabilities in the sector and even began promoting a local version of the Bayh-Dole Act for the Indian public sector in the past decade.

Furthermore, the local pharmaceutical firms did not have a very strong culture of collaboration up until 2005 because all products in the market were generics, and firms mainly competed under brand names. This affected ways and means in which collaboration could be structured on the whole. This notion is changing slowly with firms beginning to focus on private-private collaborations, but there is a need for more policies that foster public-private collaborations for product development and other emerging areas. Most firms interviewed had not collaborated with and were largely unenthusiastic on the question of collaboration with institutes in the public sector due to their lack of product development focus. The proposed governmental incentive on soft loans for collaboration with governmental research facilities is one effort to resolve this.

Post 2005 policy on implementation of the TRIPS Agreement in India has been an effort to (a) maintain the *availability of drugs* (for local consumption and exports) *at low prices* and to (b) *minimize the impact* of the patent regime on the domestic industry. The Patent (Amendments) Act of 2005 contains some key provisions that lean in favour of public health. All pre-1995 patents do not qualify for protection in India and all products with patent priority dates between 1995 and 2005 can continue to be manufactured by generic firms despite grant of a patent in India, if the generic manufacturers already had a market approved version of the patented drug, in return for payment of a “reasonable” royalties to the respective patent holder firms. The term “reasonable royalty” is not defined in the Act and therefore subject to interpretation. Section 3 (d) of the Act that deals with the definition of patentability specifies that patents will not be granted automatically for different forms of the same molecules, such as salts, esters, polymorphs and decisions will be taken case-by-case to establish novelty in an effort to

⁶⁵ Dinesh Abrol, “The Reality of Chasing Global Innovation Leadership: Lessons from CSIR, India”, Presentation at the fourth Globelics Conference, Saratov, 10-14 September 2007.

prevent ever-greening of molecules. This and several other provisions are in place in the regime to ensure a mitigated impact of the TRIPS-compliant patent regime on local pharmaceutical firms. Indian firms need time to manoeuvre themselves into the global pharmaceutical scenario for innovative R&D, and their strengths need to be harnessed to extract rents from generics and contract research and manufacturing activities: most of the policy developments in India fall into this line of vision.

However, trends in global pharmaceutical innovation reveal that investment by governments into public sector research, especially of the kind that translates research into marketable products is becoming very important the world over, and venture capital investments into biotechnology are gradually failing.⁶⁶ In this context, it is important that the government of India establishes more rigorous support structures for the sector in addition to patent interpretations that are in favour of the local sector.

4.1. The Mashelkar Committee Report

In an effort to elaborate upon the provisions of the Patent (Amendments) Act, 2005, the Indian government set up a technical expert group set up under the chairmanship of R. A. Mashelkar, Director General of the Council for Scientific and Industrial Research that examined two main issues:

- Whether it would be TRIPS compatible to limit the grant of patent for pharmaceutical substance to new chemical entity or to new medical entity involving one or more inventive steps; and,
- Whether it would be TRIPS compatible to exclude microorganisms from patenting.

The committee report found that whereas it will not be TRIPS compatible to grant pharmaceutical patents to new chemical and new medical entities only, every effort must be made to provide drugs at affordable prices to the people of India. The committee recommended that the grant of frivolous patents and 'ever-greening' should be prevented through the formulation of detailed guidelines that can be used by the Indian Patent Office for examining the patent applications on pharmaceuticals. It also concluded that it will not be TRIPS-compatible to exclude microorganisms from patenting, but detailed guidelines need to be formulated to ensure that only those patents proving 'substantial human intervention' and 'utility' are granted. The report, which was supposed to clarify the provisions of the Indian patent regime on patentability, was submitted in December 2006 was withdrawn in February 2007 on grounds of technical inaccuracy and plagiarism, thus not contributing much to clarity on the Indian patent regime. It is highly unlikely that this report will be re-submitted in the near future.

4.2. The Novartis Judgement, Tarseva and Valcyte: What is "Patentable" in India?

One of the first cases post-2005 that challenged the stance of the regime on patentability was the Novartis case. Gleevec, Novartis's anti-cancer drug, was India's first exclusive marketing right (EMR), on a beta crystalline version of the compound Imatinab Mesylate. Indian generic producers of the drug challenged the EMR on grounds that the compound Imatinab Mesylate was a derivative of a molecule that was known prior to 1995, and therefore does not qualify for patent protection. At the time when the EMR was granted, several Indian companies were producing generic versions

⁶⁶ OECD, Bioeconomy to 2030, 2008, pre-publication draft, on file with the author.

of Imatinab Mesylate, including, Cipla, Ranbaxy and Sun Pharmaceuticals. The EMR was withdrawn and Novartis was subsequently also refused a patent on Gleevec. In response, Novartis moved the Indian high court challenging the constitutional validity of section 3 (d) in the Indian Patent Act of 2005, claiming that such an interpretation is against the TRIPS Agreement. The High Court in Madras issued a judgement in 2007, deeming Section 3 (d) to be constitutional and not against the TRIPS Agreement.

The Gleevec case seems to set a precedent of sorts on what is patentable under the Indian patent regime. There are other, newer disputes on similar grounds. The Tarseva case (box 4) and the Valcyte case help show some of the loopholes in the present system, and the thin line walked on by the Indian judiciary to promote public health.

Box 4.0 The Tarseva Patent Dispute⁶⁷

The Indian Patent Office granted a patent on the lung cancer drug, Erlotinib to Roche (brand name Tarseva) earlier this year, around which time, Cipla received marketing approval for marketing a generics version of the drug from the Drug Controller's office. Cipla had made no pre-grant or post-grant opposition to Roche's patent, but having received the market approval, it went ahead and launched the drug explicitly violating the product patent on Tarseva that had been granted to Roche. At the same time, another drug company, Natco (which had made a pre-grant opposition to Erlotinib that had been rejected by the Patent Office) applied for a compulsory license to sell the drug in Nepal (a least developed country).

Roche approached the Delhi High Court requesting for the grant of an injunction stopping Cipla from marketing the product. The Delhi High Court, while denying an injunction on 18 March 2008, based the decision on three grounds:

- (a) The presence of a prima facie case
- (b) Balance of convenience, which in the court's view shifts to Cipla because it is manufacturing locally
- (c) And the degree of hardship (in terms of the price difference between the patented drug and the generics version) that will be shifted to consumers in case Roche is granted an injunction.

A new patent application by another US-based firm, OSI Pharmaceuticals on the crystalline version of the same drug is pending in the Indian patent office, which may not be granted given the Indian Patent regime's stance on crystalline versions of patented molecules. Despite this, keeping the patent application in mind, the Delhi High Court has asked Cipla to maintain accounts of the sale from this drug in case the final judgement of the case decides in favour of Roche and Cipla will have to pay royalties over the sale of the drug to Roche. If the final judgement rules in favour of Cipla, it will set a new precedent which is quite the opposite the present patent regime.

The case is still going on and Roche expects the hearing to go in its favour. The case also shows the lack of coordination between various offices, especially the patent office and the Drug Controller of India, when it comes to granting marketing approval and patents of drugs. On the issue of compulsory license that Natco has applied for, Natco claims it has a letter from the Nepalese government. Whether this is sufficient to constitute a notification under Section 92 A of the Indian Patents Act of 2005 which deals with compulsory licensing for exports to other least developed countries is unclear. Natco has also another application for a compulsory license pending for Sunitinib (Pfizer's Sutent).

Another on-going dispute concerns a patent granted to Roche on Valgancyclovir

⁶⁷ Personal communication with Deepali Talvar, Director Legal Services, Pfizer; the OPPI Representatives and Chan Park of the Lawyers Collective.

(brand name Valcyte) by the Chennai Patent Office in June 2007. Valgancyclovir is an anti-infective used to treat opportunistic infections related to HIV/AIDS.

The timeline of events in the Valcyte case are as follows:

June 1995	Roche files a patent application for the drug.
July 2006	Pre-grant opposition filed by the Lawyers Collective, an NGO, on behalf of two organizations; the Indian Network of People Living with HIV/AIDS and the Tamil Nadu People with HIV/AIDS.
June 2007	Patent grant by Chennai Patent Office.
Sept 2007	Objection to the grant of patent by Lawyers Collective, a public interest organization, on both procedural and substantive grounds.
Dec 2007	Cipla files post-grant opposition
Feb 2008	Ranbaxy files post-grant opposition.
June 2008	Post-grant opposition filed by the Delhi Network of People Positive (DNP+), which is an organization of people living with HIV/AIDS.

The Lawyers Collective objection to Roche's patent on Valcyte is based on two main grounds. Firstly, the US Patent Office rejected the patent that has been granted by the Chennai Patent Office already in 1994 on grounds that the drug had been in public domain for three years already at that time. Roche then went ahead and secured a patent on a crystalline form of the drug based on the claim that it makes the drug simpler to manufacture. The Indian patent that has been granted includes both the original use as well as the crystalline version. The objection is targeted at the Chennai office for (a) having granted a patent on a product that was declined a patent in the US for having been in the public domain; and (b) for having granted a patent also on the crystalline version of the drug which is against section 3 (d) of the Indian Patents Act. Additionally, the Lawyers Collective has also objected on procedural grounds: normally, when a pre-grant opposition is filed, the patent office is obliged to hold a hearing. However, no hearing was held in the Valcyte case. The case has become all the more complicated since Cipla and Ranbaxy have joined post-grant opposition.

As anticipated, the Indian and foreign firms were split on the implications of these legal developments.⁶⁸ Almost all the Indian companies interviewed agreed that these were good trends, both for public health and for the local generics sector. There was overwhelming consensus amongst the local firms that India's patent stance was reasonable from a public health stand point of view, and that they would continue to apply for patents on esters/salts/ polymorphs/combinations abroad to protect their interests in the export markets (field interviews).

4.3. The Reddy Committee Report on Data Protection

According to Article 39(3) of the TRIPS Agreement, member countries are under an obligation to provide protection to regulatory data submitted for receiving market approval of pharmaceutical products under specific circumstances. The Government of India constituted an expert committee in order to deal with the steps that need to be taken to comply with Article 39(3) of the TRIPS Agreement. The report (also known as the Reddy Committee Report) submitted in May 2007 acknowledges that: (a) data protection is relevant for any product at the stage of market approval, whether or not its

⁶⁸ The IPA and OPPI have expressed their divergent positions on several policy developments, including the Reddy Committee Report on Data Protection; see respective websites.

patent-protected; (b) it is a protection provided in return of submission of proprietary test data required for market approval; and (c) it protects against unfair commercial use and disclosure.

The Committee Report dealt with the issue of data protection for pharmaceuticals and agro chemicals separately suggesting different forms of protection for each of the categories. In the context of pharmaceuticals, the committee concluded that the present legal regime is probably not adequate to address issues on data protection with respect to Article 39.3, and that the Drugs & Cosmetics Act needs to have clearer legal mechanisms to ensure that undisclosed test data is not put to unfair commercial use within India. The Committee concluded that there was a need to improve the system and make necessary legal changes and explicitly provide for the minimum requirements under Article 39.3 of TRIPS.

The Report calls for a two-stage approach to data protection for all new chemical entities:⁶⁹ a transition stage and a data exclusivity regime to be enacted at the end of the transition stage. In the transition stage, the Report recommends that test data that companies seek to protect can be protected through trade secrets. During this stage, the Drug Regulator of India will continue to be the central body in-charge of market approval of drugs, and companies that wish to protect their data, they can specifically request for protection of the said data as trade secrets. The report provides that in case the data that are supposed to be protected as trade secrets are leaked out, the company in question can receive damages for trade secret violation.

It provides a model of data protection (of five years in duration) to be applied at the end of the transition period. This model of data protection incorporates several features that are meant to make it more public health-centred. The main features of the post-transition model of data protection as recommended by the Report are:

- (a) The test data will not be relied upon by the drug regulator for second or subsequent market approvals;
- (b) The protection applies with prospective effect only, for all molecules discovered after 01 January 1995;
- (c) In case of a patented drug, the data protection should not go beyond the term of protection of the patent, failing which it will lead to extension of market exclusivity to the patent holder;
- (d) The period of protection will be counted from the date of first marketing approval granted anywhere in the world in order to ensure that companies market their new drug in India at the earliest in case they wish to receive data protection for their product;
- (e) Data protection provisions will be over-ridden by all provisions in the Indian Patent Regime on compulsory licensing (sections 84 to 92 A) and Section 107 which provides for the Bolar Exception in order to ensure public health;
- (f) Date protection provisions can be waived by the government of India at any point of time due to any public health emergency;
- (g) During a public health emergency, the government can rely on data provided by the proprietary firm to grant market approval to any other firm;

⁶⁹ The report defines 'new chemical entity' for purposes of data protection as: "a chemical compound which contains an active ingredient or formulation of such an ingredient *that has not been previously approved in India* irrespective of its registration or use in any other country." (Emphasis added)

- (h) Government of India reserves the right to control the prices of the drugs under data protection;
- (i) The provision of data protection to any firm in India should not restrain manufacture of generic versions (not approved) for export to other countries that do not have data protection for the product in question, or where the data protection for the product in question has expired.

Implications of the Reddy Committee Report on Access to Medicines

There is a clear distinction between keeping information secret (data protection) and doing approvals and clinical work “relying” exclusively on the original patent holder’s data submitted to obtain regulatory approval for the patented product (data exclusivity). Article 39(3) of the TRIPS Agreement places a requirement upon member countries to provide protection to regulatory data under specific circumstances. However, it is not clear as to whether a strict reading on Article 39(3) calls for a regime of data exclusivity.⁷⁰ Data exclusivity, a relatively new form of intellectual property protection, is one such form of protection and it refers to the protection of clinical data that contain data submitted by pharmaceutical companies to regulatory agencies, such as the US Food and Drug Administration and the European Agency for the Evaluation of Medicinal Products (EMA), for the purposes of obtaining market approval of patented drugs.⁷¹ Grant of data exclusivity (five years in the case of the model proposed by the Reddy Committee Report) prevents the regulatory agency from using the data submitted by the originator company to determine bioequivalence of generic products for the said period.

The Reddy committee report is another effort by the Indian government to balance its obligations under the TRIPS Agreement with public health. The Report leaves the length of the proposed transition period in the open (it could extend to anything between five or ten years). Even after the end of the transition period, it recommends that higher standards of data protection should be provided only after careful assessment “...of its impact on the sector and public to avoid any adverse repercussions in the long run.”

Whereas the post-transition model has incorporated several safeguards in the interest of fastest introduction of generics, and public health (features (b) to (i) above), it still remains unclear why the report concluded that India needs a new system of data exclusivity. India has not had a very reliable system of test data submitted for marketing approval of products, and earlier studies of the sector have shown that domestic firms have relied on access to the data in order to be able to reverse engineer quickly and cost-effectively.⁷² That said there seem to be sufficient legal mechanisms in place to strengthen protection of test data, without having to provide a data exclusivity term of five years in order to comply with Article 39 (3) of the TRIPS Agreement. In common law (on which the Indian legal system is based), unfair commercial use is a remediable ground. Furthermore, trade secret protection, which was earlier on a weaker form of protection under the Law of Torts and Contracts in India (as the report also notes) has

⁷⁰ Carlos Correa, Protection of Data Submitted for the Registration of Pharmaceuticals: Implementing the Standards of the TRIPS Agreement, South Centre, 2002.

⁷¹ Meir Perez Pugatch, “Intellectual Property and Pharmaceutical Data Exclusivity in the Context of Innovation and Market Access”, Paper Presented at the UNCTAD-ICTSD Dialogue on Ensuring Policy Options for Affordable Access to Essential medicines, Bellagio, 12-16 October 2004.

⁷² See Lanjouw, Jean O., “Intellectual Property and the Availability of Pharmaceuticals in Poor Countries.” Innovation Policy and the Economy, Vol. 3, 2002 and Gehl Sampath (2005) in footnote 2 above.

been elevated to the status of an intellectual property category under the TRIPS Agreement. Thus, strengthening the existing regulatory mechanism for data protection within the country and relying on trade secrets seems to be sufficient to comply with the requirements of Article 39(3) of the TRIPS Agreement.

Most importantly, the challenge of the Reddy Committee Report remains its holistic enactment as India's data exclusivity regime after the completion of the transition stage. In other words, several provisions remain key to ensure that the data exclusivity regime will not run against the interest of the local pharmaceutical sector and public health. Specifically, the clauses that state that in the case of a patented drug, the data protection should not go beyond the term of protection of the patent and that the period of protection will be counted from the date of first marketing approval granted anywhere in the world are very important safeguards.

As a hypothetical exercise, if India presently had a data exclusivity regime that provided only five years of protection as stipulated by the Reddy Report, but did not contain the provision that it should be from the date of first marketing approval granted anywhere in the world, then the Valcyte and Tarseva cases would look very different. Both products would have obtained five years protection of their data under the data exclusivity regime. In such a case, regardless of whether the patents on the products were valid under the Indian patent regime, companies will not be able to obtain marketing approval for generic versions of these products, unless they repeat clinical trials. This would be expensive, ethically dubious and cause undue delays in generic entry.

5.0 ARV Production by Indian Firms and Emerging Disease Segments

The WHO estimates that by the end of 2007, there were an estimated 33.2 million [30.6 million-36.1 million] people living with HIV and about two thirds of those live in sub-Saharan Africa.⁷³ As of December 2006, only 2.2 million people were receiving treatments, and this figure had gone up to about 3 million people [2 700 000-3 280 000 people] at the end of 2007 in low and middle income countries, nearly 950 000 more compared with the end of 2006.⁷⁴ India itself has the second-highest number of people in the world living with HIV/AIDS, according to the National AIDS Control Organization (NACO) and the Joint UN Programme on HIV/AIDS and only 7% of those people have access to treatment.⁷⁵ Further, according to the WHO, only 23% of the people in need of ARVs in Africa had access to it in 2006⁷⁶ and only 31% as of 2007.⁷⁷

5.1. Impact of Changing Industry Trends on First and Second Line ARVs

⁷³ WHO, Towards Universal Access: Scaling Up Priority HIV/AIDS Interventions in the Health Sector, Progress Report, 2008, WHO Geneva.

⁷⁴ WHO, Towards Universal Access: Scaling Up Priority HIV/AIDS Interventions in the Health Sector, Progress Report, 2008, WHO Geneva; Global Fund ARV Fact Sheet, 1st December 2007.

⁷⁵ EIU Forecast 2007, p. 9; WHO, 2007. It is not clear from these statistics as to how much of this lack of access can be attributed directly to the lack of affordable drugs. Inefficiencies in drug distribution and procurement impacts upon access, but it is not the focus of this work.

⁷⁶ UNAIDS AIDS Epidemic Update: Special Report on HIV/AIDS. December 2006. Geneva, Switzerland: UNAIDS/WHO, 2006.

⁷⁷ WHO, Towards Universal Access: Scaling Up Priority HIV/AIDS Interventions in the Health Sector, Progress Report, 2008, WHO Geneva.

Amongst the top fifteen firms, only four (Ranbaxy, Cipla, Aurobindo and Hetero) manufacture first and second line ARVs. The other firms that produce ARV products – Matrix, Emcure, Strides and Micro Labs – are not amongst the top 15 in the market, but all ARV-manufacturing firms were interviewed in detail during the survey. Of these Ranbaxy, Aurobindo and Matrix Laboratories all began to produce ARVs due to the commercial incentives provided by the President's Emergency Plan for HIV/AIDS Relief Initiative (PEPFAR) that was launched in 2004.⁷⁸

Tables 5 and 6 show the global supply scenarios for ARVs: they contain a list of first line and second line ARVs, with originator/ patent holder firms, Indian generic manufacturers who are currently manufacturing the drugs, and producers in the rest of the world for the same products. The tables give us an idea of the role played by generic producers in India in making access to anti-retroviral drugs universal even after 2005 and India's compliance with the TRIPS Agreement.

⁷⁸ Cheri Grace, "The Effect of Changing Intellectual Property on Pharmaceutical Industry Prospects in India and China; Considerations for Access to Medicines", DFID Health Systems Resource Centre: London, 2004.

Table 5: First-line ARVs: Patent Holders and Generic Producers⁷⁹

First-line ARVs			
Drug⁸⁰	Originator/ Patent Holder	Indian Generic Producers	Generic Producers in the Rest of the World
Stavudine (d4T) <i>Zerit</i>	Bristol Myers Squibb	Cipla, Hetero, Matrix, Ranbaxy, Aurobindo, Strides Acrolabs, Emcure	Duopharma (Malaysia), Aspen Pharmacare (South Africa), Ranbaxy (Malaysia)
Zidovudine (ZDV) <i>Retrovir</i>	Glaxo Smith Kline (UK)	Ranbaxy, Cipla Ltd, Hetero, Strides Acrolabs, Aurobindo, Emcure, Matrix,	Aspen Pharmacare (South Africa)
Zidovundine (AZT) <i>Retrovir</i>	Glaxo Smith Kline (UK)	Matrix, Strides Acrolabs, Hetero, Aurobindo, Cipla, Ranbaxy, Micro Labs,	Aspen Pharmacare (South Africa), Apotex Inc (Canada),
Lamivudine (3TC) <i>EpiVir</i>	Glaxo Smith Kline (UK)	Cipla Ltd, Aurobindo, Micro Labs, Ranbaxy, Matrix, Strides Acrolabs, Hetero, Emcure	Aspen Pharmacare (South Africa)
Nevirapine (NVP) <i>Viramune</i>	Boehringer Ingleheim (USA)	Ranbaxy, Cipla Ltd, Aurobindo, Hetero, Strides Acrolabs, Emcure, Matrix, Micro Labs,	Aspen Pharmacare (South Africa), Huahai Pharmaceutical (China), Duopharma (Malaysia)
Efavirenz (EFV) (200 mg) <i>Stocrin 200</i>	Merck	Ranbaxy, Aurobindo, Strides Acrolabs, Hetero, Micro Labs, Cipla Ltd,	
Efavirenz (EFZ) (600 mg) <i>Stocrin 600</i>	Bristol Myers Squibb (Puerto Rico), Merck Sharp & Dohme (Australia)	Cipla, Hetero, Matrix, Aurobindo, Strides Acrolabs, Ranbaxy, Emcure, Micro Labs, Emcure	
Emtricitabine (FTC) <i>Emtrival</i>	Gilead Sciences but Merck owns the rights for Canada and Australia	Aurobindo, Matrix, Cipla	
Didanosine (DDI) (200 mg) <i>Videx</i>	Bristol Myers Squibb	Aurobindo, Micro Labs, Cipla Ltd,	
Didanosine (DDI) (400 mg) <i>Videx EC</i>	Bristol Myers Squibb	Aurobindo, Ranbaxy, Micro Labs,	

⁷⁹ Data collected from each website of all Manufacturing Companies, The Global Fund, List of ARV Pharmaceutical Products Classified According to the Global Fund Quality Assurance Policy for Single and Limited Source Pharmaceutical Products, Edition 53, June 30, 2008; CHAI, Anti Retroviral Price List, April 2008; WHO Prequalification Programme, Manufacturers And Suppliers Whose HIV-Related Medicines Have Been Found Acceptable, In Principle, For Procurement By UN Agencies, 63rd Edition, February 2008.

⁸⁰ This column contains the name of the compound, followed by its abbreviation in brackets, and the brand name from the originator firm in italics.

Table 6: Second-line ARVs: Patent Holders and Generic Producers⁸¹

Second-line ARVs			
Drug ⁸²	Originator/ Patent Holder	Indian Generic Producers	Generic Producers In the Rest of the World
Tenofovir disoproxil fumarate (TDF) <i>Viread</i>	Gilead Sciences	Cipla Ltd, Aurobindo, Hetero, Strides Acrolabs, Matrix, Ranbaxy	
Indinavir (IVD) <i>Crixivan</i>	Merck	Ranbaxy, Strides Acrolabs, Emcure, Micro Labs, Hetero, Cipla Ltd, Cadila Pharmaceuticals	
Lopinavir (LPV/r) <i>Kaletra</i>	Abbott	Aurobindo, Hetero, Emcure, Matrix, Ranbaxy, Cipla Ltd	
Nelfinavir (NFV) <i>Viracept</i>	Pfizer, but Roche has the distribution rights	Cipla Ltd, Aurobindo, Hetero, Emcure	
Abacavir (ABC) <i>Ziagen</i>	GSK	Ranbaxy, Cipla Ltd, Aurobindo, Hetero, Strides Acrolabs, Emcure, Matrix,	
Atazanavir (ATV) <i>Riyataz</i>	BMS	Hetero, Emcure, Matrix, Aurobindo	Aspen Pharmacare (SA)
Saquinavir (SQV) <i>Fortovase or Invirase</i>	Roche		
Ritonavir <i>Norvir</i>	Abbott	Aurobindo, Matrix, Ranbaxy, Cipla Ltd,	

As the tables show, whereas the market for first line ARVs is heavily commoditised with several generic manufacturers for each of the products, the second-line ARVs, especially Lopinavir/ Ritonavir and Atazanavir have limited supply and Indian firms are playing a very important role in ensuring competition in the market. According to the Global Price Reporting Mechanism (GPRM) database, generic competition amongst first line suppliers have brought down the median price of the most commonly prescribed fixed dose combination in first-line regimen (d4T 30 mg + 3TC 150 mg + NVP 200 mg) by 40% from US\$ 153 (2004) to US\$ 92 (2007) in low-income countries and from US\$ 154 (2004) to US\$ 91 (2007) in middle- income countries.⁸³

Therefore, the most important question is how India's TRIPS compliance will impact upon the emergence of an equally competitive market for second-line ARVs for local consumption and export? This is a very important issue for global access to medicines because almost all ARVs that have received pre-qualification under the WHO's prequalification programme for essential medicines as of 01 February 2008 are manufactured by Indian firms apart from the South Africa's Aspen Pharmacare's and China's Zhejiang Pharmaceutical Co (the latter has a pre-qualification only for Nevaripine).

⁸¹ Same as footnote 79.

⁸² This column contains the name of the compound, followed by its abbreviation in brackets, and the brand name from the originator firm in italics.

⁸³ A Summary Report by the Global Price Reporting Mechanism on Antiretroviral Medicines, February 2008.

Table 7: Patent Applications for ARVs Pending in India⁸⁴

Patent application	Form
Lopinavir	Crystalline/ polymorph
Ritonavir	Crystalline/ polymorph
Lamivudine+Zidovudine	Combination
Abacavir+lamivudine+Zidovudine	Combination
Tenofovir disoproxil fumarate	Ester/salt

Tenofovir disoproxil fumarate (TDF), has a ester/ salt patent whose priority patent date is 1997, and the patent holder firm is Gilead. Gilead's patent application on TDF is presently pending consideration with the Indian Patent Office. Presently, several firms (including Emcure and Hetero) have voluntary licenses to produce the product in return of which they pay an undisclosed amount of royalty to Gilead (field interviews). A recent case won by the Indian patient groups in the USA has led to the rejection of four patents on Gilead's TDF drug *Viread* on grounds that the patents did not meet certain criteria of patentability. Although this decision is not a final one, Gilead is obliged to share this information with the Indian Patent Office according to Section 8 of the Indian Patent Act.⁸⁵ What happens to Tenofovir is very important because several key countries have adopted or are currently considering adopting Tenofovir in their first-line Protocols, including Botswana, Ethiopia, Lesotho, Namibia; Nigeria, and Zambia. Given the expanding coverage of patients for first-line regimens in low and middle-income countries, the demand for Tenofovir is forecast to rise.⁸⁶

GSK has dropped patent claims on its second line ARV drug Abcavir and Trizivir, which is a combination therapy of three first and second-line ARVs. Other second-line ARVs whose production remains highly critical are: Atazanavir and Lopinavir/ Ritonavir (LPV/r). Atazanavir's patent is held by Bristol Myers Squibb (BMS), whereas the Lopinavir has a priority patent date post-1995 and Abbott holds the patent. According to the WHO's 2008 Antiretroviral Treatment (ART) Guidelines, Nelfinavir (patent held by Pfizer) has been disqualified to be a protease inhibitor, and several countries have switched to regimens with LPV/r instead. Of the 42 regimens prescribed by the 2008 guidelines, several of them contain LPV/r, such as: TDF+3TC+LPV/r, TDF+ FTC+LPV/r, *ddi*+ABC+LPV/r.

Similar price reductions have been observed in some second-line drugs, although second line treatments remain very expensive when compared to first line treatments in low-income countries, according to the WHO (2008).⁸⁷ Introduction of Lopinavir/Ritonaavir by Indian firms like Cipla saw reductions in Abbott's prices for Kaletra in the Indian market by a significant margin (field interviews). Abcavir's median price has reduced from US\$ 887 (2004) to US\$ 426 (2007) in low-income countries and from US\$ 887 (2004) to US\$ 410 (2007) in middle-income countries. However, the median price of LPV/r (133/33mg) has decreased much more in middle-income

⁸⁴ Adapted and modified from Leena Menghaney, "HIV/AIDS Treatment Legal and Political Choices for India", Journal of Creative Communications, 2006, Vol. 1, Issue 2, p. 195-202, at p. 198.

⁸⁵ Section 8 requires that patent applicants keep the Indian Patent Office informed of the status and developments regarding equivalent foreign applications.

⁸⁶ WHO, Demand Forecast for Antiretroviral Drugs in Low and Middle Income Countries 2007-2008, prepared by the WHO, UNAIDS, Clinton Foundation and the Mexican Institute for Public Health, November 2007, p. 24.

⁸⁷ WHO, Towards Universal Access: Scaling Up Priority HIV/AIDS Interventions in the Health Sector, Progress Report, 2008, WHO Geneva.

countries than in low income countries and the prices of other second-line drugs remain high.⁸⁸ This makes the issue of ensuring adequate price competition through generic firms very critical, especially so because 97% of HIV-infected persons in low-income countries are being treated with first line regimens and will need to shift to second-line regimens sometime in the coming future.

Although there are four firms presently well on their way to produce generic versions of LPV/r and heat-stable LPV/r (Aurobindo, Cipla, Matrix and Emcure) which is expected to make them widely available at cheaper prices, these firms have made investments into producing the drugs only after 2005, and hence are not protected under the clause in India's patent regime which allows continued production for the payment of a 'reasonable royalty'. This leaves the issue of validity of the manufacture of the drug by the other firms much in the open.⁸⁹ It is likely that Abbott will defend its patent in India, given that it enforces its patent rights on Kaletra strictly in China (which is why there are no Chinese manufacturers of the drug). But given the way the Tarseva case has been received by the Indian courts, there is a high probability that the judiciary will rule in favour of the local generic firms and public health. This is what the firms are also hoping for (field interviews). However, if the patent rights are upheld, they may affect the availability and use of all regimens that contain LPV/r.

It seems unlikely that BMS will defend its patent on Atazanavir in India. Presently, Aurobindo, Emcure, Hetero and Matrix are coming up with generic versions of Atazanavir (field interviews). Emcure and Aspen (SA) have received voluntary licenses from BMS, but the other three firms have come up with their own technologies for the manufacture of Atazanavir. Emcure has received WHO pre-qualification and the other two firms expect to receive WHO pre-qualification later this year. There is no procurement data available in the GPRM database for Atazanavir presently, but it is expected that the entry of several generic versions of the drug will help to lower the prices and enhance the availability of the drug as a second-line regimen.

In addition to competitive supply of Lopinavir/ Ritonavir and Atazanavir, it is important to note that Indian firms have been key players in creating fixed dose combinations of recommended first-line regimens, several of which were not available in the market by the originator companies since the early 2000s. These fixed dose combinations are a key example of how Indian firms have been active in evolving new and disruptive forms of innovation in order to create products that are pro-poor by targeting to benefit mainly from the economies of scale involved. Table 8 below contains a list of adult ARV fixed dose combinations that are presently available, and the important role played by Indian firms in this regard.

⁸⁸ A Summary Report by the Global Price Reporting Mechanism on Antiretroviral Medicines, February 2008.

⁸⁹ Aurobindo and Hetero are both suppliers to the PEPFAR initiative and this might account for their production.

Table 8: Adult Fixed Dose Combinations: Patent Holders and Generic Producers⁹⁰

Adult Fixed Dose Combinations			
Fixed Dose Combination (FDC)⁹¹	Originator/ Patent Holder	Generic Producers India	Generic Producers in the Rest of the World
Abacavir + Lamivudine 600 mg + 300 mg (ABC + 3TC)	Glaxo Smith Kline (UK)	Aurobindo, Cipla Ltd., Hetero Drugs	
Abacavir + Lamivudine + Zidovudine 300mg + 150 mg + 300mg (ABC + 3TC + AZT)	Glaxo Smith Kline (UK)	Matrix Laboratories, Ranbaxy, Aurobindo, Hetero Drugs	
Didanosine + Efavirenz + Lamivudine (ddl + EFV + 3TC) 400mg + 600mg + 300mg		Cipla Ltd.	
Efavirenz + Emtricitabine + Tenofovir 600mg + 200mg + 300mg (EFV + FTC + TDF)	Merck Sharp & Dohme (Canada; the Netherlands), Bristol Myers Squibb and Gilead Sciences Int. (Canada)	Matrix Laboratories, Cipla Ltd.	
Efavirenz + Lamivudine + Stavudine 600mg + 150 mg + 30mg/ 40 mg (EFV + 3TC + d4T)		Strides Acrolabs, Emcure, Ranbaxy	
Efavirenz + Lamivudine + Zidovudine 600mg + 150mg + 300mg (EFV + 3TC + AZT)		Ranbaxy, Strides Acrolabs, Aurobindo, Cipla Ltd., Emcure	
Emtricitabine + Tenofovir 200mg + 300 mg (FTC + TDF)	Gilead Sciences	Hetero Drugs, Strides Acrolabs	
Lamivudine + Zidovudine 150mg + 300mg (3TC + AZT)	Glaxo Smith Kline (UK), Pharmacare Ltd. (South Africa)	Cipla Ltd., Hetero Drugs, Cadila Pharmaceuticals, Ranbaxy, Matrix Laboratories, Aurobindo, Strides Acrolabs, Emcure	
Lamivudine + Nevirapine + Zidovudine 150 mg + 200mg + 300 mg (3TC + NVP + AZT)		Strides Acrolabs, Hetero Drugs Ltd.	Aspen Pharmacare (South Africa)
Lamivudine + Stavudine 150 mg + 30 mg/ 40 mg (3TC + d4T)		Cipla Ltd., Ranbaxy, Strides Acrolabs, Aurobindo, Matrix Laboratories, Hetero Drugs, Emcure	

⁹⁰ Source: Same as footnote 79

⁹¹ This column contains the name of the compounds, their strengths, followed by their abbreviations in brackets.

Lamivudine + Stavudine + Nevirapine 150mg +30mg/40 mg + 200 mg (3TC +d4T + NVP)		Cipla Ltd., Ranbaxy, Hetero Drugs, Emcure, Aurobindo, Matrix Laboratories, Micro Labs, Strides Acrolabs, Emcure	Duopharma (Malaysia)
Lamivudine + Nevirapine + Zidovudine 150 mg +200mg + 300 mg (3TC + NVP + AZT)		Matrix Laboratories, Strides Acrolabs, Hetero Drugs, Cipla Ltd., Ranbaxy, Micro Labs, Aurobindo, Emcure	Aspen Pharmacare (South Africa), Apotex Inc (Canada)
Lopinavir + Ritonavir 133.3mg + 33.3mg/ 200 mg + 50 mg (LPV + r)	Abbot Laboratories (UK and USA, Germany)	Aurobindo, Matrix Laboratories, Ranbaxy, Cipla Ltd., Hetero Drugs, Strides Acrolabs, Emcure	

The same is true also in the case of paediatric fixed dose combinations. Table 9 below contains a list of paediatric FDCs presently available. Indian firms have created value added by creating paediatric ARVs for children in association with the Clinton Foundation for HIV/AIDS (CHAI),⁹² prior to which there were no ready-to-use dosages for HIV-infected children, see table 9.

Table 9: Paediatric Fixed Dose Combinations: Patent Holder and Generic Producers⁹³

Paediatric Fixed Dose Combinations			
Fixed Dose Combination⁹⁴	Patent Holder Firm	Generic Producers India	Generic Producers In the Rest of the World
Lamivudine(20mg) + Stavudine (5mg) + Nevirapine (35 mg)		Ranbaxy	
Lamivudine (40mg) + Stavudine (10mg) + Nevirapine (70 mg)		Ranbaxy	
Lamivudine (30mg) + Stavudine (6mg)		Cipla Ltd.	
Lamivudine (60 mg) + Stavudine (12 mg)		Cipla Ltd.,	
Lamivudine (150 mg) + Stavudine (30 mg)		Cipla Ltd., Ranbaxy, Strides Acrolabs Ltd., Aurobindo, Matrix Laboratories, Hetero Drugs	
Lamivudine (30mg) + Stavudine (6mg) + Nevirapine (50 mg)		Cipla Ltd	
Lamivudine (60 mg) + Stavudine (12mg) + Nevirapine (100mg)		Cipla Ltd.	
Lamivudine (150 mg) + Stavudine (5 mg) + Nevirapine (35mg) tablet for oral suspension		Ranbaxy	
Lamivudine (150 mg) + Stavudine (10 mg) +		Ranbaxy	

⁹² DAT Overview, Clinton HIV and AIDS Initiative, 11 April 2008.

⁹³ Source: same as footnote 79.

⁹⁴ This column contains the name of the compounds, their strengths, followed by their abbreviations in brackets.

Nevirapine (70mg) tablet for oral suspension	
Lamivudine (20 mg) + Stavudine (5 mg)	Ranbaxy
Lamivudine (40mg) + Stavudine(10mg)	Ranbaxy

It is also important to consider the impact of patenting on the interests of Indian firms to create appropriate fixed dose combinations for second-line ARVs that employ Lopinavir/ Ritonavir and Abacavir, such as Abacavir + Didanosine + Lopinavir/Ritonavir (ABC + ddI + LPV/r), Lamivudine + Lopinavir/Ritonavir + Zidovudine (3TC + LPV/r + AZT), Lamivudine + Lopinavir/Ritonavir + Tenofovir Disoproxil Fumarate (3TC + LPV/r + TDF), Didanosine + Lopinavir/Ritonavir + Zidovudine (ddI + AZT + LPV/r).

5.1.1. The Situation in China and Bangladesh: Why is India's Supply Critical for Global Public Health?

Globally, there are two other countries that could potentially play the role of generic producers of important patented products: China and Bangladesh. Bangladesh has presently two firms, Square Pharmaceuticals and Beximco (the two largest local firms) that produce ARVs. Potentially, since Bangladesh (as a least developed country) is exempt from the TRIPS Agreement to implement its provisions on pharmaceutical patents until 2016, and it has an active local pharmaceutical sector, it could serve as a global supplier of public health-related drugs. However, Bangladesh needs to enact a new patent regime in order to be able to reap these flexibilities, since its present Patent Act of 1911 allows for both product and process patents on pharmaceuticals for a period of sixteen years (extendable by ten more). In the absence of a new Patent Act, it would at least need a legal ordinance or executive order that would invalidate these provisions under the Patent Act of 1911. A second requirement would be to build capacity amongst the local firms: they are presently only producing some first line ARVs. Beximco is manufacturing Lamivudine, Zidovudine, Efavirenz and Stavudine whereas Square Pharmaceuticals is manufacturing Efavirenz (Adiva), Lamivudine (Hivarif), Lamivudine and Zidovudine (Avudin), Abacavir, Lamivudine and Zidovudine (Tivizid) in the first line and only one second-line ARV, Nelfinavir, which is presently not recommended by the WHO's ART 2008 Guidelines.

The first line ARVs market is heavily commoditized and the profit margins have come down largely owing to extensive competition. Given that Bangladesh itself has a very low percentage of persons infected by HIV/AIDS, the main market for Square and Beximco would be export markets. It is unclear whether there is any price competitiveness of Bangladesh firms, given that they import most of the APIs required for the ARVs (see box 5), and the low economies of scale. Furthermore, the two firms have been unable to cater to both domestic and export markets up until now because they are not WHO pre-qualified. They also do not have a C1 status on the Global Fund's list,⁹⁵ as a result of which they are not qualified to cater to Bangladesh's own procurement of ARVs using Global Fund grants.

China has a relatively strong pharmaceutical sector⁹⁶ but since its WTO accession in 2002, it is obliged to grant patent protection to pharmaceutical products as

⁹⁵ C1 status implies WHO prequalification letter certifying the compliance of the manufacturing site with WHO GMP requirements and proof of dossier submission to WHO's Prequalification Program with acceptance letter.

⁹⁶ See Grace, 2004, footnote 78 above.

specified by the TRIPS Agreement. China could potentially play an important role by providing a compulsory licensing-friendly legal regime, where local firms secure compulsory licenses for exports, or even to fulfil local demand. However, up until now, the Chinese regime has not issued any compulsory licenses despite the fact that firms like Abbott and Glaxo Smith Kline (GSK) protect their rights over Kaletra and Lamivudine respectively in the Chinese market. In the case of GSK's Lamivudine, although the patent has expired globally, GSK enjoys a registration right on the product in the Chinese market, which is a local form of protection. This allows GSK to deter generic entry of the drug into the Chinese market.

5.1.2. Active Pharmaceutical Ingredients (API) Supplies for ARVs

An issue that emerged to be important in the field survey is the need to guard against the threat of predatory pricing in ARV drugs. There are only five pre-qualified producers of APIs for both first line and second line ARVs worldwide: Matrix Laboratories,⁹⁷ Hetero Pharmaceuticals and Aurobindo from India, and Desano and Huahai in China.⁹⁸ Aurobindo sells its ARV formulations only to the WHO and PEPFAR and tenders directly from countries, outside their main commercial activity of selling APIs to other Indian firms seeking to produce ARVs. Hetero and Matrix supply APIs to other firms, but also compete with them in the final formulations both nationally and internationally. Ranbaxy, Strides, Micro Labs, Emcure and Cipla mainly formulate the ARVs for sale. This could create scope for the integrated firms (who produce both APIs and the formulations) to hike up the price of the APIs, thus making it difficult for them to compete in the final price for formulations of first and second-line ARVs. Whereas most firms plan to continue the production of first and second-line drugs that presently a part of their product portfolios, they expressed severe scepticism to enter newer segments if the procurement of ARVs focused only on the price of the final product (field interviews).⁹⁹ Some of the formulator firms have made representations to WHO pointing out to this problem, the receipt of which was also confirmed by the WHO during this study.

Box 5.0 Securing Competitive API Supplies for ARVs¹⁰⁰

The cost of API as percentage of total cost of finished dosage form varies significantly from molecule to molecule. For instance, high value-low volume drugs like cardio vascular medicines where it is common to have tablets of 1mg or 5mg may have higher component of the API when compared to low value-high volume drugs (with tablets of 250mg or 500mg). The latter kind of drugs will have relatively lower component of API in the cost of the finished dosage form. On average though, one could consider API as 50% of total cost of finished dosage form. In the case of ARVs, most firms in India and Bangladesh were of the view that API costs comprise around 40% the total cost of the finished formulation. In the case of very high API component drugs, such as those for Cardiovascular system disorders, the API component of the drug could be as much as 90%.

More specifically, the public tenders for ARV have focused on the cheapest price supplier; most often the cheapest manufacturer not only wins, it wins the entire tender to

⁹⁷ Matrix has a strategic alliance with Mchem in China for API production, but Mchem's APIs for ARV production are not yet pre-qualified.

⁹⁸ Cipla has a 20% stake in Desano. Desano is WHO pre-qualified and Huahai is FDA approved.

⁹⁹ All firms quoted the example of paediatric ARVs.

¹⁰⁰ Dilip Shah, President of the IPA and other field interviews with ARV manufacturing firms and Dr. Satish Reddy, Chief Operating Officer, Dr. Reddy's Laboratories.

the exclusion of the other firms that compete in the tenders. This undoubtedly led to severe and quick price reductions in the market for first-line ARVs, but the procurement guidelines may call for a re-think focusing more on both price and quality for second-line and paediatric ARVs. Presently, it is quite likely that most firms are not really making profits by supplying the ARVs, but continue to do so since they are already manufacturing the drugs, and secondly, they may be compromising on quality in order to cut costs by importing APIs from non pre-qualified manufacturers (field interviews). This is unclear and could not be conclusively captured by the survey. However, given the importance of India as a global generics supplier of second-line ARVs, and in the interest of preserving incentives for further such drugs, it seems important to make sure that such concerns do not materialise.

Several second-line ARVs are very complex structures to manufacture. All the firms pointed attention to the inherent difficulties and the huge investments that they will need to make in terms of production technologies in order to make newer and more efficient processes for their manufacture. Lopinavir, for instance, has a twelve step synthesis chemistry and is very difficult to duplicate and the Indian firms are not able to offer huge price reductions over the patent holder firm for LPV/r mainly due to the difficulties in synthesising the product. Similarly, Atazanavir is synthesized from four different compounds and the production efficiency of the intermediates will dictate generic price efficiency.¹⁰¹ Increasing access to medicines in these categories is synonymous with increasing the incentives of firms to invest in mechanisms that enhance production efficiency. National and international procurement guidelines may need to be revised to reflect these concerns.

5.2. Malaria, Tuberculosis and Other Disease Segments

Malaria: The most common Artemisinin-based combination therapy (ACT) for first-line treatment is Coartem, patent holder Novartis and ASAP, where the patent holder is Sanofi Aventis. There are three Indian firms that produce anti-malarial combination therapies: Cipla, Strides and Ipca, of which all do not have WHO prequalification for their first line ACT, the generic version of Coartem. Ipca has WHO pre-qualification only for a second-line therapy using artemisinin; namely Artemisin Amodiaquine. Strides has developed its own technologies for ACT combinations and presently produces several of them. The company has considerable acreage of Artemisinin (the plant that is used to produce ACT drugs) in Vietnam. Ranbaxy's joint collaboration with MMV for the development of an anti-malarial drug has been discontinued recently, despite which Ranbaxy has proceeded with the development of the drug. According to the field interview with the company in April 2008, the drug is presently in clinical trials, and is a substitute for the artemisinin combination therapy recommended by the WHO. However, it is not clear whether Daiichi's recent takeover of the company will impact upon this in any way.

Tuberculosis: Strides and Lupin are also into the production of anti-tuberculosis drugs, for both MDR and HDR Tuberculosis. Strides is the largest producer of first-line TB drugs, for which it has developed the technologies in an alliance with Sandoz. Strides

¹⁰¹ Brenda Waning and Cheryl Cashin, Development of a Simulation Model to Measure Potential Cost Savings from Reducing Treatment Costs for Antiretroviral Medicines, DFID Draft, 25 March 2008, on file with the author.

however, expressed scepticism to enter into production of second-line MDR TB drugs. Lupin remains the sole API manufacturer within India for this segment.

Other public health drugs: As opposed to widely available drugs to treat opportunistic infections such as Ciprofloxacin and Flucanazole, there are drugs for treating opportunistic infections, such as Valgancyclovir and Valacyclovir that are not available for use in resource-poor settings due to their high prices. The Indian patent situation and the on-going dispute on Roche's Valcyte (Valgancyclovir) could pave the way for cheaper substitutes of such drugs. In the case of Valgancyclovir, Ranbaxy has recently received market approval for the generic version of Valcyte, and Cipla plans to enter the market with its own version of the drug in July 2008. There are huge price differences between the originator firm's price (which is somewhere between 900 to 1000 Rupees for a 450 mg tablet, approximately between 20-25 USD) and Cipla's price, which is estimated to be around 240 rupees (6 USD). Several public health agencies, such as the Clinton HIV and AIDS Initiative (CHAI) are keen to promote more widespread use of drugs such as Valgancyclovir in developing and least developed countries¹⁰² and Indian firms will potentially play a large role in this endeavour. The flexible patent interpretations could also pave the way for cheaper generics of other important drugs to treat opportunistic infections, which are presently being manufactured only by the patent holder firm, such as Rifabutin, Famcyclovir and Valacyclovir.¹⁰³

Drugs for lifestyle diseases: There is an increasing incidence of lifestyle and other diseases that are associated with industrialized countries in India (WHO, 2007; see table in Grace, 2005, p. 23) and the incidence of chronic diseases is forecasted to rise substantially by 2015 (McKinsey, 2007). Coronary heart disease is expected to rise from 3.31% in 2005 to 4.91% in 2015, diabetes from 2.80 in 2005 to 3.70 in 2015, Asthma from 2.5% in 2005 to 2.70% in 2015, obesity from 1.3% in 2005 to 2.7% in 2015, and cancer from 0.18% in 2005 to 2% in 2015 (Ibid. p. 11). Changing disease portfolios of Indians, with an increase in global diseases is a trend in favour of the firms, since the prospect of an assured domestic market attenuates risk of failure in other international markets. A major factor that may impact of availability of drugs in the local market may however be the Indian government's plan to bring over 300 drugs in various categories under price control.

The Pharmaceutical Pricing Policy of 2006, expected to be enacted soon, contains provisions to bring all medicines listed in the national list of essential medicines that has been prepared in 2003 under price control. The National Pharmaceutical Pricing Authority (NPPA) will then be in-charge of price control of the drugs as specified by the pricing policy. It is unclear how the imposition of price controls on drugs is ensuring their wider availability, especially against the backdrop of India's own experience with drug price control. The price of the drug is only one component in access to medicines, and India's past experience with price control shows that ensuring effective competition in the local market (with public health as the primary concern) is perhaps the more reasonable way achieve greater access. The Drug Price Control Order of 1979, which brought 354 drugs under price control resulted in a huge investment hiatus from the domestic firms between 1979 and 1986. Domestic firms simply changed their product portfolios to avoid producing drugs that were under price control during this time. Since

¹⁰² Grace and Gehl Sampath, Potential Market Impact of In-Kind Donations to the Global Fund, A Report to the Global Fund to Fight TB, AIDS and Malaria, Draft, 14 July 2008.

¹⁰³ Same as above.

1986, successive price control orders, including the Drug Price Control Order of 1995 have focused on lower price controls with sufficient safeguards to ensure the growth of competition in all key therapeutic categories, which have promoted abundance of medicines locally.

All firms interviewed for the survey reacted aversely to the prospect, both domestic and foreign.

6.0 Conclusions

This study has analysed the response of the Indian pharmaceutical sector to product patent protection using both secondary and primary sources. The field survey of 49 firms based on a ranking derived using total revenues was used to understand the variegated hues of innovation in the sector, factors that impact upon it including recent regulatory changes in the patent regime and data protection, as well as changes in global innovation environment for the pharmaceutical sector. The conclusions and policy recommendations that arise from the analysis are presented here under three separate headings: those of concern to the pharmaceutical sector, those related to the regulatory environment and those that are directed towards enhancing access to medicines.

6.1. On the Pharmaceutical Sector

There is an emergence of a new industrial structure due to the gradual integration of the Indian firms with the global pharmaceutical industry, increased modularization of pharmaceutical innovation globally and outsourcing possibilities. Indian firms have seized opportunities arising from pressures in the global innovation environment, but they have also been innovative in building their own niches. To a large extent, their model has been and continues to be one where they seek to disrupt global patterns of innovation through the introduction of products that are cheaper, affordable and in some cases, as in the case of the HIV/AIDS drugs, targeted towards the masses. In such cases, the economies of scale results in benefits that only focusing on high-value added products would not. Maintaining this diversified product portfolio is enabled by the strong domestic base at home that offers an opportunity to manufacture drugs for a wide range of diseases, including global diseases.

However, this mainstreaming of Indian firms into the global industry implies also a greater sensitivity to changes in global regulatory structures that seek to favour multinational firms and make it difficult for new entrants to establish themselves globally.¹⁰⁴ The recent Ranbaxy-Daichii Sankyo deal serves as a reminder of the turbulent market in which the firms presently operate: the difficulties of integrating and making a place in global innovation are as numerous as the opportunities they pose. The global realities of pharmaceutical innovation is presently such that even established firms in developed countries rely more and more on government sponsored 'translational' public sector research to create marketable products and venture capital

¹⁰⁴ See Joyce Tait, Joanna Chataway and David Wield, "The Case for Smart Regulation", *Appropriate Governance of the Lifesciences – 2*, Innogen Policy Brief, 2007, where the authors note that global regulatory initiatives have discriminated among particular products with the intention of enabling or encouraging innovation in particular directions, for example the US FDA Fast Track and the Orphan Drugs Act. They also note that the more usual pattern is that of structuring regulatory constraints on the development of new drugs that support the reinforcement of current innovation models and industry structures.

institutions are increasingly coming under strain. Indian firms, seeking to compete globally in this changing scenario, will require much more strategic policy support by the government.

This strategic governmental support should be aimed both at (a) encouraging firms to disrupt patterns of global innovation in the pharmaceutical sector to create products for the poor the world over, making medicines more accessible; and (b) to help them focus their efforts on accumulating greater technological capabilities while maintaining their strength as low-cost innovators of high-value pharmaceutical products. This will include the following.

1. The role of the CSIR as a pro-active, industry-oriented public sector institute needs to be revived apart from efforts to strategically allocate public sector resources to support the firms.
2. A wider range of initiatives for enhanced collaboration between various actors in the pharmaceutical innovation system needs to be put in place.
3. There is a need to re-think the relationship between price control and drug availability and affordability that takes into account two important features of the market:
 - a. The amount of competition in the market and the mark-ups in pharmaceutical products (due to unregulated intermediary stages) before it reaches the consumers;
 - b. The importance of encouraging practices amongst Indian firms that allow for price discriminations between regulated and unregulated markets. Their products are intrinsically cheaper at the present, but this might become an issue in the future with rising costs of conducting R&D in India.
4. There is a need to enhance incentives for firms to invest into anti-retroviral drugs and drugs for Malaria and Tuberculosis. There have been no new entrants in the ARV market over the past three years, except Emcure and Cadila and the markets for Malaria and Tuberculosis remain largely stagnant. There is a need to envision newer incentives that focus on how to promote R&D in India for these diseases in addition to the production of generic versions.

The newly created Department of Pharmaceuticals could play a critical role in enabling support structures of relevance to the sector's performance and growth.

6.2. On the Regulatory Framework

The way the Indian patent regime is being implemented calls for legal clarity. There is a need for greater clarity on what is patentable in India, when (and for which categories) can local companies apply for compulsory licenses, and under what conditions can patents granted within India be over-ridden by Indian firms. There is also a need to establish clearly how patents will be granted and what procedures will be followed for pre and post grant oppositions. In the absence of this, extended legal battles between local firms, MNCs and civil rights groups are costly and difficult to sustain. India also needs to establish that it can not only grant but also enforce patents on pharmaceutical products in cases where the applications are consistent with the requirements of the Indian Patent Act. The Tarseva case for example, leaves one wondering about the sanctity of the patents acquired in India. It is clear that the patent's absence would be a major boon for public health. However, this decision needs to be

made at the *ex-ante* stage as to whether at all such products should be granted patents in India.

That said, the spate of patent disputes shows how Indian legislators and courts are seriously engaged in finding ways to promote access to medicines despite their obligations under the TRIPS Agreement. This commitment is extremely valuable, and should be fostered further through technical advice on how to achieve legal certainty in interpretations of the Indian patent regime that balance the country's obligations under the TRIPS commitments and public health objectives.

There is a need for enhanced coordination (and not linkage) between the Patent Office and the Drug Controller of India, which is in-charge of granting market approval to all new drugs.¹⁰⁵ There is also a need for more transparency in the workings of the patent offices in the country. The Office of India's Controller General of Patents, New Delhi is now conducting an investigation on whether the grant of a patent on Valgancyclovir (Valcyte) violated Indian patent rules. These forms of institutional costs can be avoided by creating patent databases that allow for better functioning of the Patent Offices around the country, and also help clarify the status of patent grants to those interested in industry. Pre- and Post-opposition procedures also need to be clarified, the Valcyte case again being a case in point.

It is still not clear why India needs a data exclusivity regime as suggested by the Reddy Committee Report after the transition phase. Although the regime suggested by the Reddy Committee is in the interest of public health, the question that looms large is whether and if this regime will be implemented in its entirety eventually? As this study shows, leaving out one or two stipulations of the report will have far-reaching repercussions on public health.

6.3. On Enhancing Access to Medicines

This study shows that Indian firms continue to play a critical role as suppliers of drugs for public health post 2005, especially HIV/AIDS, Malaria, TB and other opportunistic infections. Given the fact that their presence has already brought about some price reductions in Lopivavir/Ritonavir similar to what was observed in the case of first-line ARVs, and their potential to further enhance competition in existing and future drug categories for these diseases, much more effort is required to expand the role as well as interest more firms in focusing on product portfolios that include these drugs. The lack of capacity (both regulatory and technological) in Bangladesh and the lack of political willingness to grant compulsory licenses on drugs of importance to public health in China reinforce the findings of this study on the role played by Indian firms. Given the importance of capabilities and economies of scale to engage in such activities, scarce international resources seem better spent to facilitate Indian firms to enhance their activities, rather than focus on building capacity in sectors in other least developed countries.

¹⁰⁵ There is presently a debate on the statutory and public health implications of allowing a formal linkage between the office of the Drug Controller of India and the Patent Office. It has been felt that making regulatory approval contingent on clarity of patents on the product may delay generic entry, among others. See "Is the Indian Drug Controller Participating in the ACTA Negotiations", *Managing Intellectual Property*, June 19, 2008, available at: <http://spicyipindia.blogspot.com/2008/06/is-indian-drug-controller-participating.html>

This study also shows that a large number of firms are focusing on global diseases. Though this may be important, given the expanding number of persons with global diseases in India and much of the developing world, there is a case for encouraging Indian firms to invest further into R&D as well as generics production of drugs that help cure HIV/AIDS, Malaria, TB and other such neglected diseases. Such efforts should go beyond production of generics, and target the creation of R&D ventures, both through public-private partnerships and private-private initiatives. These efforts should include a re-think on international procurement guidelines for ARVs in order to focus them on price-quality rather than the cheapest price, in order to prevent the scope for any predatory pricing practices amongst the generic producers. There is a need to preserve maximum dynamic competition in this segment in the interest of global public health. Most of the ARV producing firms interviewed for this study expressed difficulties of working with tenders that merely focused on price to supply newer ARV drugs that required greater technological inputs and increased formulation capabilities.

Specifically on the domestic regulatory strategies to enhance access to medicines within India, there is not much correlation between local production and marketing possibilities for various therapeutic categories of products and government's access to medicine strategies. Especially, there seems to be a very clear disjuncture between the government's plan to bring over 300 categories of drugs under price control and the extent of competition witnessed in the market for key therapeutic categories. Mistaken policy making in this regard may be detrimental to the interests of the sector at this point of time. Price control should clearly be the solution only for those categories of drugs where there are not many sources of cheap supply. In the absence of such a criteria, the price control mechanism may be a severe disincentive to firms to invest in important product categories. In the worst case, firms may just focus on export markets (earlier experience with price control shows that firms simply discontinued manufacturing particular products), at the expense of local public health.

Annex 1: Terms of Reference

Impact of India's New Patent Regime on Access to Medicines in Developing Countries

Background

Following India's adoption of product patent protection in 2005 to conform with its WTO obligations under the TRIPS agreement, an issue of concern has been the impact on Indian firms' ability to supply generic drugs in the local market and to other developing countries. Prior to 2005, generic versions of drugs patented elsewhere produced by Indian pharmaceutical firms offered direct price competition to international pharmaceutical companies in third countries, thus enhancing access to medicines worldwide. India's present patent regime contains several interesting and important flexibilities that allow the local generic sector to continue producing generic versions of existing drugs at lower costs.

These include:

- (a) Provisions to limit "evergreening" of patents;
- (b) Provisions that enable firms to continue manufacturing generic versions of drugs patented between 1995 and 2005, against payment of a "reasonable" compensation to the original patent holder firm; and,
- (c) Efforts to check collusions between firms that manufacture patented drugs and generic firms, to delay introduction of generic versions of drugs; and,
- (d) Provisions that encourage the production of generic drugs through compulsory licensing, as envisaged by Paragraph 6 of the Doha Declaration.

Some of these provisions have been a source of controversy and legal action (as can be seen in the cases of Gleevec and Tenofovir, amongst others). In particular the section of the Indian law intended to restrict "evergreening" has been challenged by Novartis in the Indian courts.

Moreover, because companies can now patent new products in India, it is uncertain how this might affect the worldwide pricing and the accessibility of new products, and how, in the absence of potential competitive pressure, pricing of the kind that has emerged to date in the global antiretroviral market can be sustained. The extent of economic incentives for firms to continue manufacturing drugs for other developing countries under compulsory licensing is also not clear.

These issues call for a clear assessment of the implications of the present patent regime and the uncertainties related thereto, on economic incentives of firms and access to medicine issues.

Study focus

The purpose of this study will be to investigate the present patent regime and the state of India's pharmaceutical sector, in order to analyse its implications for access to medicines. The analysis will review developments concerning the implementation of the Indian Patent Act since Grace (2005). This will especially focus on the issues raised by

(a) the Mashelkar report (and its aftermath), (b) the Novartis case, and (c) the Reddy report on data protection.

The main research questions will be:

- (i) What are the developments since 2005 in the legal and economic framework in India that have implications for firms' behaviour and access to medicines? This section will particularly focus on the issue of pricing and availability of second line ARVs.
- (j) How do emerging disease trends in the country (especially the growing importance of non-communicable diseases) and in other developing countries affect issues of availability and pricing of medicines in these segments?
- (k) How important are issues related to transparency and registration of patent information and the viability of a patent database for effective manufacture of generics by the Indian firms? Transparency and registration of patent information is an issue that affects the way most Indian firms deal with the emerging situation. In a survey of the sector in 2005, most firms interviewed complained about the difficulties in obtaining patent-related information from the patent office, and that such a lack of information affected their product choice and often also led to losses since they invested time to reverse engineer drugs without having information on process/ product or formulation patents on them (Gehl Sampath, 2005). Improving the efficiency of the patent office to disseminate patent-related information could help firms deal with the emerging situation in a very important way.

Methodology

The study will be based on secondary data as well as a survey of top Indian firms, in order to assess the implications of the new developments in the legal and economic framework on firms' behaviour and constraints. The questionnaire survey will be conducted using semi-structured questionnaires, in conjunction with a local team, and will be substantiated through extensive interviews with company executives, as well as other key informants, such as those from Ministries of Health, Petrochemicals, Industry and Commerce and the Patent Office.

Annex 2: List of People Interviewed

People Interviewed	
No.	Names and Affiliations
1	Dr. B.P.S Reddy, CEO, Hetero Pharmaceuticals
2	Tapan Ray, Director General, OPPI
3	Aloka Sengupta, Vice President, ATM, Strides Acrolabs Limited
4	Dr. Shipla Patel, Medical Director, Wyeth Limited
5	Hasit Joshipura, Vice President, South Asia and Managing Director, India Operations, Glaxo SmithKline Pharmaceuticals Limited
6	Shirish Ghoghe, Senior Director, Sanofi Aventis
7	M. G. Rao, Executive Vice President, Unichem Laboratories Ltd
8	K. Subharaman, Head, Legal and Company Secretary, Unichem Labs Ltd
9	Ulhas Joshi, Vice President, Strategy and Business Development, Unichem Laboratories Ltd
10	Uday Baldota, Vice President, Sun Pharmaceutical Industries Ltd
11	Glenn Saldanha, Managing Director and CEO, Glenmark Pharmaceuticals Ltd
12	N. V. Ramana, Executive Director, Divi's Laboratories
13	Sudarshan Jain, Director-Marketing, Abbott India Limited
14	Dr. R. Sankaran, Senior Director, Intellectual Property Rights, Dabur Research Foundation
15	Dr. Surendra Tyagi, Chief Scientific Officer, Dabur Research Foundation
16	Dr. S. Padmaja, Vice-President, Intellectual Property, Aurobindo Pharma Ltd
17	Dr. J. M. Khanna, Executive Director and President, Life Sciences Division, Jubilant Organosys
18	Dr. Satish Reddy, Chief Operating Officer, Dr. Reddy's Laboratories Ltd
19	Dr. Raj Kumar, President, R&D and Commercial, Dr. Reddy's Laboratories Ltd
20	Gurdial Singh Sandhu, Joint Secretary (Pharmaceuticals industry), Department of Chemicals and Petrochemicals
21	Rahul Kapadia, Ipca Laboratories
22	Dilip Shah, President, Indian Pharmaceutical Alliance
23	Jaideep Godgay, Medical Director, Cipla Pharmaceuticals
24	Deepali Talwar, Director Legal Services and General Counsel, Pfizer Limited
25	Anglo French Drugs & Industries Ltd.
26.	Francoise Renaud-Thery, WHO AMDS
27.	Boniface Dongmo Nguimfack, WHO AMDS
28.	Yves Marchandy, MSF
29.	Dai Ellis, Clinton HIV and AIDS Initiative
30.	George Baguma, Quality Chemicals, Uganda

Annex 3: Top Indian Pharmaceutical Firms Surveyed

Top Indian Pharmaceutical Firms Surveyed			
No.	Pharmaceutical Firm	No.	Pharmaceutical Firm
1	Shasun Chemicals and Drugs Ltd.	26	Claris Lifesciences
2	Caplin Point Laboratories Ltd.	27	Torent Pharmaceuticals Ltd.
3	PI Drugs & Pharmaceuticals Ltd.	28	Medicamen Biotech Ltd.
4	Penam Laboratories Ltd.	29	Strides Acrolabs Ltd.
5	Glaxo SmithKline Pharmaceuticals Ltd.	30	East India Pharmaceutical Works Ltd.
6	Vivimed Labs Ltd.	31	Ind-Swift Laboratories Ltd.
7	Granules India Ltd.	32	Dr. Morepen Laboratories Ltd.
8	SMS Pharmaceuticas Ltd.	33	Ku-dos Chemi Co. Ltd.
9	Haffkine Bio Pharmaceuticals Corporation Ltd	34	Venus Remedies Ltd.
10	Emmellen Biotech Pharmaceuticals Ltd.	35	Nectar Lifesciences Ltd.
11	Neuland Laboratories Ltd.	36	Surya Pharmaceuticals Ltd.
12	Divis Laboratories	37	Arch Pharmalabs Ltd.
13	Sven Genetech Ltd	38	Transchem Ltd.
14	Natco Pharma Ltd.	39	Pfizer India
15	Matrix Laboratories Ltd.	40	Marksans Pharma Ltd.
16	Aurobindo Pharma Ltd	41	Ind-Swift Lab. Ltd.
17	Suven Life Science	42	Malladi Drugs & Pharmaceuticals
18	Cadila Pharmaceuticals	43	Orchid Chemicals & Pharmaceuticals Ltd.
19	Zydus	44	Panacea Biotech Ltd.
20	Arvind Remedies Ltd.	45	Jagsonpal Pharmaceuticals Ltd.
21	Genom Biotech Pvt Ltd.	46	KDL Biotech Limited
22	Intas Biopharmaceuticals Ltd.	47	J.B. Chemicals & Pharmaceuticals Ltd.
23	Apex Laboratories Ltd.	48	Unichem Laboratories
24	Aristo Pharmaceuticals Pvt. Ltd.	49	Hetero Drugs Ltd.
25	Anglo French Drugs & Industries Ltd.		

Annex 4: List of Top 100 Companies for the Firm-Level Survey

Top 100 Pharmaceutical Companies				
Company	City	Total Revenues (\$ Mn)	Net Profit (Loss) (\$ Mn)	Fiscal Year
Dr. Reddy's Laboratories Ltd.	Hyderabad	1,146,456	298,771	Mar 2007
Ranbaxy Laboratories Ltd.	Gurgaon	1,024,179	158,159	Dec 2006
Cipla Ltd.	Mumbai	945,659	169,594	Mar 2007
Sun Pharmaceutical Industries Ltd.	Mumbai	633,529	159,667	Mar 2007
Aurobindo Pharma Ltd.	Hyderabad	543,960	58,157	Mar 2007
Lupin Ltd.	Mumbai	542,424	75,649	Mar 2007
Jubilant Organosys Ltd.	Noida	495,103	58,769	Mar 2007
GlaxoSmithKline Pharmaceuticals Ltd.	Mumbai	453,277	138,489	2006
Nicholas Piramal India Ltd.	Mumbai	449,731	47,799	Mar 2007
Cadila Healthcare Ltd.	Ahmedabad	428,256	51,968	Mar 2007
Wockhardt Ltd.	Mumbai	315,171	54,214	2006
Orchid Chemicals & Pharmaceuticals Ltd.	Chennai	278,825	24,532	Mar 2007
Aventis Pharma Ltd.	Mumbai	260,576	42,978	2006
Ipca Laboratories Ltd.	Mumbai	259,033	31,031	Mar 2007
Torrent Pharmaceuticals Ltd.	Ahmedabad	236,936	28,677	Mar 2007
Glenmark Pharmaceuticals Ltd.	Mumbai	230,891	34,222	Mar 2007
Panacea Biotec Ltd.	NewDelhi	220,129	37,271	Mar 2007
Pfizer Ltd.	Mumbai	208,888	26,842	2006
Matrix Laboratories Ltd.	Secundrabad	201,610	25,288	Mar 2007

Divi's Laboratories Ltd.	Hyderabad	185,410	48,680	Mar 2007
Alembic Ltd.	Vadodara	181,140	17,944	Mar 2007
Novartis India Ltd.	Mumbai	155,773	22,480	Mar 2007
U S V Ltd.	Mumbai	154,133	34,268	2006
Unichem Laboratories Ltd.	Mumbai	144,872	22,869	Mar 2007
Nectar Lifesciences Ltd.	Chandigarh	144,293	14,280	Mar 2007
JB Chemicals & Pharmaceuticals Ltd.	Mumbai	143,412	18,030	2007
FDC Ltd.	Mumbai	125,976	16,332	2007
Elder Pharmaceuticals Ltd.	Mumbai	117,017	12,498	2007
Strides Acrolabs Ltd.	Bangalore	116,095	9,185	2006
Ind Swift Ltd.	Chandigarh	112,435	5,275	2007
Plethico Pharmaceuticals Ltd.	Mumbai	110,465	32,584	2007
Shasun Chemicals & Drugs Ltd.	Chennai	107,631	9,718	2007
Merck Ltd.	Mumbai	97,743	33,854	2006
Arch Pharmalabs Ltd.	Mumbai	96,055	7,659	2007
Ind Swift Laboratories Ltd.	Chandigarh	94,245	4,915	2007
Indoco Remedies Ltd.	Mumbai	88,713	10,673	2007
Surya Pharmaceuticals Ltd.	Baddi	88,393	6,014	2007
Wyeth Ltd.		85,331	23,448	2007
Dabur Pharma Ltd.	NewDelhi	84,308	6,410	2007
Unimark Remedies Ltd.	Mumbai	83,331	6,377	2006
Dishman Pharmaceuticals & Chemicals Ltd.	Ahmedabad	80,673	15,453	2007
Aristo Pharmaceuticals Ltd.	Mumbai	80,249	14,476	2002
Astra Zeneca Pharma India Ltd.	Bangalore	78,979	12,374	2006
Aarti Drugs Ltd.	Mumbai	78,071	3,242	2007

Claris Lifesciences Ltd.	Ahmedabad	76,146	5,438	2005
Marksans Pharma Ltd.	Mumbai	74,600	1,759	2007
Ankur Drugs & Pharma Ltd.	Mumbai	70,137	7,101	2007
Hikal Ltd.	Mumbai	67,228	8,571	2007
Ajanta Pharma Ltd.	Mumbai	64,986	3,481	2007
Neuland Laboratories Ltd.	Hyderabad	56,558	2,295	2007
Natco Pharma Ltd.	Hyderabad	56,159	7,733	2007
Burroughs Wellcome India Ltd	Mumbai	55,539	(1,475)	2003
Twilight Litaka Pharma Ltd.	Pune	52,430	3,577	2007
Granules India Ltd.	Hyderabad	50,140	2,569	2007
S M S Pharmaceuticals Ltd.	Hyderabad	50,094	5,324	2007
Organon India Ltd.	Mumbai	48,766	4,552	2006
Arvind Remedies Ltd.	Chennai	46,438	1,112	2007
Themis Medicare Ltd.	Mumbai	45,476	2,110	2007
Raptakos, Brett & Co. Ltd.	Mumbai	44,212	3,935	2006
Sharon Bio-Medicine Ltd.	Mumbai	43,592	4,265	2007
K D L Biotech Ltd.	Mumbai	43,041	(3,440)	2007
Solvay Pharma India Ltd.	Mumbai	41,767	4,755	2006
Fulford India Ltd.	Mumbai	41,274	3,237	2006
Albert David Ltd.	Kolkata	41,196	3,349	2007
Wanbury Ltd.	Mumbai	41,120	5,288	2007
Zandu Pharmaceutical Works Ltd.	Mumbai	38,396	3,707	2007
Venus Remedies Ltd.	Panchkula	37,261	7,291	2007
Hiran Orgochem Ltd.	Mumbai	35,067	274	2007
Jagsonpal Pharmaceuticals Ltd.	New Delhi	34,461	711	2007

Blue Cross Laboratories Ltd.	Mumbai	34,125	5,121	2005
Morepen Laboratories Ltd.	New Delhi	32,874	(42,452)	2007
R P G Life Sciences Ltd.	Mumbai	32,681	2,092	2007
Suven Life Sciences Ltd.	Hyderabad	29,010	2,874	2007
Jupiter Bioscience Ltd.	Hyderabad	28,246	4,775	2007
Ambalal Sarabhai Enterprises Ltd.	Vadodara	27,855	(7,504)	2007
Vorin Laboratories Ltd.	Secunderabad	26,017	(2,442)	2003
Vivimed Labs Ltd	Hyderabad	25,887	2,777	2007
Kudos Chemie Ltd.	Chandigarh	25,154	1,830	2007
Medley Pharmaceuticals Ltd.	Mumbai	24,245	658	2005
Anuh Pharma Ltd.	Mumbai	23,199	1,744	2007
East India Pharmaceutical Works Ltd.	Kolkata	23,153	625	2007
Mangalam Drugs and Organics Ltd.	Mumbai	22,529	193	2007
Apex Laboratories Ltd.	Chennai	22,054	840	2006
Anglo French Drug & Industries Ltd.	Bangalore	20,434	71	2007
Avon Organics Ltd.	Hyderabad	19,812	(4,796)	2007
Bal Pharma Ltd.	Bangalore	19,784	513	2007
Transchem Ltd.	Thane	19,416	378	2007
Fem Care Pharma Ltd.	Nashik	18,568	3,181	2007
S T S Chemicals Ltd. [Merged]	Mumbai	17,827	823	2005
Sanofi-Synthelabo India Ltd.	Mumbai	17,205	840	2006
Flamingo Pharmaceuticals Ltd.	Mumbai	17,179	8	2005
Shilpa Medicare Limited.	Raichur	17,113	1,782	2007
Lincoln Pharmaceuticals Ltd.	Ahmedabad	16,621	764	2007
Syncom Formulation India Ltd.	Mumbai	16,024	1,036	2007

Medicorp Technologies India Ltd.	Chennai	15,915	(2,770)	2003
Medicamen Biotech Ltd.	New Delhi	15,862	383	2007
Caplin Point Laboratories Ltd.	Chennai	15,288	487	2007
Malladi Drugs & Pharmaceuticals Ltd.	Chennai	15,286	3,120	2002
Dey'S Medical Stores Mfg. Ltd.	Kolkata	14,648	411	2006