United Nations Development Programme

POVERTY REDUCTION AND HIV/AIDS

FIVE YEARS INTO THE PRODUCT PATENT REGIME: INDIA'S RESPONSE

FIVE YEARS INTO THE PRODUCT PATENT REGIME: INDIA'S RESPONSE

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December 2010

United Nations Development Programme
One United Nations Plaza
New York, NY 10017
U.S.A.

Website: *www.undp.org/poverty*

UNDP is the UN's global development network, advocating for change and connecting countries to knowledge, experience, and resources to help people build a better life.

Cover Photo: Mohammad Moniruzzaman / UNDP Picture This.

Design: Alex Majumder.

Printing: Consolidated Graphics, New York, USA.

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This study was commissioned by the United Nations Development Programme (UNDP) under the auspices of the Intellectual Property and Access to Medicines Capacity Building Initiative, a cross-practice project between UNDP's Poverty Group and the HIV/AIDS Group. The project initiated in 2004 seeks to support the building of developing country and broader Southern capacity to sustainably access affordable HIV/AIDS drugs in the context of the implementation of the World Trade Organization (WTO) Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS) and intellectual property provisions in other trade agreements (e.g. bilateral and regional trade arrangements). Since 2009, the project has broadened its focus in understanding various dimensions and policy interventions to direct health innovation towards meeting long term public health goals, including sustainable access to affordable medicines. In terms of the Millennium Development Goals (MDGs), the project aims to contribute directly to the achievement of MDGs 6 and 8 (and indirectly to MDG 1) by seeking to facilitate a policy environment in which generic drugs will be more accessible to those who need them, in particular poor and vulnerable populations.

The tension between the need to promote innovation and development of new healthcare technologies (which some parties argue require higher standards of patent protection) and the promotion of sustainable access to affordable medicines is not new — it has come to the fore in many developing countries as a result of their implementation of certain provisions of the TRIPS Agreement. Developments in India have impacts well beyond its borders, given the reliance thus far of much of the global market, especially in developing and least developed countries (LDCs), on the supply of low-cost, quality Indian generic pharmaceutical products. This study is intended to be a contribution towards understanding the continued role of India as a supplier of affordable medicines five years after having complied with the TRIPS Agreement. The study analyses the role of both the Indian pharmaceutical industry and the Indian legal system in building a post-TRIPS scenario that continue to be conducive to sourcing affordable medicines.

Chapter 1 of this study (written by Sudip Chaudhuri) looks at the changes in the Indian pharmaceutical industry and the strategies adopted by surviving generic companies as well as the emergence of new originator companies and how this could impact availability of affordable medicines. Chaudhuri further analyses and presents options available and makes recommendations for policy makers including using flexibilities under the Patent law to the fullest which may be critical to promote the revival of a robust generic industry.

Chapter 2 of this study comprises two sections and analyses the response of the Indian legal system. The first section (written by Chan Park) analyses whether Indian patent offices and courts of law have made full use of flexibilities within the new patent act as well as whether they have interpreted provisions in favor of public health. Focusing on the strict patentability criteria in the Indian law, Chan additionally analyses applications that have been granted patents in all of the patent offices in the country foreseeing possible trends and establishes the need for continued strict interpretation of patentability criteria. In his recommendations, Chan also urges for more transparency by the Patent Offices.

The second section (written by K. M. Gopakumar) takes a closer look at the pharmaceutical patent applications in India's 'mailbox'. The mailbox was a transitional mechanism required under TRIPS that was established to accept patent applications between 1995 and 2004. Based on databases of the mailbox applications, medicines approved during this period for marketing both in India and the US and their patent history, Gopakumar examines the potential of some of the safeguards in India's patent law to keep space for generic competition open. He urges the strict application of the safeguards in the Indian law as well as institutional

reforms and capacity building for the safeguards to be truly effective and finds that the Indian experience has some important lessons for LDCs seeking to implement the TRIPS Agreement in the coming years.

The study has benefitted from several inputs and comments from various experts including through a national validation meeting organized by UNDP which was attended by various stakeholders including from the government, private sector, national experts and civil society. Initial drafts of the study benefitted from inputs and comments provided by Tenu Avafia, Luisa Bernal, Biplove Choudhary, Kamal Malhotra, Luciana Mermet, Savita Mullapudi Narasimhan, Cecilia Oh and Yumiko Yamamoto.

During the national validation and technical consultation meeting comments and inputs were provided by Tenu Avafia (UNDP); Jayant Dasgupta (Economic Advisory Council, India); Arun Jha (Department of Pharmaceuticals, India); K S Kardam (Deputy Controller of Patents and Design, India); Yogendra Kumar (Ministry of External Affairs, India); Dinesh Abrol (NISTADS, India); Kajal Bharadwaj (national expert); Reji Joseph (RIS); Radhika Lal (UNDP); M. Santhosh (CENTAD); Leena Menghaney (MSF); Savita Mullapudi Narasimhan (UNDP); Yogesh Pai (CENTAD); Rathin Roy (UNDP); D G Shah (IPA); Madhukar Sinha (Center for WTO Studies) and Juliana Vallini, (ANVISA, Brazil). Support from UNDP India Country Office in the organization of the workshop is gratefully acknowledged, including from Deepti Handa, Alka Narang and Shashi Sudhir.

UNDP hopes that the findings of this study will be used to design appropriate policy approaches for the consideration of different stakeholders in India, including the ministry of health, patent offices, ministry of trade, department of industrial policy, pharmaceuticals, agrochemicals, the justice department, national policy experts and civil society. Outside India, the findings may provide useful policy lessons for policy makers in other developing countries seeking to balance similar tensions in policy objectives. It is hoped that this study shall provide much needed insight into India's continued role as a supplier of affordable medicines to the developing world. Additionally, it can be used as an entry point towards exploring strategic south-south cooperation mechanisms on seeking solutions for health innovation to meet human development goals.

The overall coordination and editing was facilitated by Savita Mullapudi Narasimhan.

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List of Acronyms and Abbreviations

ACTA	Anti Counterfeiting Trade Agreement
AGE	Advanced Glycation End product
ANDA	Abbreviated New Drug Application
ANVISA	Agência Nacional de Vigilância Sanitária (Brazil)
API	Active Pharmaceutical Ingredient
ARIPO	African Regional Intellectual Property Organization
ARV	Anti Retroviral
AZT	zidovudine (ARV drug)
CARG	Compound Annual Rate of Growth
CDRI	Central Drug Research Institute
CDSCO	Central Drug Standards Control Organization (India)
CENTAD	Centre for Trade and Development
CIPI	Confederation of Indian Pharmaceutical Industries
CIPIH	Commission on Intellectual Property Rights, Innovation and Health (WHO)
CMIE	Centre for Monitoring Indian Economy
CRAMS	Contract Research and Manufacturing Services
CRO	Contract Research Companies
CSIR	Council of Scientific and Industrial Research (India)
DCGI	Drug Controller General of India
DGCI&S	Directorate General of Commercial Intelligence and Statistics
DMF	drug master file
EC	European Commission
EFTA	European Free Trade Association
EMR	exclusive marketing rights
EPC	European Patent Convention
EPO	European Patent Office
EU	European Union
FTA	Free Trade Agreement
GATT	General Agreement on Tariffs and Trade
GMP	Good Manufacturing Practices
GSK	GlaxoSmithKline
IBSA	India Brazil South Africa (trilateral grouping)
IMPACT	International Medical Products Anti-Counterfeiting Taskforce (WHO)
INN	International Non-proprietary Name
IPAB	Intellectual Property Appellate Board (India)
LDCs	Least Developed Countries
MMV	Medicines for Malaria Venture (MMV)
MNC	Multi National Corporation
MRP	Maximum Retail Price
MSF	Médecins Sans Frontières
NCE	New Chemical Entity
NDA	New Drug Application
NME	New Molecular Entity
NDDS	Normal Drug Delivery System
NISTADS	National Institute of Science Technology and Development Studies (India)
NIPO	National Intellectual Property Organization (India)
NME	New Molecular Entity
OAPI	Organisation Africaine de la Propriété Intellectuelle
OSDD	Indian Government's Open Source Drug Discovery
PAT	Profit After Tax
PCT	Patent Co-operation Treaty
R&D	Research and Development
TDF	Tenofovir Disoproxil Fumarate
TEG	Technical Expert Group on Patent Law Issues (India)
TNMSC	Tamil Nadu Medical Services Corporation
TRIPS	Agreement on Trade Related Intellectual Property Rights (WTO)
UK	United Kingdom
UNDP	United Nations Development Program
US	United States
USFDA	United States Food and Drug Administration
USPTO	United States Patent and Trademark Office
USTR	United States Trade Representative
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

"We are truly at a turning point in our response to the pandemic of HIV/AIDS. The goal of putting three million people into treatment by the end of this year has prompted a reservoir of hope. But for that hope to be fulfilled, generic drugs must be available. People Living With AIDS stand poised between life and death. The Parliament of India can make it possible for millions of people to embrace life.

Excellencies, we urge that every flexibility offered by the TRIPS Agreement be incorporated in the President's Patent Ordinance and that no "TRIPS-plus" provisions are included which would jeopardize the continued supply of crucial, affordable AIDS therapies and other essential medicines by India to the world. It is not possible to exaggerate the international importance of the decisions facing India."

- Dr. Nafis Sadik and Stephen Lewis to the Indian Prime Minister and President, 11 March 2005

In 2005, the UN Special Envoys of the UN Secretary General on HIV/AIDS in the Asia Pacific and Africa collaborated for the very first time to write to the Indian government highlighting the importance of generic HIV medicines from India to the achievement of universal access to treatment goals. Along with the UN Special Envoys, the world was watching closely to see how India would balance its obligation to comply with the TRIPS Agreement deadline to amend the Indian Patents Act, 1970 with its role as the leading supplier of safe, effective and affordable generic HIV medicines.

The substance of the original Indian Patents Act, 1970 abolished product patent protection in pharmaceuticals in order to ensure that medicines were available to the public at reasonable prices and was largely based on the recommendations of a report of a commission chaired by the jurist Rajagopala Ayyangar in 1959 which stated that laws "have to be designed, with special reference to the economic conditions of the country, the state of its scientific and technological advance, its future needs and other relevant factors…so as to minimize if not eliminate the abuses to which a system of patent monopoly is capable of being put."

The resulting Indian law did not provide patent protection for pharmaceutical products and as a result, India's generic manufacturers were able to offer triple-combination anti-retrovirals (ARVs) at a fraction of the price being offered by patent-holding multinational pharmaceutical companies. The lack of patent barriers also allowed Indian generic companies to manufacture fixed dose combinations of ARVs that have become the weapon of choice in the global scale up of ARV treatment.

But to comply with TRIPS, India amended her patent laws and re-introduced product patent protection in pharmaceuticals from 1 January 2005 leading to global concerns about the continuing ability of Indian generic companies to supply these medicines. These concerns were taken seriously by the Indian Parliament, which aware of its responsibility not only to Indians but to patients across the world adopted the only pragmatic solution available — to utilize flexibilities available under TRIPS in an attempt to secure the availability, affordability and accessibility of medicines.

Five years after India changed its Patent regime this Study examines the impact of these safeguards on access to medicines analyzing the impact of TRIPS on the Indian Pharmaceutical Industry as well as the response of the legal system.

The Indian Pharmaceutical Industry after TRIPS, Sudip Chaudhuri

The Indian pharmaceutical industry occupies a special position among developing countries having demonstrated strong innovation capabilities, strength in developing cost-efficient processes and significant capacity in setting up manufacturing plants for drugs satisfying international quality norms, earning worldwide recognition as the 'pharmacy of the developing world'. This study examines how Indian generic companies are responding to the new policy environment of the TRIPS regime, the impact on their growth and the fruition of the promises of the TRIPS regime to deliver increased, more relevant R&D. The analysis of the performance of the Indian pharmaceutical industry is largely based on a sample of 166 large and medium sized Indian companies. The study explores changes in the domestic and export markets as well as in the research and development area.

In terms of the domestic market, the study finds that Indian companies continue to maintain their dominance though there is renewed interest from MNCs. Changes in the domestic *patented* market are yet to take effect fully and will be heavily influenced by the manner in which India's amended patent law is applied. The Indian companies are taking various responses including filing oppositions to ensure the robust application of India's patent law, exploring voluntary licensing, engaging in patent disputes and resisting the enforcement of greater patent rights in order to restrict the scope of the patented market.

The domestic *generic* market, which comprises the bulk drugs market and the retail formulations market on the other hand, has seen significant changes. For bulk drug manufacturers, TRIPS hardly makes a difference as they already operate in a very competitive environment and will continue to do so even after patents expire. In the post-TRIPS situation large firms that cannot initiate the manufacturing of new drugs as they did earlier will be the most adversely affected. Anticipating the shrinkage in domestic operations due to TRIPS, Indian companies have been introducing new products and promoting these aggressively resulting in the expansion of the retail formulations market. Market concentration is also rising with negative implications for pricing. The market share of the top 20 companies has increased while more than half of the small-scale pharmaceutical units operational in India have closed down in the last two years.

In terms of exports, the study finds that the export market is larger than the domestic market not only for large companies but also for smaller companies. However, only a small number of companies have been able to undergo the full transition to exports to regulated markets. For the larger companies, there is an increasing interest in developed markets like the US (which is now the largest export partner in both bulk drugs and formulations) and their role in these markets ranges from supplying generics where patents have expired to an increase in their own patenting practices and patent challenges. Exports to developing countries including LDCs is an area that will be most affected after the TRIPS regime when patents are granted in India and to utilize India's capability and capacity for enhancing the access to essential medicines in developing countries, compulsory licensing or other measures will be of vital importance.

To facilitate their international operations, Indian companies have also set up subsidiaries and acquired companies abroad. Some of these acquisitions however have caused severe financial strains for some companies. They are also facing MNCs as competitors in the generics market. Certain policy initiatives and actions at the behest of MNCs and developed countries are also jeopardizing exports such as the seizure of several consignments of Indian exports meant for Africa and Latin America at European ports on allegations of the violation of intellectual property rights at the transit point.

Relationships between the generic industry and foreign companies are also changing including tie-ups for marketing and distribution, increasing mergers and acquisitions as well as contract research and manufacturing. For instance, recent acquisitions include Ranbaxy by Daiichi Sankyo and strategic alliances have been reported between Pfizer and Aurobindo and between GSK and Dr. Reddy's. The Study finds that in the pre-TRIPS situation, because of competition in patented drugs in India, both consumers and Indian producers were able to benefit from the policy environment. After TRIPS, the new policy environment has led to collaborations between Indian companies and MNCs that are restricting competition and both of them are gaining at the cost of consumers.

The study also specifically explores the claim that strong patent protection will be beneficial for India. The TRIPS negotiations were driven by specific claims that TRIPS-compliant patent protection would prompt developing-country companies to conduct greater R&D for the development of new drugs more suited to local needs. The study finds that among a sample (see Annex I) of 166 companies only 37 were major R&D spenders (increasing steadily from 3.89 percent in 2001 to 8.35 percent in 2005/06) while the rest maintained their R&D expenditure around 1 percent. As seen above, the Indian pharmaceutical industry is highly export oriented. Significant R&D efforts are directed towards developing processes and products to get regulatory approvals for entry and growth in patent–expired generic markets in developed countries. Thus much of R&D by Indian pharmaceutical companies is not related to TRIPS. It is the result of increasing export orientation of Indian pharmaceutical companies and diversification to the regulated markets, particularly to the US.

While for the R&D spenders there has been a significant amount of investment, no NCE developed by an Indian company has yet been approved for marketing in India. For companies that invested heavily in NCE development there have been significant setbacks to the extent that eventually these companies have had to reduce their R&D expenditure and some have de-merged their NCE R&D business. The study also finds that the anticipated benefit of TRIPS that the product patent incentive will prompt local companies to put resources in developing drugs more suited to developing countries has not materialized with NCEs being developed by Indian companies aimed at global diseases that have lucrative markets.

While the Indian pharmaceutical industry has performed well since the beginning of the TRIPS regime it is also very heterogeneous. The larger and export oriented companies have done much better than the smaller and domestic market oriented companies. However there has been a sharp decline for the medium and smaller sized companies. Even for the larger companies, the figures hide some important differences.

Highlighting these differences, the study presents case studies of the strategies of key Indian generic companies including Ranbaxy, Dr. Reddy's and Cipla. Ranbaxy and Dr. Reddy's have pursued a 'high-risk-high-gain' strategy investing in NCE R&D, while Cipla, the other company in the group of "Big three", opted for a 'safer" strategy. Interestingly enough, in the post-TRIPS situation, Cipla, which is more critical about the

advantages of TRIPS, has done much better than Ranbaxy or Dr. Reddy's, with Ranbaxy having reached a point where it was sold to Daiichi Sankyo, a Japanese multinational company. The general picture that comes out from the case studies is that companies which have been able to expand in the domestic market and which have avoided high risks in foreign markets and in R&D have done well.

Analyzing the findings the study concludes that little has changed to dispute the conventional wisdom that developing countries should not grant product patent protection in pharmaceuticals. They are already paying the cost of high prices of patent protected products without having seen the supposed concomitant technological benefits. While R&D activities have diversified, efforts in the full development of NCEs are yet to succeed and are focused on lucrative developed country markets; there have been several setbacks and the partnership model has not always worked properly. What Indian companies have really demonstrated is the ability to develop generics — an ability acquired and improved during the pre-TRIPS period. Industry gains are evident in the new relationships with MNCs. But from a public health perspective these can hardly be a justification for a country such as India to grant such patent protection. The author accordingly recommends as follows:

- **Policy Implications**: The Government must continue to play an important role in the development of the pharmaceutical industry in India as it has in the past and adopt policy initiatives that ensure a larger space of operations to generic companies which will in turn drive down prices.
- **Preserving generic competition**: In the immediate context, the Government should utilize fully the flexibilities provided under TRIPS, and reject TRIPS-plus measures including those being pushed through Free Trade Agreements (FTAs). In particular the Government could introduce an easy to use compulsory licensing system. In this regard the procedure in the Indian law is overly complicated as it allows patent holders to delay the process. A significant step to improve access to essential medicines without violating TRIPS is to revive and utilize the capacities of public sector units to manufacture patented drugs and supply these through public health care facilities on a no-profit basis.
- **Addressing pricing**: Controlling the prices of patented drugs as well as the improvement of public healthcare and insurance facilities are also required.
- **TRIPS review**: Finally, the Indian experience as evidenced in the study, along with that of several other developing countries and LDCs, provides sufficient evidence for a proper review and renegotiation of TRIPS. Indeed, with fifteen years of experience with the TRIPS regime, such a review is overdue.

The Interpretation of TRIPS by the Indian Legal System

The 'Interpretation of TRIPS by the Indian legal System' was done through two separate studies. In an effort to gauge the potential reach and impact of the safeguards in India's patent law, a review of 'mailbox' applications pending before the Patent Offices was conducted. Separately, to determine how these safeguards are being applied by the Indian Patent Office, a sample of the pharmaceutical product patents that have been granted since the introduction of the product patents regime in 2005 was reviewed and analyzed.

The Implementation of India's Patent Law: A review of patents granted by the Indian Patent Office, Chan Park

India's compliance with the TRIPS Agreement in 2005 led to a global concern about the continuing ability of generic companies to supply these medicines. One of the chief concerns at the time was the growing prevalence of what are known as 'secondary' patents — i.e., patents covering various ancillary features of existing medicines. Such secondary patents, often of questionable validity, have been known to be strategically used by patent holding pharmaceutical companies to 'evergreen' their patent monopoly periods and thus unduly delay the entry of generic competition.

In response to these concerns, the Indian Parliament integrated some unique provisions including pioneering the exercise of what had been a largely overlooked TRIPS 'flexibility' — that of setting strict criteria for patentability. Particularly relevant in the pharmaceutical context are the following exclusions which represent some of the most common forms of secondary patents applied for by pharmaceutical companies:

- New uses of known substances (section 3(d));
- New forms of known substances, without significant enhancement in efficacy (section 3(d));
- "Mere admixtures" (section 3(e));
- "Any process for the medicinal…therapeutic or other treatment of human beings" (section 3(i)).

The study reviews key decisions of the Indian Courts and the Indian Patent Office and finds fairly strong positions on the interpretation and application of these safeguards. Among these are:

- The recognition that the legislative intent of Parliament in enacting section 3(d) was to protect public health and prevent evergreening;
- Thus, Patent Offices must recognize that "pharmaceutical product [patents] in India should be granted with utmost care and should be granted only to very genuine cases;"
- Specifically, in interpreting the meaning of 'efficacy' in Section 3(d), an extremely high standard applies; an 'advantageous property' is not the same as efficacy and 'new forms' that result in advantageous properties with respect to bioavailability, stability, etc., are not patentable;
- With respect to 'mere admixtures,' compositions, dosage forms, formulations, and combinations, these are not patentable unless there is a demonstrable synergistic effect between the components.
- With respect to both the 'enhanced efficacy' requirement of section 3(d) and the 'synergistic effect' requirement of section 3(e), data sufficient to establish this must be clearly set out in the specification, and not proffered at a later date during the opposition hearing.
- With respect to the 'new use' exclusion of section 3(d), it is insufficient to merely reformulate a 'new use' claim as a composition claim for such use.

To determine how these safeguards in India's patent law and the interpretation emerging from judicial and Patent Office decisions are being interpreted and implemented by the Indian Patent Office, a study examining four years of the implementation of the product patent regime in India by the Indian Patent Office

was conducted. Identifying and obtaining granted patents including their specifications was a significant challenge for the study. It relied on information available from the Patent Office which at the time the research was conducted was difficult to obtain. The author was finally able to obtain copies with specifications of 84 granted patents that were identified as likely to be secondary patents and which were reviewed for this study.

An analysis of the claims contained in the 84 granted patents to determine how these strong legal positions were being applied shows that patents relating to composition/formulation constituted by far the largest proportion (67 percent) of secondary patents that were reviewed. Additionally, a significant number (16 patents or 19 percent of the sample) of patents reviewed were formulated as composition claims but were in fact 'new use' or 'method of treatment' claims 'in disguise'. A number of patents relating to other secondary features, such as salt forms, esters, prodrugs, enantiomers, etc., were also granted (8 patents, or 10 percent of the sample). Other key findings of the Study include:

- **Application of patent law safeguards**: The review showed an apparent inconsistency in how many of the safeguards of India's patent law are being applied to specific patent applications. For example, it appears that a number of patent applications relating to a specific polymorphic form of a known compound have been granted, despite the lack of any data provided in the application with respect to enhanced efficacy.
- **Patents granted in India, but rejected by United States Patent and Trademark Office (USPTO) and/or the European Patent Office (EPO)**: More troubling are those instances where the patent application not only appeared to clearly fall under one or more of the exclusions contained in Indian patent law, but were also deemed to lack novelty or inventive step in jurisdictions that have much more liberal patentability criteria than India. Thus applications rejected in the United States (US) and the European Union (EU) have been granted in India, a matter that is puzzling particularly since the prosecution history of the equivalent US application is available online.
- **Method of treatment claims reformulated as composition claims; Swiss-style claims**: Indian patent law contains two complementary provisions that could potentially exclude a large number of 'new use' and 'method of treatment' claims from patentability — Section 3(d) and Section 3(i). Although decisions of the Patent Office have rejected such claims as merely a reformulation of a new use claim, this does not appear to be a consistent practice. There were several 'composition' claims that in fact appeared to be essentially 'new use' or 'method of treatment' claims. If a patent application covering a new use of an old substance can be patented in India simply by reformulation as a composition claim, then the safeguards in Indian law would be quite easily circumvented.

One of the most striking findings of this review was an unexpected and a rather unfortunate one: the sheer difficulty of obtaining what should be publicly available information from the Patent Offices. For potential generic competitors, such a lack of transparency introduces a large amount of legal uncertainty. The Indian Patent Office appears to be aware of the problem, and has made significant progress in providing this information online including the recent availability of granted patents with their specifications. However, the difficulties in obtaining what is legally required to be publicly available information since 2005 has hindered the ability of civil society groups, generic competitors and other interested parties to participate to the fullest extent in preventing questionable patents from being granted.

The author concludes that the Indian patent law contains robust safeguards that, if strictly interpreted and applied, have the potential to eliminate a significant amount of patent barriers to affordable generic production. As the review of some of the more recent case law and other precedents from the Indian courts and Patent Offices indicate, many of these provisions are in fact being interpreted and applied in a robust manner. However, it does not appear to be the case that such provisions, absent an opposition from a civil society group or generic competitor, are being applied in a consistent manner. Regardless, based on the initial analysis, the author identifies a few policy reform options that the Indian Government might consider undertaking immediately including:

- **Expedite the process of making patent information online** and fully searchable, including published applications, granted patents, complete specifications, examination reports, patent office decisions, details of oppositions filed, and correspondence between the applicant and the Patent Office;
- **Facilitate access to information at each of the Patent Offices**; decentralize information so that information about patent applications filed/granted in any of the Patent Offices are available at all of them;
- **Clarify through patent examination guidelines or through legislative change the robust exclusions** of new use claims, method of treatment claims, 'Swiss-style' claims, in order to ensure that applicants may not simply 'draft around' any such exclusions;
- **Strengthen the interpretation of section 3(e)** to clarify that composition, formulation and dosage form claims require a strong showing of synergy; clarify that this is independent of satisfying inventive step, and that as "a general rule, formulation techniques and the range of compounds that may be used for developing pharmaceutically viable products in different forms are well known to a person skilled in the art" (Correa, 2007);
- **Clarify**, through patent examination guidelines or through legislative change, that various common 'advantageous properties' arising from converting a known drug into a new form are not patentable under section 3(d), including (but not limited to): improvements in a drug's bioavailability, potency, stability, hygroscopicity, flow properties, ease of manufacture, etc.

The Landscape of Pharmaceutical Patent Applications in India and Implications for Access to Medicines, K.M. Gopakumar

The second part of the study of India's public health safeguards is based on India's use of the entire transition period allowed under TRIPS for developing countries, which offers an opportunity to examine the nature and trends in patent applications that were filed in the mailbox and to determine the potential of key safeguards contained in India's patent law to create a viable space for continued generic production of medicines.

This study explores the potential of three key safeguards in India's patent law as follows: (i) medicines invented prior to 1995 are considered to be in the public domain; (ii) restriction on the scope of patentability in relation to known substances; and (iii) patented medicines already being produced and marketed before 1 January 2005 may continue to be manufactured by the generic company on the payment of a reasonable royalty.

To this end, three databases were created: (1) mailbox applications filed in India between 1995 and 2004 to indicate who the major players and countries are and the trends in patent applications filed during this period; (2) marketing approvals and patent history of New Molecular Entities (NMEs) approved by the United States Food and Drug Administration (USFDA) in the same time period to allow through a process of elimination to determine which applications resulted in approved products and are therefore of importance and which one were invented prior to 1995; and (3) marketing approvals of NMEs given by India's drug regulator between 1995 and 2004 to determine which medicines, even if patented, could continue to be produced by generic companies on a payment of royalty.

The database of mailbox applications shows that 14 countries together accounted for almost 90 percent of the applications of which all except India are developed countries. It also showed the level of concentration of applications within a few multinational companies with 12 leading multinational companies accounting for 32 percent of the applications. A title search of the 'mailbox' applications which has several limitations and is not a scientifically accurate representation of the exact claims of the patent applications nevertheless provides an indication of the number of mailbox applications claiming patents on known substances and a greater concentration of applications in certain disease areas such as cancer, HIV/AIDS, diabetes and cardiovascular diseases.

With the limitations of title searches and the lack of publicly available and fully searchable specifications of the mailbox applications, the study analysed information from the USFDA *Orange Book* that details all medicines that have received marketing approval from the USFDA, classifies which are NMEs and provides the patent history of approved medicines. The analysis showed that of the 301 NMEs approved for marketing between 1995 and 2004, only ten were invented after 1995. However, as noted above, there are nearly 10,000 applications in India's mailbox. It is evident after comparing these different sets of data that applications related to the other 291 NMEs relate to patents on known substances. Assuming that the Indian Patent Office is successful in the strict application of the patentability criteria under India's patent law, the primary concerns in terms of access to treatment relate to seven NMEs. The ten post-1995 NMEs are for the treatment of cancer, HIV/AIDS, osteoarthritis, epilepsy, hyperactivity disorder, erectile dysfunction and for the imaging of appendicitis.

The marketing approvals of NMEs given by India's drug regulator between 1995 and 2004 to determine which medicines even if patented could continue to be produced by generic companies on a payment of royalty. The marketing approval data from India's Central Drug Standard Control Organization (CDSCO) shows that it gave marketing approval for 128 generic versions of the 301 NMEs approved by the USFDA during the same time period allowing generic companies manufacturing these NMEs to continue doing so on the payment of a reasonable royalty. Of the post-1995 NMEs, 3 have received marketing approval in India prior to 2005.

Based on the three databases, case studies for medicines for diabetes, hypertension, cardiovascular diseases, cancer and HIV/AIDS were conducted. The case studies showed that if the safeguards in India's laws were applied properly, there would be few medicines where generic competition would be prevented. For instance, in the case of medicines for diabetes, of the 13 NMEs approved for marketing by the USFDA between 1995 and 2004, 12 were invented prior to 1995 and therefore patent applications on them should attract the scrutiny of section 3 of India's patent law while 9 were approved for marketing in India prior to 2005 and can continue being supplied even if patented on the payment of royalty.

The information from the databases created as part of this study indicates that the application of strict patentability criteria by the Indian Patent Office can be expected to significantly reduce the number of patents granted in India on the mailbox applications. As is evident from the USFDA *Orange Book* listings, NMEs approved between 1995 and 2004 are predominantly pre-1995 medicines and therefore in the public domain. The only way that patent applicants can claim patents on these are to file for patents on known substances, which would automatically attract the provisions of section 3(d). Even where some of these patents are granted, the case study of the five major diseases areas indicates that several generic versions of these NMEs were already on the Indian market prior to 2005. However, the effectiveness of these flexibilities is only as extensive as their application by the Indian Patent Office. In light of the findings of the study, the author recommends:

- **Absolute exclusion of patents on substances in the public domain prior to 1995**: The Indian Patents Act should have ideally excluded patents on substances known prior to 1995 instead of the window provided by section 3(d) which allows patent applicants to get patents on known substances if they demonstrate increased therapeutic efficacy. This has resulted in an increased burden on patent offices as well as providing greater room for patents on known substances to be granted.
- **Improvement in infrastructure and human resources in the Patent Office**: There has been a fourfold increase in the patent applications in India between 1995/96 and 2007/08 and a 17-fold increase in the granting of patents in the same period. Countries with limited infrastructure need to apply more stringent safeguards to prevent the patenting of known substances. Support and funding for patent oppositions should be provided to assist Patent Offices in their scrutiny of patent applications.
- **Mandatory declaration of international non-proprietary name (INNs) in patent applications**: The name of an NME, often the INN, provides a face to an otherwise abstract patent application. A declaration of the INN would lessen the burden of Patent Offices in examination and help other stakeholders identify those applications that are of the greatest concern.
- **Creation of a regularly updated database of NMEs by the Indian Patent Office**: This would enable to examine these applications more accurately and help Patent Offices in identifying patent applications on known substances. Governments should also analyze these NMEs to determine the public health importance of the patent applications, the cost of production, the technological dimension, the patent status (current and potential), potential candidates for compulsory licenses and other patent flexibilities.
- **Establishment of an Institutional Mechanism for the review of granted patents**, their impact on access to medicines with an operational mandate to recommend the use of TRIPS flexibilities.

The future of Access to Affordable Medicines and India's Role Post-TRIPS

In December 2009, UNDP organized a technical consultation to discuss India's role in the domain of sustainable supply and access to affordable medicines. The consultation reviewed the studies in this publication. Comments and recommendations of participants were considered by the authors in the finalization of the studies. The deliberations also provided policy recommendations from a national and international perspective to sustain global access to affordable medicines. The frontiers of South–South collaborations in this area, especially using existing networks such as the India-Brazil-South Africa (IBSA) framework, were also explored.

The discussion was underscored by the emerging crisis in HIV treatment with a scale-down of funding for treatment on the horizon. The decreasing avenues for generic production only threatened to deepen the crisis. Discussions at the consultations focused on some key issues including the full use of safeguards by India, the demand for data exclusivity and its negative impact on access to medicines, India's FTA negotiations, the seizures of Indian generic medicines in transit and the increasing confusion between the enforcement of intellectual property and fake medicines in the 'counterfeit' debate.

Discussions at the meeting also highlighted the potential of South-South collaboration in R&D, protection of traditional knowledge, transfer of technology, the promotion of access to medicines and the implications of greater intellectual property protection. Participants felt that there was a window of opportunity for cooperation to address the various challenges posed by the TRIPS regime. The IBSA framework could act as an important entry point in these areas as well as for collaboration in building capacity in a cost effective manner to counter the impact of shrinking generic competition for access to medicines. Other suggestions included the use of the IBSA forum by governments to refine their negotiating positions on several issues and to initiate policy dialogue with civil society. The challenges of taking such initiatives forward were also the subject of much discussion. This included the increasingly entrenched interests in international forums and the changing scenario with the economic and financial crisis. In undertaking such initiatives, South–South cooperation may not be enough and greater international support, tax incentives and international funding would be required, for instance, to focus on neglected diseases.

Some of the issues that were brought up at the technical consultation were discussed at the *Academic Forum of the 4th India-Brazil-South Africa (IBSA) Dialogue Process*, 2010. This consultation presented to the heads of the three states several recommendations including cooperation between patent offices in the IBSA countries; consultation between IBSA countries on FTAs; sharing information on cost effectiveness analysis undertaken by the three countries and collaboration in R&D especially on priority and neglected diseases.

CHAPTER 1: THE INDUSTRY RESPONSE
THE INDIAN PHARMACEUTICAL INDUSTRY AFTER TRIPS

Sudip Chaudhuri ◊

I. Introduction

The Indian pharmaceutical industry occupies a special position among developing countries. It has demonstrated strong innovation capabilities, tremendous strength in developing cost-efficient processes and significant capacity in setting up manufacturing plants for drugs satisfying international quality norms. As a result India has received worldwide recognition as a low-cost producer of high-quality drugs. Médecins Sans Frontières (MSF, 2007) describes India as the 'pharmacy of the developing world'. In the case of HIV medicines, while several factors have contributed to enhanced access to treatment around the world, the increased availability of generic anti-retrovirals (ARVs) manufactured by Indian companies and their consequent price reductions has been one of the most important.[1]

Taking advantage of the freedom countries had before the creation of the WTO, India abolished product patent protection in pharmaceuticals in 1972. This operated as a pull mechanism by providing Indian companies the space and opportunity to develop and innovate. Aided by the push mechanism of public investments in manufacturing and in R&D, Indian pharmaceutical companies made enormous progress (Chaudhuri 2005, chapter 2).

But to comply with the TRIPS Agreement, India amended her patent laws and re-introduced product patent protection in pharmaceuticals from 1 January 2005. Earlier from 1 January 1995, a 'mailbox' facility was put in place to receive and hold product patent applications.[2] Under TRIPS, these applications are being processed since 1 January 2005 for grant of patents. For those drugs on which patents are granted, Indian generic

◊ The author thanks Kamal Malhotra and Cecilia Oh for discussions at the initial stages of this study and Luciana Mermet, Tenu Avafia and others at UNDP for comments on earlier drafts. The author is particularly grateful to Savita Mullapudi Narasimhan and Kajal Bhardwaj for various suggestions and comments. The latter also provided inputs to fill up some gaps in the earlier draft. The author also benefited tremendously from interviews, particularly, with Ashok Kumar, Secretary, Department of Pharmaceuticals, Government of India, Rajiv Kher, Joint Secretary, Department of Commerce and Industry, Government of India, Hasit Joshipura, Managing Director, GlaxoSmithKline, India, Mumbai, N. H. Israni, Chairman, Bluecross Laboratories, Mumbai (formerly President of Indian Drug Manufacturers Association), Srinivas Lanka, formerly Whole-time Director of Aurobindo Pharma, Hyderabad, Himanshoo Nayak, General Manager, Business Development, Elder Pharmaceuticals, Mumbai, Achin Gupta, Vice President, Corporate Strategy, Glenmark Pharmaceuticals, Mumbai and V. V. Krishna Reddy, Executive Director, Sri Krishna Pharmaceuticals, Hyderabad.

1 See Avafia and Narasimhan (2006) for a discussion of these factors.

2 As a developing country, although India had to provide patent protection for pharmaceutical products introduced from 1 January 1995, it did not have to provide such protection till 2005. Thus, under Articles 65.2 and 64.4 of TRIPS, India had time till 1 January 2005 to introduce product patent protection in pharmaceuticals. But Articles 70.8 and 70.9 put a limitation on the transition period allowed under Article 65 — India was required to introduce provisions on the "mail box" and for "exclusive marketing rights" from 1 January 1995.

companies would not be able to manufacture them unless a voluntary or compulsory license is granted. These changes to India's patent law have led to concerns being expressed in different circles regarding India's continued ability to supply affordable drugs. It has also been argued, however, that strong patent protection will be beneficial for India. The TRIPS negotiations were driven by specific claims that TRIPS-compliant patent protection would prompt developing-country companies to conduct greater R&D for the development of new drugs more suited to local needs.

In the post-TRIPS situation, Indian generic companies have the following basic options:

- For non-patented or patent-expired drugs:
  - To continue to cater to domestic and export markets
- For patented drugs:
  - Undertake R&D for development of new drugs
  - Collaborate with innovator companies for manufacturing, marketing and R&D
  - Manufacture patented drugs through compulsory or voluntary licensing

How are Indian generic companies responding to this new policy environment? What has been the impact on their growth? Are Indian generic companies mature enough to take advantage of stronger patent protection? Does India's experience suggest a re-thinking about the relationship between patents, R&D and innovation in developing countries? What policy interventions are needed to sustain the growth of the industry so that generic competition can continue to ensure that the human development objective of access to affordable medicines is satisfied?

This chapter examines these questions and discusses the nature of the different markets that Indian companies operate in, the changes taking place in these markets, how activities of Indian pharmaceutical companies have changed and the implications for access to medicines. The methodology followed for this study is discussed in Annex I. Section II focuses on domestic operations and Section III on export-related activities. Section IV examines the R&D activities of Indian companies while Section V looks at the financial performance of Indian pharmaceutical companies. This chapter also includes case studies highlighting the different approaches taken by key Indian companies in response to the new policy environment and their varying outcomes. Finally, Section VI discusses findings and their policy implications.

II. Domestic Market

The pharmaceutical market is usually segmented into two types of markets dealing with patented drugs and generic products respectively. Before TRIPS, in the absence of product patent protection in India, the entire market was generic. After TRIPS, not only is the patented product market developing, the generic market is also undergoing a significant transformation in response to TRIPS and other factors. This section discusses these changes and focuses on the responses of Indian companies to the changing situation.

Features of India's domestic market

Before discussing the changes in India's domestic market, it would be useful to understand some basic features of this market including the focus of manufacturing activities and the traditional and new players in the arena. Manufacturing activities of the Indian pharmaceutical industry can be classified into (i) the production of active pharmaceutical ingredients (APIs) present in the drugs (also known as bulk drugs) and (ii) the production of formulations, i.e., processing of APIs into finished dosage forms such as tablets, capsules, ointments, etc. While a major segment of the APIs manufactured in India is exported, the major segment of formulations manufactured is sold domestically.[3] The domestic formulations market can be further classified into: (a) retail and (b) institutional. In India, the institutional drug market is quite limited accounting for only 15 percent of total formulations sales (IBEF, 2008, p. 4).

Dominance of Indian Companies

The retail formulations market in India is dominated by Indian companies. For 2007/08[4], of the 468 companies considered by ORG-IMS[5], only 46 are controlled by foreign companies accounting for 20 percent of the market. This is a distinctive feature of the situation in India. In fact, India and Japan are the only two countries where pharmaceutical companies of the US and Europe do not dominate. Some of the large formulators in India include these companies (for example, GlaxoSmithKline (GSK), ranked 3rd (among ORG-IMS companies) with 4.71 percent market share in 2007/08, Pfizer, 9th with 2.46 percent, Abbott, 11th with 2.29 percent, Sanofi-Aventis, 13th with 2.25 percent and Novartis, 22nd with 1.66 percent) but most have a very small market presence (including, Eli Lilly, ranked 60th with 0.3 percent market share, Bayer, 78th with 0.2 percent, Johnson & Johnson, 98th with 0.13 percent) and only two feature among the top 10 companies—GSK (3rd) and Pfizer (9th).

Of the 20 largest companies, 16 are Indian controlled (including Cipla, Ranbaxy, Dr. Reddy's, Lupin, Sun Pharmaceuticals, Piramal Healthcare and Cadila Healthcare) and only four are MNCs.[6] In contrast to the situation in the early 1970s, 39 of the top 50 companies today are Indian companies. The market share of MNCs has declined over the years, even after the introduction of product patent protection in January 2005 — from 23 percent in December 2004, to 22 percent in March 2006 and 20 percent in March 2008. As we will see below, the Indian pharmaceutical industry has become highly export intensive and for many of the larger companies the export market is larger than the domestic market. But the domestic market has also expanded at a very rapid rate. As Table 1 shows, domestic formulation sales have increased at an annual compound rate of growth of 17 percent since 1995/96 for a group of 15 large formulators. Some have improved their market share (for example, Cipla saw an increase in its market share from 4.18 percent in 1995/96 to 5.24 percent in 2007/08) while others like Cadila Healthcare, Sun Pharmaceuticals, Dr. Reddy's and Glenmark have experienced an annual growth of over 20 percent.

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3 Only about 10 to 20 percent of the APIs manufactured are domestically used, but two-third of the formulations manufactured are domestically consumed ("Pharmaceuticals: Cover Story — Manufacturing Opportunities for Indian pharmaceutical players", pp. 1-2 (*www.crisilresearch.com*)).

4 In India, the financial year starts on 1 April and ends on 31 March. Accordingly these figures are for the financial year April 2007 to March 2008.

5 Proper statistics are not available for most of the pharmaceutical units in India. Our discussion on the market structure of the retail market is based on the market surveys of ORG-IMS which is a standard source of information (see Annex I).

6 The term MNC is used in this study to denote foreign pharmaceutical companies. For an explanation of which companies are classified as MNCs/foreign companies for the purposes of this study, please refer to Annex I.

Table 1: Growth of Retail Formulations sales of top Indian companies

Company	Retail sales, 1995/96 (INR million)	Market share, 1995/96 (percent)	Retail sales, 2007/08 (INR million)	Market share, 2007/08 (percent)	CARG, 1995/96 to 2007/08 (percent)
Cipla Ltd.	2863	4.18	16831	5.24	15.91
Ranbaxy Laboratories Ltd.	2686	3.92	15995	4.98	16.03
Alembic Ltd.	1664	2.43	6075	1.89	11.40
Torrent Pharmaceuticals Ltd.	1540	2.25	6584	2.05	12.87
Lupin Ltd.	1536	2.24	8513	2.65	15.34
Piramal Healthcare Ltd.	1363	1.99	11592	3.61	19.53
Cadila Healthcare Ltd.	1323	1.93	11902	3.71	20.09
Wockhardt Ltd.	998	1.46	6361	1.98	16.69
Unichem Laboratories Ltd.	931	1.36	5002	1.56	15.04
Ipca Laboratories Ltd.	796	1.16	4015	1.25	14.44
Sun Pharmaceutical Inds. Ltd.	722	1.05	10684	3.33	25.17
U S V Ltd.	599	0.87	4579	1.43	18.47
Dr. Reddy's Laboratories Ltd.	557	0.81	7490	2.33	24.18
J B Chemicals & Pharmaceuticals Ltd.	495	0.72	2058	0.64	12.61
Glenmark Pharmaceuticals Ltd.	460	0.57	4369	1.36	20.63
Elder Pharmaceuticals Ltd.	417	0.61	2912	0.91	17.58
TOTAL (15 companies)	18950	27.55	124962	38.93	17.02

Source: ORG-MARG, *Retail Store Audit*; ORG-IMS, *Stockist Secondary Audit*.

Expansion of MNCs

But the situation has been changing. There has been a renewal of interest in the Indian domestic market on the part of MNCs with some entering India directly by establishing subsidiaries (for example, Bristol Myers Squibb and Eisai) or indirectly through licensing arrangements with Indian companies for the marketing of their products (for example Schering AG and Boehringer Ingelheim) (Ernst & Young, n.d., pp. 5, 8). MNCs have also started buying up Indian companies — the most notable being the acquisition of India's largest pharmaceutical company, Ranbaxy by the Japanese MNC, Daiichi Sankyo in June 2008. Other acquisitions of Indian companies include Dabur by Fresenius, Matrix by Mylan and Shanta Biotechnics by Sanofi-Aventis.

MNCs have started introducing patented drugs to the Indian market which Indian companies can no longer manufacture; 17 of these were introduced in the first four years (2005-2008) of the new patent regime (Ernst & Young as quoted in IBEF, 2008, p. 8). More such drugs are expected to be marketed though New Chemical Entities (NCEs) patented after 1995 will not immediately be put in the market. Industry sources[7] suggest that

7 See, for example the interview of Yusuf K. Hamied, Chairman and Managing Director of Cipla, India by Knowledge@ Wharton, 7 May 2009 (accessed from *http://knowledge.wharton.upenn.edu/india*).

considering the time lag between the time when an NCE is patented and when it is finally marketed, they will really hit the market around 2012-2015. In the product patent regime, the prices of such patented drugs will depend on:

- What prices MNCs holding the patents would charge;
- What steps are taken to regulate such prices (including through price control or price negotiation); or
- What steps are taken to provide competition from generic producers through voluntary or compulsory licensing, which may have an impact on the prices of patented products as well.

If MNCs charge affordable prices for patented drugs in developing countries, access may not be adversely affected. Or if they give voluntary licenses to generic companies to manufacture the patented drugs, the consequent competition could make drugs more affordable. An examination of experiences with the access strategies employed by MNCs in India and other developing countries indicates the extent to which such voluntary mechanisms are likely to be successful from a public interest point of view.

Several MNCs have special programmes to improve access in developing countries (Chaudhuri 2007b, Table 1).The 'Abbott Access to HIV Care' programme aims to provide the ARV combination *lopinavir+ritonavir* (marketed by Abbott as Kaletra) to African countries and other LDCs at 'no profit' while the 'Gilead Access Program' provides for the supply of *tenofovir disoproxil fumarate* or TDF (marketed by Gilead as Viread) at 'no profit' to several developing countries. On the face of it, these programmes appear impressive. However, a deeper analysis of their implementation and impact raises serious doubts as to their ability to address the problem of access to medicines. It is difficult to cite cases where such programmes have been introduced when the patents that relate to the medicines are not under dispute or there is no threat of generic competition or of compulsory licensing.

Thus, Brazil has negotiated price discounts for key ARVs such as *nelfinavir*, *efavirenz*, *lopinavir/ritonavir* and TDF after making announcements of compulsory licensing (Love 2007). For *lopinavir/ritonavir*, Abbott's price reductions for non-LDC countries came only when generic competition from India was imminent. Moreover, these discount prices are often not available in reality as the companies have not registered or started marketing the drugs in countries eligible for the discounts. Nor are the price discounts available to all developing countries — restrictions are imposed to exclude relatively richer developing countries.[8]

If GSK's policy is any guide, MNCs may not even be keen on any significant differential pricing in pharmaceutical products. GSK, for example, has introduced the anti-breast cancer drug *lapatinib ditosylate* (marketed by GSK as Tykerb) in May 2008 in India. It will soon introduce another new drug *ethromopag olamine* (marketed by GSK as Promacta). It has also started selling vaccines for rotavirus and cervical cancer. GSK's policy seems to be to introduce new drugs whenever they are ready. These will be at some discounts compared to their prices in developed countries but will still be very high compared to prices which would have resulted from generic competition. GSK is charging a price of about USD 20,000 or approximately INR 903,299.80[9] per person per year for *lapatinib ditosylate* even after a 25 percent discount.[10]

8 See Chaudhuri, 2007b for examples and data sources.

9 EDITOR's Note: The Indian Place Value system differs from the US place value system. For example, INR 100,000 is termed as INR 1 Lakh (5 zeros) and INR 10 million is termed INR 1 Crore (7 zeros).

10 Interview with Hasit Joshipura, Managing Director, GlaxoSmithKline, India, 12 May 2008.

In the case of voluntary licenses given by some MNCs to generic companies, these have mainly been given for products which have very little patent life left and have rarely been given voluntarily (Amin and Radhakrishnan, 2007). Usually they follow some public or legal action and sometimes they have been used as a strategy to thwart oppositions by generic companies. (See the discussion in the next section on Gilead's voluntary licenses for TDF).

For patented medicines, the replication of the impact that Cipla's offer of supplying the triple combination of ARVs (*stavudine+lamivudine+nevirapine*) at USD 350 per person per year in 2000 had in triggering generic competition and a drastic fall in prices will now only be possible through a compulsory or fair voluntary licence. Without which Cipla (or any of the other generic companies) will not be able to manufacture patent protected ARVs such as *raltegravir* (Merck), *etravirine* (Tibotec) or *entecavir* (BMS) though it is willing to do so, on payment of a royalty of 4 percent of the sales.[11]

Thus the negative impact of product patent protection is already being felt and it is very important to put in place mechanisms to control the prices of new patented drugs. If the patentees continue to charge high prices then the public policy focus should be to ensure the entry of generics as early as possible; if necessary through the grant of compulsory licenses.

The entry of MNCs and their increasing sway can also influence public policy decisions taken by the Indian government. An important issue which may delay the entry of generics in this context is data exclusivity. If the demand of MNCs to grant data exclusivity is accepted, then they will have the right to exclude others, including drug regulatory authorities from using the clinical and pre-clinical data which they submit while seeking approval to market a drug. The safety and efficacy of a new drug is decided on the basis of such data submitted by the original applicant. The current practice is that generic companies are not required to again conduct studies to establish the safety and efficacy of their products. They can rely on the data already available to establish that their products are bio-equivalent to products already found to be safe and effective. If the demand for data exclusivity is accepted, then even when MNCs have not applied for patents, patents have been denied or compulsory licenses have been granted, generics companies will either have to do their own clinical studies or wait till the period of exclusivity ends. Since such studies are too costly for generic companies, effectively that will mean the delayed entry of generics (WHO, 2006). The Indian government is currently considering whether or not to adopt data exclusivity rules (Sampath, 2008, p. 39). The demand for data exclusivity has also arisen in the context of FTAs being negotiated by India. It has been widely argued and accepted that TRIPS does not require member countries to adopt data exclusivity and India should exercise this freedom.[12]

Changes in the Domestic Patented market

Changes in the domestic patented market will be heavily influenced by the manner in which India's amended patent law is applied and the resulting scope of the generic market for Indian companies to continue manufacturing and supplying to. A vigorous application of the public health safeguards in India's patent law will restrict the patented market and preserve a significant space for generic competition. One key area of concern for the domestic pharmaceutical industry will be the extent to which secondary patents are granted

11 P. T. Jyoti Dutta, 'Concern over access to next-gen AIDS drugs,' *Hindu Business Line*, 6 February 2009.

12 See Chaudhuri, 2005, pp. 80-83 for a review of these issues.

in India. Indian companies are evolving various responses including filing oppositions to ensure the robust application of India's patent law, exploring voluntary licensing, engaging in patent disputes and resisting the enforcement of greater patent rights to restrict the scope of the patented market.

Under Article 70(3) of TRIPS, a WTO member country has no obligation to provide patent protection for any subject matter which has fallen into the 'public domain' before the WTO came into being, i.e., before 1 January 1995. Thus any drug patented abroad before 1995 can continue to be manufactured and sold in India after 1995 even though these may be under patent protection in other countries. Drugs patented after 1 January 1995 can be classified into the following categories:

1. Those involving NCEs patented after 1995; and
2. Those involving NCEs developed before or after 1995 but with patents for:
    a. new uses
    b. new formulations and compositions
    c. new combinations
    d. new chemical derivatives (salts, esters, etc.)

According to Article 27(1) of TRIPS, patents are required to be provided for inventions, which are "new, involve an inventive step and are capable of industrial application." The agreement however does not define these terms. This provides some flexibility which India has taken advantage of by enacting section 3(d) in its amended patent law and restricting product patents to some extent. Under this provision, India does not grant patents for new uses. Nor will patents be granted for new formulations/combinations/chemical derivatives of NCEs "unless they differ significantly in properties with regard to efficacy."

India's law also includes or makes use of various other TRIPS flexibilities (see Box 1).

Oppositions and Patent Disputes

After 1 January 2005, when the Indian Patent Office started examining the 'mailbox' applications and these were made public, it was discovered that a large number of product patent applications are actually secondary patent applications. Several generic companies including Ranbaxy, Cipla, Natco and Hetero are now involved in formal opposition proceedings in the Patent Office. Where patent applications have been filed on key medicines, a number of health groups and civil society organizations (including networks of people living with HIV and groups working on cancer) have also filed oppositions.[13] While some patent applications have been rejected (like Boehringer Ingelheim's patent application for *nevirapine hemihydrate*), others have been withdrawn (like GSK's withdrawal of its patent application for *zidovudine/lamivudine*, where both the NCEs involved in the product were pre-1995 NCEs but GSK claimed that it used a novel binding agent to combine the NCEs).[14]

13 See *Details of Pre-grant Oppositions filed during 1st January, 2005 and 31st March, 2009 — Statement referred to in reply to Lok Sabha Unstarred Question No. 2784 for answer on 7.12.2009*, Answer, Minister of State in the Ministry of Commerce and Industry (Shri Jyotiraditya M. Scindia), Lok Sabha, 2009 (*http://164.100.47.132/LssNew/psearch/QResult15.aspx?qref=79951*).

14 See Julie George (with R. Sheshadri and A. Grover), "Intellectual Property and Access to Medicines: Developments and Civil Society Initiatives in India", in Intellectual Property Rights and Access to Medicines, Brazilian Interdisciplinary AIDS Association, Rio de Janeiro, 2009 (*www.abiaids.org.br*).

BOX 1: TRIPS Flexibilities Incorporated in India's Patent Law

Exemptions from grant of patents in certain cases: Under Article 27(1) of TRIPS, patents will have to be provided for inventions which are "new, involve an inventive step and are capable of industrial application". The agreement however does not define these terms. This provides a flexibility which India has used to some extent. The Patents Amendment Act of 2005 has provided the important qualification that salts, esters, polymorphs, particle size, combinations and other derivatives of known substances cannot be patented "unless they differ significantly in properties with regards to efficacy" (explanation to section 3(d)). In other words secondary patents are not permitted unless these are therapeutically significant.

Compulsory licensing and government use: Article 31 of TRIPS, the Doha Declaration and the 30 August 2003 WTO decision allow for the issue of compulsory licenses in various circumstances. India's patent law contains detailed provisions regarding compulsory licenses including those that generic companies can apply for, government use licenses, those issued in cases of national emergency, extreme urgency and public non-commercial use and compulsory licenses for exports.

Exceptions to exclusive rights in certain cases: Article 30 of TRIPS permits member countries to "provide limited exceptions to exclusive rights conferred by a patent..." The following three are the most significant and common exceptions:

- **Early working:** Also known as the Bolar exception — under section 107A(a) of India's Patents Act, 1970 use of a patent for development and submission of information for regulatory approval will not be considered an infringement of the patent. Thus generic companies need not wait till the actual expiry of the patents to develop generic products and hence can introduce generics immediately after the expiry of patents.
- **Parallel imports:** Under section 107A(b), "importation of patented products by any person from a person who is duly authorized by the patentee to sell or distribute the product shall not be considered as an infringement of patent rights." Thus, if need be, India can shop around the world and import patented drugs from the cheapest source.
- **Research and experimental use:** Under section 47, patented products/processes may be made or used by any person for the "purpose merely of experiment or research including the imparting of instructions to pupils".

Opposition and revocation proceedings: Section 25 provides for pre-grant and post-grant opposition proceedings before the Indian Patent Office. Section 64 also allows for revocation petitions to be filed at any time; revocation may also be applied for as a counter-claim during the course of an infringement suit.

Limits on data protection: India's Drugs and Cosmetics Act, 1940, which regulates the marketing approval of new drugs, as well as the amended Patents Act, 1970 do not contain any provisions relating to data exclusivity. Thus test and clinical data relating to safety and efficacy of drugs submitted by the patent holder can be used by generic companies and the drug regulator for introducing and approving generic products.

No links between patent status and marketing approvals: This is not required under TRIPS and India has kept the two issues separate — drug approval procedure does not require consideration of patent status.

In other cases, MNCs are fiercely fighting patent battles. Decisions of the Patent Office and judgments of the courts have not favoured MNCs in four high profile cases involving Roche's anticancer drug, *erlotinib* (marketed by Roche as Tarceva) and the drug used for HIV/AIDS infections, *valganciclovir* (marketed by Roche as Valcyte), Novartis' anti-cancer drug *imatinib mesylate* (marketed by Novartis as Gleevec) and Gilead's anti-HIV/AIDS drug *tenofovir disoproxil fumarate* (marketed by Gilead as Viread). Some of these decisions are discussed in greater detail in Chapter 2A. While these are positive developments, the situation is far from clear. The MNCs have filed various appeals. Once section 3(d) was introduced in India's patent law, law-abiding applicants should have withdrawn all the patent applications which are not valid under this provision. Not only is this not being done, MNCs are involved in extended patent litigation with Novartis challenging the validity of section 3(d) and after a negative ruling now approaching the Supreme Court to challenge the interpretation of the provision (for further details, see chapter 2A).

Voluntary licenses

As noted above, the extent to which generic competition can bring down the prices of patented drugs could depend on voluntary licenses given by patent holders. Such licenses are however, seldom given without some form of pressure. For instance, Gilead entered into non-exclusive voluntary license agreements with several Indian generic companies in September 2006, to produce and sell TDF in the 97 countries covered under its Access Programme. Gilead had previously been approached by Indian companies after it had received its approval for marketing TDF from the USFDA in 2001, yet the voluntary licenses came only when oppositions were filed against Gilead's patent applications for TDF in India. Gilead's move can be seen as a strategy to ward off such oppositions. The Indian generic companies that took the voluntary licenses adopted a 'low-return low-risk' strategy. Their calculations individually seem to have been that if Gilead got the patent and others accepted the license and they did not, they would be left out of the market.

However, the terms and conditions of these licenses are also important. Cipla decided to take the risk of not taking Gilead's licenses. It found the agreement too restrictive and objected to the condition that all technological advances relating to the product and the APIs involved would have to be passed on to Gilead on a royalty free basis. Cipla was also not willing to pay the royalty of 5 percent unless Gilead was actually granted the patent for TDF in India.[15] *Tenofovir* was developed and patented in 1986 by a Czech academic institution, the Institute of Organic Chemistry and Biochemistry. In 1991, Gilead signed a license agreement with the Czech institute and developed and patented TDF, a salt of *tenofovir* in 1996. It got marketing approval in the US in 2001. Thus Gilead's application is for a new form of an existing compound and hence under section 3(d) of India's Patents Act, 1970 not eligible to get a patent unless it is established that it is a significant improvement in terms of efficacy. The Indian Patent Office rejected Gilead's patent application for TDF on 30 July 2009.[16]

Resisting greater patent rights

The domestic patented market will be influenced not only by the patent law but also to the extent that MNCs can enforce greater patent rights than those required under TRIPS. One area of concern is the attempts by

15 This account on Gilead is based on Chaudhuri, 2007b.

16 See the note of Lawyers Collective, Mumbai circulated in Ip-Health, 1 September 2009 and the news item, "India says No to HIV Patents" in *www.nature.com*, 3 September 2009 for the decision of the Patent Office.

MNCs to link the patent status of a drug with its marketing approval. For instance, in the case of the anti-cancer drug, *erlotinib*, for which Roche has obtained a patent in India, Cipla sought to manufacture and market a generic version after getting marketing approval from the Drug Controller General of India (DCGI). The latter could do so because in India, drug regulatory authorities are not required to consider the patent status for granting marketing approvals. MNCs are trying to frustrate such efforts in various ways. Roche has sued Cipla;[17] Cipla in turn has counter claimed that the patent granted is invalid and should be revoked. While the final judgment on the validity of the patent is awaited, the courts have refused Roche's plea for a preliminary injunction against Cipla marketing its generic version of the medicine during the pendency of the case on various grounds including public interest.

The reaction of another MNC, Bayer, has significant long term implications. It has sued the Indian Government and the DCGI to enforce patent linkages. Bayer approached the Delhi High Court to stop the DCGI from granting marketing approval to Cipla for the anti-cancer drug *sorafenib tosylate* (marketed by Bayer as Nexavar). Bayer wants drug regulatory authorities to consider the patent status before granting marketing approval to any generic company. Linking patent status to marketing approvals is not required under TRIPS. Thus India has been entirely justified in keeping the two issues separate. In their eagerness to enjoy and enforce greater patent rights, the MNCs are not hesitant to challenge such TRIPS flexibilities. Bayer's case was rejected by the Delhi High Court and it has now approached the Indian Supreme Court in this matter.[18]

Compulsory licensing

With patent disputes on critical provisions of India's patent law continuing, generic companies, civil society organizations or the government are yet to consider applying for or asking for compulsory licenses.

Currently three texts — the TRIPS Agreement, the Doha Declaration and the WTO Decision on Paragraph 6 — collectively provide the legal framework concerning the grant of compulsory licenses (Oh, 2006).

TRIPS does not include the phrase "compulsory license." Article 31 refers to "use without authorization of the right holder," and includes both use by third parties (what is usually referred to as compulsory licenses) and use by government. Article 31 of TRIPS does not place any restriction on the grounds for issuing a compulsory license can be given. In case there were any doubts, the Doha Declaration on the TRIPS agreement and public health[19] has made it clear that "Each member has the right to grant compulsory license and the freedom to determine the grounds upon which such licenses are granted." The only requirement under TRIPS is that once the decision to award a compulsory license has been taken certain conditions have to be satisfied. These include: (i) that authorization of such use will have to be considered on its individual merits, (ii) that before permitting such use (except in such cases as situations of national emergencies, extreme urgency, public non-commercial use), the proposed user will have to make efforts over a reasonable period of time to get a voluntary license on reasonable commercial terms, (iii) that the legal validity of the compulsory licensing decision and the remuneration will be subject to judicial or other independent review and (iv) the compulsory licenses can be terminated if and when the circumstances which led to it cease to exist and are

17 See 'Cipla gets HC relief in Roche Case,' *Mint*, 25 April 2009 and 'SC dismisses Roche petition on Tarceva,' *DNA – Daily News and Analysis*, 28 August 2009.

18 "Bayer's attempt to stop Cipla drug sale fail", *Business Standard*, 19 August 2009 (*www.business-standard.com*).

19 WTO, "Declaration on the TRIPS agreement and public health", WT/MIN(01)/DEC/2, adopted on 14 November 2001 (available at *www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm*).

unlikely to recur. However as several commentators have argued, including Watal (2001) and Love (2001), the grounds and the procedure can be so specified as to make these conditions less onerous than what these appear to be.

The Doha Declaration affirmed the right of member countries to take appropriate measures to protect public health. It is of immense help to developing countries in that it acknowledges that a conflict may exist between intellectual property standards and public health concerns and indicates that the former should not be an obstacle to the realization of the latter (Correa, 2002). The Doha Declaration also noted in its paragraph 6 the difficulties of countries with insufficient or no manufacturing capacities to effectively use compulsory licensing provisions and instructed the Council of TRIPS to find an expeditious solution to the problem. The subsequent WTO decision in August 2003[20] permitted within the TRIPS framework, production and exports of patented drugs to countries without sufficient manufacturing capacities.

To what extent has India effectively utilized the TRIPS flexibilities relating to compulsory licensing? To understand the Indian situation it is important to make a distinction between the following three regimes:[21]

1. The Patents and Designs Act of 1911 which was in force in India till 1972 and which provided for product patent protection and also had elaborate provisions relating to compulsory licenses for products including pharmaceuticals;
2. The Patents Act, 1970 which eliminated product patent protection in pharmaceuticals but inherited the same compulsory licenses structure of the Act of 1911 for other products; and
3. The amended patents law which has not only re-introduced product patent protection in pharmaceuticals from 1 January 2005 but has basically retained and made applicable to all products including pharmaceutical products the same compulsory licensing structure from the Act of 1911.

The basic problem with the amended patent law in India is that it lacks any positive strategy. It appears that adequate attention has not been devoted to design the law to take advantage of the flexibilities which TRIPS provides. The amended patent law has elaborate provisions on compulsory licensing in chapter XVI which was introduced in 2002 (sections 82 to 94).[22] But the entire amendment has been carried out very mechanically. It starts with the relevant text of the Patents Act, 1970 and then makes some changes to make it TRIPS compliant. This has been done by deleting some clauses of the original Patents Act, 1970 (for example, abolition of special license of right or compulsory licensing provisions relating to pharmaceutical processes) and lifting some clauses from TRIPS and inserting these in the amended Act. The whole of Article 7 of the TRIPS agreement on Objectives and Article 8 on *Principles* are listed in the Act. Paragraph 4 of the Doha Declaration relating to the right of governments to take measures to protect public health, is also incorporated.

20 WTO, "Implementation of paragraph 6 of the Doha Declaration on the TRIPS Agreement and public health", Decision of the General Council of 30 August 2003WT/L/540 and Corr.1, 1 September 2003 (*www.wto.org/english/tratop_e/trips_e/implem_para6_e.htm*).

21 This discussion on CL system in India unless otherwise mentioned is based on Chaudhuri, 2005, pp. 83-116.

22 Amendments to India's patent law to make it TRIPS compliant were made in three phases, First in 1999, then 2002 and finally in 2005. The provisions on compulsory licensing provide details of general principles applicable to the working of patented inventions; grounds for grant of compulsory licenses; matters to be taken into account by the Controller of patents while considering applications for compulsory licenses; the procedure for dealing with compulsory licensing applications; general purposes for granting compulsory licenses; terms and conditions of compulsory licenses.

India's patent law also has provisions for compulsory licensing for export in light of the WTO's 30 August 2003 decision for countries that have insufficient or no marketing capacity. The only case in India of an application for a compulsory license has been made under this provision. (See discussion below under 'Export Market')

Article 31 of TRIPS dealing with compulsory licensing provides for special provisions "in the case of a national emergency or other circumstances of extreme urgency or in cases of public non-commercial use." Public use of patents or 'government use' is a standard feature of patent laws in many countries. Under US patent law (28 USC Sec 1498), the US government can use a patent or authorize third parties to use patents for virtually any public purpose and the government has actually made good use of it. For any such use, the government is not required to negotiate with the patent owner. Nor is the latter provided any injunctive relief. All that it can expect is payment of compensation for the use (Love, 2001).

Following the British patent law, the Indian patent law also provided for government use of patents and these provisions have been retained in the recent patent amendments. The central government or anyone authorized by it may use (i.e., "make, use, exercise or vend") an invention or acquire an invention for the purpose of the central government, state Governments or a government undertaking on payment of adequate remuneration or compensation (Sections 99 to 103).[23] Except in circumstances of national emergencies or extreme urgency or public non-commercial use, the government need not even inform the patentee about such use. The patent owner, however, can challenge such use or the terms of such use. Any such disputes are required to be judicially settled at the level of the High Court. Under the original Patent Act, 1970, the right to use included "the right to sell the goods." In the amended Act, the right of the government is restricted to the "right to sell, on non-commercial basis." This is an important difference. But still, in the amended Act, the government has wide ranging powers to make drugs more affordable and available. If the patented drugs are too expensive, then the government can produce or authorize others to produce and distribute these through public clinics.

The outcome of the various cases and the decisions in hundreds of product patent applications pending before Indian Courts and the Indian Patent Office will determine the development of the domestic patented market. In cases where Indian companies were already producing and marketing these products before 1 January 2005, they need not suspend production even if MNCs get the patents. Under section 11A(7), they can continue to produce on payment of 'reasonable royalty'. But in other cases, to the extent MNCs are successful in getting patents, Indian companies will not be able to manufacture the products and will have to rely on voluntary licenses from patent holders. If such licenses are not given or are given on restrictive terms, there will be negative consequences for competition and prices. Public policy interventions, including the grant of compulsory licenses, will become absolutely necessary to make drugs affordable.

Changes in the Domestic Generic market

To understand the changes in the domestic generic market, we need to understand some of the characteristics of the Indian policy environment.

In patent protected markets, such as the US, when a pharmaceutical MNC develops and puts a new drug into the market, it is sold not under its generic name but under a brand name. But when the patents expire, other

23 The government also has the power to revoke patents if the patentee has "without reasonable cause failed to comply with the request of the central government" to use the patent (section 64(4)) or if the patent and the way it is exercised is "mischievous to the State or generally prejudicial to the public" (section 66).

firms which enter the market usually sell the medicines under their generic names. Hardly any branding takes place in such generic markets as all generic products are considered to be bio-equivalent to the branded patented drug. The strict drug regulatory standards of USFDA ensure that there is no quality difference and hence one hardly observes any price difference between competing generic products.

In pre-TRIPS India, in the absence of product patent protection, the entire industry was a generic market. But the structure has been more complicated than the US generics market — there have been different types of generics markets with different types of competition and hence prices.

To introduce any new drug, it is mandatory to obtain marketing approval from the DCGI. For drugs already approved abroad, the requirement in India is for limited Phase III clinical trials to be conducted. Usually only larger Indian companies can afford the expense of generating and submitting product dossiers to the DCGI for marketing approval. After four years, however, any company may take a manufacturing license without submitting product dossiers and clinical data.

Thus when a new drug was introduced in India, generic competition meant that its price would be significantly lower than the high patented protected monopoly price abroad. But the regulatory barrier during the first four years led to restricted competition and hence prices higher than the market prices after four years when other companies entered and pushed down the prices further.

The bulk drugs market closely resembles a perfectly competitive market with a large number of firms and where both the buyers and sellers are firms. Unlike in the case of the formulations market as discussed below, those who buy bulk drugs are aware not only of the prices charged by the different firms but also of their quality reputation. The buyers can avoid the poor quality producers and shop around in the market to buy from the cheapest reliable supplier. Such competition among the firms has resulted in very low bulk drugs prices (Chaudhuri, 2005, pp 233-237).

But in the retail formulations market, even though prices decline, they do not equalize. Unlike the US generics market, significant price differentials exist and all the firms do not sell under generic names in India. The larger ones, in particular use brand names to sell their generic products allowing product differentiation. Like the MNCs abroad in patent protected markets, the Indian generic companies target doctors for promoting prescription drugs and consumers directly for non-prescription drugs. Typically market leaders charge higher prices but still manage to retain dominant market shares. This is primarily because of imperfections in the market –buyers do not have knowledge about the prices and quality of all the other products available in the market. A still evolving and improving drug regulatory system means that not all products available in the market in India are considered to be equally effective or safe allowing leading firms backed by sales promotion and better reputations to charge higher prices without losing market dominance (Chaudhuri, 2005, chapter 7; Sengupta et al. n.d., p. 10). These prices are significantly higher than the prices at which institutional buyers such as public health authorities buy through competitive bidding processes. Because of competition, the prices of the drugs procured by the Tamil Nadu Medical Services Corporation (TNMSC), for example, have been significantly below retail prices, particularly compared to those of leading brands (Srinivasan, 1999; Sakthivel, 2005). The example of TNMSC is important because it has been able to economize on prices through competitive bidding without compromising quality — bids are restricted to manufacturers who have the capacity and the capability to supply quality products (Lalitha, 2008).

In the industry, the main beneficiaries of the pre-TRIPS market have been the larger companies who were the first to introduce new drugs and enjoyed a premium from restricted competition. Typically, they would themselves manufacture the APIs initially. Over time, as the number of competitors increased and prices of APIs fell, they often found it cheaper to buy the APIs from other firms rather than producing them themselves (subject to the ratio parameters mentioned below). They could shift to newer APIs while continuing to manufacture and market the formulations in their brand names. For the API manufacturers such as Sri Krishna Pharmaceuticals, which are involved in manufacturing bulk drugs at the mature stages, TRIPS hardly makes a difference. They operated in a very competitive environment earlier and will continue to do so even after patents expire.[24] In the post-TRIPS situation, large firms cannot initiate the manufacturing of new drugs as they did earlier. Consequently, they are also the ones to be most adversely affected.

Expansion of the Retail Formulations Market

Anticipating the shrinkage in domestic operations due to the TRIPS regime, Indian companies particularly the larger ones have not only been introducing new products but also promoting these very aggressively.[25] The retail formulations market has been increasing at a fast and steady rate — at around 14 percent the last three years, 2005/06, 2006/07 and 2007/08. The market is estimated to be INR 320,958,000 (USD 7,103,196.34 billion)[26] in 2007/08. While factors such as rising income levels, urbanization, and rural penetration have contributed to the expansion in the retail market, ORG-IMS data shows that a major growth driver has been the introduction of 'new' products. ORG-IMS considers as a new product not only a NCE or a new chemical derivative but also new combinations of existing drugs or a new formulation or composition. Companies such as Cipla, Lupin and Intaas are not only diversifying to new therapy classes by introducing new brands where they are not currently present but also introducing new drugs in therapy classes where they are already present (Care Research n.d., p. 27). The number of products marketed by Cipla, for example, has increased from 92 in December 1994 to 139 in June 1997, to 504 in June 2002, 694 in October 2004, 779 in December 2006 and 803 in March 2008.[27]

The acceleration of new product introduction by large companies has been aided by several other factors. What has changed since the mid-1990s is not only the patent regime. Several policies which restricted the activities of large units have been withdrawn.[28] Industrial licensing has been abolished. Earlier, large units were required to take permission from the government to manufacture (in addition to the marketing approvals from the drug regulatory authorities). The licence, among other things specified the volume of production. This is no longer required. Earlier large units had to manufacture the APIs in specified ratios to be eligible to get licences for manufacturing formulations. Thus, unless they were prepared to also manufacture the APIs, they could not have undertaken formulations' manufacturing and marketing. Such ratio parameters have been withdrawn. The larger units are no longer required to manufacture APIs to manufacture or market formulations. Another

24 Interview with V. V. Krishna Reddy, Executive Director of Sri Krishna Pharmaceuticals, 23 April 2008, Hyderabad.

25 A news report in a leading English daily in India reported various incentives being provided by pharmaceutical companies to doctors to prescribe their brand of medicines including foreign trips, expensive gifts, etc. See Rema Nagarajan, "Are your drugs boosting your doc's lifestyle? Pharma Firms Openly Bribe Doctors With Freebies, Junkets", *Times of India*, 15 December 2008.

26 See Editor's note ibid, USD billion (9 zeros) is equivalent of INR 100 Crore.

27 IMS, *Stockist Secondary Audit*.

28 *Modifications in Drug Policy, 1986*, National Pharmacuetical Pricing Authority, Department of Chemicals and Petrochemicals, Ministry of Chemicals and Fertilizers, New Delhi, 1994 (accessed from *www.nppaindia.nic.in*).

significant change has been the dilution of price control measures. The Drug Price Control Order, 1995 has reduced the number of bulk drugs under price control from 142 to 74 accounting for about 30 to 35 percent of the market compared to about 70 percent earlier (Chaudhuri 2005, p. 304).

Shrinkage of the small scale generic industry

Market concentration in the generic industry in India is also rising with negative implications for pricing. The market share of top 20 companies has in fact increased from 46 percent in December 1994 to 56.8 percent in March 2008 and that of top 50 companies from 74.3 percent to 81.3 percent. The trend will intensify in future. According to the Confederation of Indian Pharmaceutical Industries (CIPI), a nation level group of small-scale pharmaceutical associations in various states, more than half of the small-scale pharmaceutical units operational in India have either closed down or indefinitely suspended business activities in the last two years (Jayakumar, 2008). This is partly because of the inability to withstand the competition from larger units in the changed business environment. In the retail formulations market, the smaller units are increasingly finding it difficult to compete with the larger units, which have greater marketing and other resources.

Another factor which has gone against the smaller units is the amendment of Schedule M of the Drugs and Cosmetics Act, 1940 to comply with the Good Manufacturing Practices (GMP) standards of the WHO.[29] Manufacturers are required to follow Schedule M to ensure that their products are consistently produced and controlled according to quality standards and in 2004 it became mandatory for all manufacturers to adhere to the amended Schedule M. A large number of units, primarily in the small scale sector, operating on thin profit margins having neither the resources nor the incentive to upgrade their facilities in accordance with the new GMP standards have exited from business (Jayakumar, 2008).

If proper implementation of Schedule M improves quality standards and ushers in a greater degree of price based competition rather than brand based competition, prices will be more affordable. Recent US experience shows that strict regulatory standards are not inconsistent with competitive prices — drugs are sold there at USD 4 per month thanks to supplies from India satisfying the strict USFDA norms (Ministry of Commerce and Industry, 2008, p. 98). But ultimately what matters is not just the specification of standards. What is critical is to monitor whether the manufacturers are following the procedures and abiding by the safeguards to produce drugs which are safe and effective and if they are not, then to take corrective action. This is an area where India's drug regulatory authorities must improve their ability to take appropriate action where manufacturers knowingly or unknowingly produce drugs which do not satisfy quality requirements. Recent amendments to India's drug regulatory laws have enhanced punishments for spurious drugs.[30] It remains to be seen whether this will bring about a perceptible change in the situation.

Tie-ups with foreign companies

Another opportunity for generic manufacturers which is becoming increasingly visible is to tie up with foreign companies to market and distribute their products. This is mutually profitable. Foreign companies, particularly the smaller ones, that are not willing or able to invest in creating marketing infrastructure, can

29 Another factor which has changed the environment of the small scale sector is the policy of maximum retail price (MRP) -based excise duty and the creation of some excise free regions in the country. New units have come up in these regions at the cost of those in other regions.

30 The Drugs And Cosmetics (Amendment) Act, 2008, No. 26 of 2008.

use the marketing and distribution set-up of the Indian companies. On the other hand, Indian companies can market new products which otherwise are not accessible to them on grounds of technology or patents. Tie ups can take different forms, for example (i) importing the APIs and formulating in India; (ii) importing the formulations; and (iii) manufacturing the product here with technology dossiers supplied by foreign companies for which they receive royalties. Some companies, such as Elder Pharmaceuticals, have been doing it for quite some time. But the trend has accelerated post-TRIPS. Among the in-licensing deals struck by Indian companies are Cadila Healthcare with Schering AG, Boehringer Ingelheim, Piramal Healthcare with Ethypharm, Eli Lilly, Biogen, Laboratories, Pierre Fabre (Ernst & Young, n.d., p. 8). In the pre-TRIPS situation, because of competition in patented drugs in India, both consumers and Indian producers were able to benefit from the policy environment. After TRIPS, the new policy environment has led to collaborations between Indian companies and MNCs that are restricting competition and both of them are gaining at the cost of consumers.

III Export Market

The growth in exports has been one of the most outstanding features of the Indian pharmaceutical industry. Negligible before the 1970s, exports started picking up after the abolition of product patents in 1972, accelerating in the 1980s and then growing rapidly since the mid-1990s. In recent years, exports have been increasing annually at more than 20 percent.[31] Company-wise export figures are available for 120 Indian companies for 2007/08 from the Centre for Monitoring Indian Economy (CMIE) Prowess database (see Annex I). These companies exported drugs worth INR 221,594.8 million (USD 5.5 billion) in 2007/08 which makes up about three fourths of India's total drug exports (INR 291,395.7 million or USD 7.2 billion in that year). The proportion of exports in net sales for these 120 companies is 44 percent. The export market, as detailed in Table 2, is larger than the domestic market not only for large companies, such as Ranbaxy (61.7 percent of net sales), Dr. Reddy's (59.7 percent), or Cipla (50.1 percent), but also for smaller companies such as Granules (68.9 percent), Shilpa Medicare (73.5 percent), Kopran (60.5 percent), Transchem (54.6 percent), and Pure Pharmaceutical (51.9 percent).

From semi-regulated to regulated markets

The export market can be broadly classified between regulated markets and semi-regulated markets. In the former, there are regulatory barriers in the sense that exporters are required to fulfill elaborate registration requirements and in some countries, inspection procedures, to satisfy drug regulatory authorities about the efficacy and safety of medicines. Such requirements are absent or are not as elaborate in the latter. The stricter the regulations, the tougher the entry barriers, and accordingly, the higher the prices. Regulated markets are restricted to the countries in North America and Western Europe,[32] as well as to Japan, Australia and New Zealand. The remaining countries in Asia Africa, Latin America and Eastern Europe have relatively lower regulatory standards that vary across countries and for the purposes of this paper are categorized as semi-regulated.

31 Calculated from Directorate General of Commercial Intelligence and Statistics (DGCI&S), data obtained from CMIE India Trades database.

32 Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Netherlands, Spain, Sweden, United Kingdom, Norway, and Switzerland.

The pharmaceutical industry in India has grown in the following sequence:

- Production for the domestic market
- Exports to semi-regulated markets
- Exports to regulated markets

The motivation for moving up the stages has been larger markets and higher price realizations. Again with each market, the tendency has been to move up the value chain and target value-added segments. However, only a small number of companies have been able to undergo the full transition to exports to regulated markets. The vast majority of exporters are stuck at the first stage — exports to semi-regulated markets.

By the time TRIPS came into effect, India was already a substantial exporter to regulated markets. These markets accounted for about 43.9 percent of India's total pharmaceuticals exports in 1994/95. Since then, the importance of the regulated and semi-regulated markets has remained roughly the same (see Table 3). But significant country-wise changes are noticeable. European countries (including both the regulated Western European markets and semi-regulated Eastern European markets) and the Asian markets accounted for more than two-thirds of India's exports in 1994/95. Their share by 2007/08 had reduced to less than half. The growth has been much faster in the US, African and Latin American markets. The share of the US market has gone up from 10.7 percent in 1994/95 to 19 percent in 2007/08 and that of the African market from around the same level to 14.7 percent. There has been a significant jump in Latin American exports too — the share rising from 2.5 percent to 7.9 percent.

The US is now India's largest export partner in both bulk drugs and formulations. It

Table 2: Pharmaceutical exports of Indian companies, 2007/08 (based on a sample of 120 companies)

Company	Exports (INR million)	Exports as percent of sales	Exports as % of India's pharmaceutical exports
Ranbaxy Laboratories Ltd.	25172.8	61.7	8.64
Dr. Reddy's Laboratories Ltd.	22599.1	59.75	7.76
Cipla Ltd.	21017.4	50.08	7.21
Lupin Ltd.	13555.3	52.73	4.65
Aurobindo Pharma Ltd.	13395	58.96	4.6
Orchid Chemicals & Pharmaceuticals Ltd.	10085.6	81.49	3.46
Divi'S Laboratories Ltd.	9628.2	92.95	3.3
Jubilant Organosys Ltd	8562.5	42.78	2.94
Sun Pharmaceutical Inds. Ltd.	8064.5	35.01	2.77
Glenmark Pharmaceuticals Ltd.	6774.1	50.31	2.32
Matrix Laboratories Ltd.	6124	64.4	2.1
Ipca Laboratories Ltd.	5164.1	47.4	1.77
Biocon Ltd.	4776.3	54.38	1.64
Piramal Healthcare Ltd.	4536.5	23.89	1.56
Cadila Healthcare Ltd.	4358	25.41	1.5
Nectar Lifesciences Ltd.	3842	52.03	1.32
Wockhardt Ltd.	3632	30.97	1.25
Strides Arcolab Ltd.	3222.1	81.83	1.11
J B Chemicals & Pharmaceuticals Ltd.	3181.7	57.14	1.09
Alembic Ltd.	2939.8	29.67	1.01
Shasun Chemicals & Drugs Ltd.	2817.8	64.89	0.97
Plethico Pharmaceuticals Ltd.	2765.2	62.64	0.95
Hikal Ltd	2459.2	81.76	0.84
Dishman Pharmaceuticals & Chemicals Ltd.	2349.2	65.44	0.81
Torrent Pharmaceuticals Ltd.	2221.8	22.32	0.76
U S V Ltd.	2048.5	30.21	0.7
Fresenius Kabi Oncology Ltd.	1750	73.12	0.6
Ind-Swift Laboratories Ltd.	1697.9	38.19	0.58
Neuland Laboratories Ltd.	1486.5	68.09	0.51
Ajanta Pharma Ltd.	1286.3	45.15	0.44
Granules India Ltd.	1277.4	68.88	0.44
Unichem Laboratories Ltd.	1106.5	19.14	0.38
Aarti Drugs Ltd.	1093	35.18	0.38

Table 2: Pharmaceutical exports of Indian companies, 2007/08 (contd.)

Company	Exports (INR million)	Exports as percent of sales	Exports as % of India's pharmaceutical exports
Emcure Pharmaceuticals Ltd.	1019.8	23.85	0.35
Natco Pharma Ltd.	929.6	41.08	0.32
Themis Medicare Ltd.	881.7	40.3	0.3
Indoco Remedies Ltd.	771.9	22.09	0.26
Shilpa Medicare Ltd.	712.4	73.46	0.24
Arch Pharmalabs Ltd.	700.4	13.62	0.24
Vasudha Pharma Chem Ltd.	626.2	37.94	0.21
Panacea Biotec Ltd.	616.8	7.36	0.21
Suven Life Sciences Ltd.	612.3	52.23	0.21
Kopran Ltd.	564.6	60.53	0.19
Syncom Formulations (India) Ltd.	548	79.58	0.19
Marksans Pharma Ltd.	530.9	22.42	0.18
S M S Pharmaceuticals Ltd.	507.6	24.23	0.17
Medicamen Biotech Ltd.	504.4	65.61	0.17
Anuh Pharma Ltd.	495.3	44.68	0.17
R P G Life Sciences Ltd.	426.5	36.06	0.15
F D C Ltd.	392.8	8.06	0.13
Vivimed Labs Ltd.	389.8	25.26	0.13
K D L Biotech Ltd.	313.6	28.15	0.11
Bal Pharma Ltd.	312.7	36.69	0.11
Hiran Orgochem Ltd.	292.4	24.51	0.1
P I Drugs & Pharmaceuticals Ltd.	284.7	42.27	0.1
Smruthi Organics Ltd.	259.4	47.89	0.09
Anu'S Laboratories Ltd.	256	17.65	0.09
Zandu Chemicals Ltd.	254	79.95	0.09
Indian Immunologicals Ltd.	236.5	12.36	0.08
Elder Pharmaceuticals Ltd.	233.1	4.26	0.08
Twilight Litaka Pharma Ltd.	232.1	7.87	0.08
Tonira Pharma Ltd.	231.2	71.47	0.08
Fermenta Biotech Ltd.	217.1	70.79	0.07
Lincoln Pharmaceuticals Ltd.	154.2	17.88	0.05
Transchem Ltd.	150.8	54.58	0.05
Tyche Industries Ltd.	128.1	43.82	0.04

Source: ORG-MARG, *Retail Store Audit*; ORG-IMS, *Stockist Secondary Audit*.

accounted for 23 percent of India formulations exports and 14 percent of bulk drugs exports in 2007/08.[33] In fact larger Indian companies, which have the resources to do so, are increasingly targeting the more lucrative regulated markets in North America and Europe; particularly the US generics market. Thus the US and European markets already constitute the major markets for companies such as Ranbaxy, Dr. Reddy's Laboratories and Wockhardt. The reason is simple — these regions provide larger markets and higher price realizations. Price realizations are higher because regulatory requirements to enter these markets are stricter and entry is more difficult. Indian companies exporting to the US are required to file a Drug Master File (DMF) for APIs and an Abbreviated New Drug Application (ANDA) for formulations and set up dedicated plants. These are costly and time consuming, which most companies are unable to afford, and so they concentrate on the semi-regulated markets (Chaudhuri, 2005, chapter 6).

The behaviour of the larger Indian companies in semi-regulated markets is quite different. Consider for example the role of Indian companies in Tanzania.[34] The generic market in Tanzania, particularly in rural areas, is highly competitive and price sensitive. The larger and more reputed Indian companies with larger overheads and larger investments in GMP plants are finding it very difficult to compete in these markets with smaller suppliers including from India who are less quality conscious. In some of the products, these larger companies have become non-competitive. Zydus Cadila, an Indian company

33 Data source same as in Table 3.

34 The discussion in this paragraph is based on Chaudhuri, 2008a which also provides references to sources used.

has decided to withdraw from Tanzania. The other larger Indian companies such as Ranbaxy, Cipla, Sun, Glenmark have not withdrawn and are trying to target niche markets in urban areas where there are entry barriers and branding is possible. It helps these companies as a result to survive and perhaps also to grow. But it hardly satisfies the cause of most of the poor people who need essential drugs.

Table 3: India's exports of drugs & pharmaceuticals

	1994-1995		2007-2008	
	USD million	Percent of India's total exports	USD million	Percent of India's total exports
Regulated Markets	**351.4**	**43.9**	**3160.8**	**43.6**
Europe	229.2	28.6	1449.2	20.0
US	85.8	10.7	1375.4	19.0
Others	36.4	4.6	336.2	4.6
Semi-regulated Markets	**448.9**	**56.1**	**4080.6**	**56.4**
Asia	206.3	25.8	1369.1	18.9
Africa	85.3	10.6	1064.8	14.7
Latin America	20.2	2.5	572.6	7.9
Eastern Europe	110.5	13.8	699.1	9.6
Others	**26.6**	**3.4**	**375**	**5.3**

Source: Author's calculation based on DGCI&S, export data obtained from CMIE India Trades database.

Exports to Patented Markets

So far as patented markets are concerned, even before TRIPS, India could enter an export market only after the patents expired. In the absence of product patent protection in India, even when it was legal for India to manufacture and export, countries which recognized product patents could not import the products so long as the patents were in force there. In Africa, for example before TRIPS, all the countries except Angola, Djibouti, Eritrea, Ghana and Somalia, recognized product patents in pharmaceuticals.[35] Where opportunities arose for generic competition as for example in patented ARVs, Indian generic companies played a very positive role as we have mentioned above. After 2005, Indian companies will be prevented from manufacturing new ARVs that may be patented and other new patented drugs, hence India's role as a 'pharmacy of the developing world' will be severely restricted.

To utilize India's capability and capacity for enhancing the access to essential medicines in developing countries, compulsory licensing or other measures are of vital importance.

Of these measures, it is important to note that following the WTO's 30 August 2003 decision on the Doha Paragraph 6 issue, India inserted a provision (Section 92A) during the 2005 amendments to permit compulsory

35 Ghana now has a product patent regime but the other four still do not have one. See Chaudhuri, 2008a, pp. 23-24.

licenses for the purpose of manufacturing and exporting patented drugs to countries with insufficient or no manufacturing capacity. Under the provision if any other country issues a compulsory license or a notification or in any other manner allows for the import of a drug patented in India, a compulsory license for export must be granted. But the 30 August 2003 decision imposes several conditions requiring not only that a very cumbersome procedure be followed for such export, but that this procedure be followed each time a country exports or imports and thus acts as a serious disincentive for the parties involved in the system, particularly generic suppliers (Chaudhuri, 2005, pp. 113-114).

In India, there has so far been only one example of a generic company making an application under this provision for export. The company was NATCO which was looking to export the anti-cancer medicine *erlotinib*, patented by Roche in India, to Nepal. Although the provisions of the law do not provide for objections by the patent owner, the Indian Patent Office notified them anyway and the result was protracted hearings in the Delhi Patent Office on whether the patent holder should be heard and the requirements of the WTO 30 August 2003 decision among other things. In its decision, the Patent Office did not accept the documents provided by NATCO to support export under a compulsory license to Nepal on various grounds, including the non-fulfillment of the requirements of the WTO 30 August 2003 decision even though such decision is not included in the patent law.[36] The compulsory licence application was ultimately withdrawn. These proceedings reflect once more, the need for simple and easy to use compulsory license provisions.

Of course even if this provision were applied effectively in India, the ability of Indian companies to export to patented markets will also depend on how these markets apply patent laws and whether, like the Indian law, they follow a model that restricts the patent market or not.

Exports to the US

The increasing focus on the US market is one of the most important changes in the behaviour of Indian pharmaceutical companies after TRIPS. Market size and returns have been the key considerations for this change. But transparent regulatory procedures and linguistic convenience have also played their roles. Europe is a more difficult market due to different regulatory systems of different countries, complex pricing systems and linguistic differences (Sampath, 2008, p. 22).

But because of the resources required for getting regulatory approvals and setting up dedicated plants, only a few Indian companies have been able to effectively tap the opportunities in the US market. As can be seen from Table 4, among the CMIE companies (see Annex I), 54 have filed DMFs and of these, 18 have also obtained ANDAs. These companies[37] with DMFs and/or ANDAs in the US, exported drugs worth INR 206,552.3 million (USD 4,634.854) which constituted about 70 percent of India's total drugs exports in 2007/08 (calculated from Tables 2 and 4).

Indian companies in the US can be classified into (i) those heavily involved in both DMFs and ANDAs (for example, Ranbaxy, Dr. Reddy's, Sun, Aurobindo, Wockhardt, Cadila Healthcare, Lupin), (ii) those which are mainly in DMFs but also have ANDAs, (for example, Matrix, Cipla, Ipca, Natco) and (iii) those with only DMFs

36 Delhi Patent Office, *In the matter of Patent Application No. IN/PCT/2002/00785/DEL (Patent No. 209251) and In the matter of application for compulsory licence u/s 92(A) and Rules 96-97 filed by M/s Natco Pharma Ltd. and In the matter of Interlocutory petition filed on 27.02.2008 by M/s Natco Pharma Ltd.*, July 2008.

37 Except Hetero for which exports data are not available from the CMIE Prowess data base for 2007/08.

(for example, Divi's, Neuland, Shasun, Alembic, Biocon, Granules, Hikal, Suven). In 1995, India had only 11 USFDA approved plants. The number went up to 44 by 2005 and is now 119. This is the highest number of USFDA approved plants outside the US. In 2007, companies from India got 132 ANDA approvals compared to 169 by companies from the US. In DMFs, India is the largest filer with 274 compared to only 90 from China (Ministry of Commerce and Industry, 2008, pp. 17-18).

Most Indian companies operate in commodity generics where, apart from regulatory barriers, there are practically no other entry barriers. These markets are characterized by intense competition among a large number of companies, with low prices and profit margins. Indian companies in fact compete a lot amongst themselves. The success of one Indian company in a field often induces the entry of other Indian companies in the same field (Chaudhuri, 2005, pp. 198-201). Indian companies have contributed significantly to the lowering of generic drug prices in the US market. Relying on Indian supplies, Wal-Mart Stores Inc, a leading US based retail company, has been able to provide select drugs at USD 4 a month (Ministry of Commerce and Industry, 2008, p. 98). Such price decreases have taken place through competition without any complaint about quality. Thus with reference to our discussions on the imperfections in the Indian and Tanzanian generics markets, consumers in these countries could also benefit if drug regulation improved.

Smaller than predicted generic market

Indian companies were lured to the US market by the prospects of a huge generic market. India's Minister of Commerce and Industry, while justifying the Patent Ordinance, which introduced product patent in pharmaceuticals in India from 1 January 2005, pointed out that drugs worth USD 60 billion were are going off-patent in the next five years and that India could "grab a lion's share of this."[38] But these prospects have been grossly overestimated. As generics enter, prices fall sharply to 80 percent of the branded price and lower.[39] Assuming 90 percent price erosion, a USD 60 billion market is effectively reduced to USD 6 billion. Bulk drugs account for about 15 percent of the price. Hence the total bulk drugs market where Indian exporters are primarily involved would be less — around USD 0.9 billion during the five year period (Chaudhuri, 2005, p. 213). Indian companies through intense competition, including amongst themselves, have contributed to even sharper price erosion and hence lower opportunities. Further statements claiming that drugs are going off-patent do not represent an accurate picture as several of the medicines concerned continue to be protected by so-called secondary patents.

Increasing trend of patenting by generics

A few Indian companies have lately started targeting value-added segments in different ways. In these markets due to some entry barriers, the number of players is limited. The ability to introduce products in the relatively early stages of the product cycle has a significant impact on price realization. The generic company which is the first to launch (or among the first few to launch), gets a much better price than in the case of commodity generics. One way of doing so is to enter into products where only select companies have technical competence and dedicated facilities. Dabur, for example, was the first company to get USFDA approval in September 2006 for an anti-cancer drug that is difficult to manufacture (Greene 2007, p. 24).

38 'Kamal Nath, 'Statement On The Ordinance Relating To Patents (Third) Amendment', Press Release, Department of Commerce, Ministry of Commerce and Industry, Government of India, New Delhi, 27 December 2004.

39 "Generic Competition and Drug Prices", *www.fda.gov/cder/ogd/generic_competition.html*.

Some Indian companies, for example Sun Pharmaceuticals, Ranbaxy, Orchid Chemicals and Pharmaceuticals, have been successful in identifying and entering niche mid-size and smaller markets where opportunities are less but competition is also limited.[40] Another way is to develop non-infringing processes of manufacturing where the product patent has expired but the patent holder has prevented generic entry through patents for a number of processes. Matrix Laboratories, for example was the first company to develop a non-infringing process for a difficult to manufacture drug, *citalopram*. With restricted competition it was able to reap huge benefits.[41]

Another thrust area for many larger Indian companies has been developing new formulations by modifying existing drugs. The idea is to develop new formulations, get patents on them and sell at a higher price. The new formulations include novel drug delivery systems (NDDS) such as developing a controlled or extended release formulation of existing oral therapies to reduce side effects or increase patient compliance; developing alternative delivery routes, including oral as opposed to injectables, to increase patient convenience and compliance, and enhancing purification of the product to reduce dosing and side effects (Datamonitor 2001, p. 37). Among the Indian companies, an example of commercial success is that of the NDDS developed by Ranbaxy for *ciprofloxacin*, whereby patients are required to take the drug once a day against the twice-a-day dosage earlier. It took out a patent and licensed it to Bayer, which held the product patent for the drug. The latter has put the new dosage form in the market after approval from the USFDA. Ranbaxy receives royalty on the sales of the product though the patent on the original molecule has expired (Singh, 2006, pp. 195-196).

Thus, apart from DMFs and ANDAs, patenting in the US is becoming increasingly important for generic companies desiring to move up the value chain. Before 1995, only Ranbaxy had patents in the US. Since then, other companies have joined in and there has been a sharp upward trend (Chaudhuri, 2009, pp. 286-287). Table 4 lists 27 companies with patents in the US. The big three are Ranbaxy (with 93 patents), Dr. Reddy's Laboratories (83) and Dabur (now known as Fresenius Kabi Oncology) (39). Other major patentees include Orchid (27), Lupin (25) and Wockhardt (20). Indian companies are active in patenting in other countries too (Dhar and Gopakumar, 2006, p. 44).

Decreasing gains from patent challenges

Among the actions of Indian companies in the US market, patent challenges by a few of these companies have attracted the most attention. The USFDA provides for two types of applications: (i) the New Drug Application (NDA) for seeking permission to market a new drug and (ii) ANDA for seeking to market a generic drug. When the NDA is filed (for any drug product other than biologicals and vaccines, for which the system is different), the applicant must also provide the USFDA with certain information regarding the patents relating to the product for which permission is sought. When an ANDA is filed, the application must contain a certification with respect to the patents so listed in the *Orange Book*. There are four certification options. One of these is a Para IV application. For the latter, the generic company certifies that the patent is invalid or will not be infringed by the generic drug for which the ANDA applicant seeks approval.[42] Para IV certification is relevant because

40 "Pharmaceuticals: Formulations Exports — Opportunities growing bigger", 31 December 2008, pp. 7-9, *www.crisilresearch.com*.

41 Matrix Laboratories Ltd., *Annual Report, 2005-06*.

42 The other certifications are known as Para I, II and III respectively are: (I) the required patent information has not been filed; (II) the patent has expired; (III) the patent has not yet expired and approval is sought after patent expiration.

Table 4: Activities of Major Indian pharmaceutical companies

CMIE companies	CMIE-rank	No. of DMFs	No. of ANDAs	No. of US Patents	NCE R&D	Mergers and Acquisitions
Cipla Ltd.	1	117	12	17		
Ranbaxy Laboratories Ltd.	2	93	244	93	✓	✓
Dr. Reddy's Laboratories Ltd.	3	134	140	83	✓	✓
Lupin Ltd.	4	72	73	25	✓	✓
Sun Pharmaceutical Inds. Ltd.	5	66	157	13	✓	✓
Aurobindo Pharma Ltd.	6	119	137	10		✓
Jubilant Organosys	7	26	18	6		✓
Piramal Healthcare Ltd.	8	8		5	✓	✓
Cadila Healthcare Ltd.	9	61	79	5	✓	✓
Glenmark Pharmaceuticals Ltd.	10	28	45	12	✓	✓
Orchid Chemicals & Pharmaceuticals Ltd.	11	53	45	27	✓	✓
Wockhardt Ltd.	12	42	89	20	✓	✓
Ipca Laboratories Ltd.	13	42	8	4		
Divi'S Laboratories Ltd.	14	33		2		
Torrent Pharmaceuticals Ltd.	15	10	11	8	✓	✓
Alembic Ltd.	16	22		6		
Matrix Laboratories Ltd.	17	105	20	3		✓
Biocon Ltd.	18	16		6	✓	✓
Panacea Biotec Ltd.	19	0		14		
Hetero Drugs Ltd.	20	49	4	16		
Nectar Lifesciences Ltd.	21	2				
U S V Ltd.	22	21		4		
Unichem Laboratories Ltd.	24	13	4			
J B Chemicals & Pharmaceuticals Ltd.	25	7	10	2		
Elder Pharmaceuticals Ltd.	26	0				✓
Arch Pharmalabs Ltd.	27	5				
F D C Ltd.	29	12				
Ind-Swift Laboratories Ltd.	30	12		1		
Plethico Pharmaceuticals Ltd.	31	0				✓
Shasun Chemicals & Drugs Ltd.	32	23		2		✓
Emcure Pharmaceuticals Ltd.	33	4		1		
Strides Arcolab Ltd.	34	0				✓

Table 4: Activities of Major Indian pharmaceutical companies (contd.)

CMIE companies	CMIE-rank	No. of DMFs	No. of ANDAs	No. of US Patents	NCE R&D	Mergers and Acquisitions
Dishman Pharmaceuticals & Chemicals Ltd.	35	4				✓
Indoco Remedies Ltd.	36	2				
Aarti Drugs Ltd.	37	9				
Hikal Ltd.	38	8				✓
Fresenius Kabi Oncology Ltd.	41	8	11	39	✓	
Marksans Pharma Ltd.	42	1				✓
Natco Pharma Ltd.	43	22	4	1		✓
Neuland Laboratories Ltd.	45	29				
S M S Pharmaceuticals Ltd.	48	11				
Granules India Ltd.	51	13				
Vasudha Pharma Chem Ltd.	54	3				
Vivimed Labs Ltd.	56	1				
Jagsonpal Pharmaceuticals Ltd.	57	1				
Zandu Pharmaceutical Works Ltd.	59	2				
Morepen Laboratories Ltd.	61	6				
R P G Life Sciences Ltd.	63	2				
Suven Life Sciences Ltd.	64	8			✓	✓
K D L Biotech Ltd.	66	1				
Anuh Pharma Ltd.	67	2				
Gufic Biosciences Ltd.	86	5				
Smruthi Organics Ltd.	87	4				
Krebs Biochemicals & Inds. Ltd.	88	6				
Alpex International Ltd.	94	3				
Tonira Pharma Ltd.	98	3				
Zandu Chemicals Ltd.	99	2				

Source: (i) CMIE-rank: rank in terms of net sales in 2007/08 among Indian companies listed in Table A (see also Annex I); (ii) For DMFs, see *www.fda.gov/cder/dmf/*. (Retrieved on 7 August, 2008); (iii) for ANDAs, See Electronic *Orange Book*, accessed on 18 August, 2008 from *www.fda.gov* (searched by applicant holder for both prescription and OTC drug products); (iv) for patent data, see *www.uspto.gov* (searched issued patents by assignee name, accessed 30 April, 2009; (v) for NCE R&D, company Annual reports and websites; (v) for mergers and acquisitions, CMIE, Mergers & Acquisitions database and Cygnus 2008.

Notes: (i) The companies listed in the table are those from Table A of Annex I which are active in the US with DMFs/ ANDAs/US patents and/or are involved in NCE R&D and/or have acquired companies abroad; (ii) Sun Pharmaceuticals includes Caraco; Dr. Reddy's Laboratories includes Dr. Reddy's Research Foundation; Fresenius Kabi Oncology is the new name of Dabur, which includes the Dabur Research Foundation.

even when the patent on the active ingredient (NCE) expires, there can be other patents on formulations for example, which may still be valid. In almost all Para IV ANDA cases, the generic applicant is sued by the patent holder (Federal Trade Commission, 2002). By successfully contesting these patent cases, if a generic company obtains a Para IV ANDA, it gets market exclusivity for 180 days. During this period no other generic company is permitted to enter the market.

Any successful first to file Para IV ANDA can bring immense returns to the company as shown by Dr. Reddy's Laboratories experience. Dr. Reddy's was the first Indian company to get the 180-day exclusivity for marketing *fluoxetine* (marketed by Eli Lilly as Prozac) 40 mg capsule in August 2001.[43] Dr. Reddy's Laboratories and Ranbaxy are two Indian companies which have been very active in challenging patents in order to be the first to enter the generics market. They have recently been joined by a few others such as Sun Pharmaceuticals, Glenmark, Lupin, Aurobindo and Wockhardt.[44] Patent challenges involving litigation is a high-risk-high-gain strategy. A failure means a loss of several years of hard labour and huge legal expenses (Chaudhuri, 2005, pp. 205-206).

The generic companies have been successfully contesting patent litigations in most of the cases.[45] But the gains from such patent challenges have decreased in recent years. An important policy change in the US in 2003 introduced 'shared exclusivity'. Earlier only one company, the first company to file Para IV ANDA, enjoyed the 180-day exclusivity. After 2003, all the companies filing the ANDA on the same day are eligible for the exclusivity. With generic companies competing among themselves intensely, shared exclusivity has been the rule rather than the exception. For instance, Ranbaxy and Dr. Reddy's shared the exclusivity with 11 other companies in *fluconazole* tablets and 12 other companies in *ciprofloxacin* tablets. None of the smaller Indian companies which have been targeting the value added Para IV markets have received 180-day exclusivity alone.[46]

The MNCs have always fought patent challenges very hard. Where they fail to prevent early generic entry, they launch authorized generic products, i.e., issuing licenses to generic companies to market their products. As a result, even in cases where generic companies are able to get 180-day exclusivity, the gains are significantly reduced. For instance, Dr. Reddy's, competed with Teva in *finasteride* 5 mg tablets and with Ranbaxy in *simvastatin* 80 mg as an authorized generic company (Espicom 2009, p. 27). Another tendency that the Federal Trade Commission too has observed is going for out of court settlements (Federal Trade Commission, 2002). This low risk-low gain option is becoming increasingly popular for both MNCs and generic companies. Indian companies such as Ranbaxy, DRK, Lupin and Sun Pharmaceuticals have opted for such settlements in a number of cases.[47]

43 About half of Dr Reddy's operating profits in 2001/02 came from this product alone. See Dr. Reddy's Laboratories Ltd, *Annual Report, 2001-02*.

44 "Pharmaceuticals: Sector Strategy", *IDFC-SSKI India Research*, 15 February 2008.

45 The Federal Trade Commission (2002, p. 20) found that generic applicants won 29 out of 40 patent litigations (73 percent).

46 They have shared it with others in products such as *divalproex sodium* tablets, *zalephon* capsules, *meloxicam* tablets. Espicom, *The World Generic Market Report, 2009: Volume 1: Global Overview and Company Profiles*, pp. 8-12, January 2009.

47 "Light at the End of Tunnel", Sector Report/India Research, Angel Brooking, March 2008.

Mergers and Acquisitions

To facilitate their international operations, Indian companies have been setting up subsidiaries abroad. In the US, 11 Indian companies have 18 subsidiaries including Ranbaxy Pharmaceuticals Inc., Dr. Reddy's Laboratories Inc., Sun Pharmaceutical Industries Inc, Lupin Pharmaceuticals Inc., Aurobindo Pharma USA Inc. (Espicom 2009, p. 13). They are also acquiring companies abroad to speed up their entry into foreign markets. Such acquisitions not only provide them with a ready basket of products but also with established marketing and distribution networks. The Indian companies also benefit from the reputation and influence of local companies. Table 4 lists 23 companies which have acquired companies abroad.

The US continues to be a major target market for acquisitions. Other target markets include Germany, France, United Kingdom (UK) and South Africa. The top acquirers are: Ranbaxy (with acquisitions in France, Germany, Romania, Spain, US, South Africa); Dr. Reddy's (in Germany, Italy, UK, US, Mexico); Wockhardt (France, Germany, Ireland, UK), Zydus Cadila (in France, Italy, Spain, Brazil, Japan and South Africa), Sun Pharmaceutical (in US, four companies), Israel and Hungary); Lupin (in Germany, Australia, Philippines and South Africa). Dr. Reddy's acquisition of betapharma of Germany has been the largest acquisition. Other major deals include: Ranbaxy (Terapia, Romania), Wockhardt (Negma, France; CP Pharmaceuticals, UK, Pinewood, Ireland), Sun Pharmaceuticals (Taro, Israel).[48]

As discussed in the section below, some of these acquisitions have caused severe financial strain on some companies leading to the question whether some of the acquisitions were premature.

Changing relationships and roles of MNCs and generic companies

The structure of the generics market is changing not only in developed countries but also in developing countries. The strategies of MNCs and generic companies, and the relationships between them, have been undergoing a transformation.

Traditionally the roles of MNCs and generic companies have been quite distinct — the former marketing patented new drugs and the latter, patent expired drugs. While MNCs continued to stay in the market even after generic entry, the focus of their activities had been on the patented drugs market. After patent expiry and with generic entry as the revenue from patent expired drugs fell, they could shift to new patented drugs and maintain, even increase their profitability. This was possible because of a steady flow of new drugs in the market. But lately, while the size of the market of drugs going off-patent has been on the rise, the number of NCEs approved for marketing has been decreasing. MNCs are finding it increasingly difficult to compensate for the loss of markets to generic companies by putting in new patented products in the market.

The result is that MNCs themselves are now targeting generic markets. They are doing so not only in developed countries but also in emerging countries, where the market has been and is expected to grow at a faster rate. Previously Novartis was the only major MNC with a strong generic arm through Sandoz. Now others are adopting different strategies to enter and grow in the generic market. As noted above, in the US, MNCs are trying to counter patent challenges from generic companies by going for out of court settlements or by launching authorized generic products. Other ways include acquiring generic companies, for example Ranbaxy by Daiichi Sankyo and entering into strategic alliances, for example between Pfizer and Aurobindo

48 CMIE Mergers & Acquisitions Database; Cygnus 2008; Espicom 2009, pp. 51-52.

and between GSK and Dr. Reddy's. GSK will market about 100 formulations manufactured by Dr. Reddy's for several developing country markets (excluding India). Aurobindo similarly will manufacture more than 100 formulations for Pfizer for both the regulated markets of the US and EU and also for about 70 semi-regulated markets.[49] Increasingly, exports by Indian companies are taking the form of Contract Research and Manufacturing Services (CRAMS).

Contract Research and Manufacturing Services (CRAMS)

CRAMS can be divided into two major business segments — contract research and contract manufacturing. Contract research involves research activities for the development of new molecules and pre-clinical and clinical research. Some pharmaceutical companies have diversified to clinical trials but these are mainly done by specialized Contract Research Companies (CROs) set up in India in recent years, for example Vimta Laboratories, ClinInvest Research, Wellquest, Lambda Therapeutics. Contract manufacturing consists not only of the supply of intermediates, APIs and formulations of drugs already in the market but also involves customs synthesis, i.e., process development and manufacture of new drugs for pre-clinical and clinical trials.

Contract manufacturing is nothing new in India. What is new is the acceleration and emergence of specialized CRAMS companies in India. For some of the Indian generic companies such as Dr. Reddy's Cadila Heath Care, Lupin, IPCA, Sun Pharmaceuticals and Biocon, CRAMS is only one of the many activities. For example, for Dr Reddys and Cadila Heath Care they constitute only about 10 percent of total revenues. But there are companies which have specialized in CRAMS, such as Jubilant Organosys, Dishman, Divi's Shasun, Suven Life Sciences and Hikal. For these companies, CRAMS is a major or dominant activity contributing 100 percent of the revenue for Suven, 75 percent for Dishman and 55 percent for Jubilant in 2007/08 (Ernest & Young, n.d., p. 11; Anandrathi Research 2008, pp. 3, 8). The Indian CRAMS market is growing at a rapid rate but was still only about 2 percent of the global pharmaceutical outsourcing market of USD 52 billion in 2006 (Anandrathi Research, 2008, p. 15).

Several factors have contributed to the emergence of CRAMS. MNCs have been experiencing significant profit erosion. With rising R&D expenditure, there has been an upward pressure on costs. But there has been a downward trend in prices. The flow of new products has slowed down and generic competition has intensified. There is also the pressure to contain costs in the face of rising healthcare expenditure. The MNCs have been forced to be cost conscious and are trying to outsource activities to cheaper sources. With India's demonstrated skills in process chemistry, cost-competitive research base, large and skilled work force, not only larger MNCs but also smaller companies are tying up with Indian companies for CRAMS (Cygnus 2008(b), Ernst & Young, n.d.).

Indian companies have their own reasons for collaborating. Unlike in the past, generic companies have now started investing in new medicines. But the lack of adequate resources and skills has compelled them to enter alliances with MNCs. CRAMS do not give any spectacular returns as in the case of patent challenges but they are steady over a long period (around 5 years or more). With the intensification of competition in larger generic markets such as the US, CRAMS is developing as an attractive option for larger Indian companies which can undertake the necessary manufacturing investments and satisfy the quality and other requirements of MNCs.[50] Indian companies are also realizing that it is quite difficult to grow in different markets in different countries simultaneously with their own marketing network. Companies such as Glenmark and Dr. Reddy's

49 "Recent MNC Alliances: Signaling Paradigm Shift?", *IDFC-SSKI India Research*, 30 June 2009.

50 "India Pharmaceutical CRAMS; the Imminent Growth Opportunity", *Reliance Money Sector Report*, 15 July 2008.

have re-worked their strategies and have withdrawn from some markets and are focusing on select markets.[51] As in the Pfizer-Aurobindo and GSK-Dr. Reddy's deals mentioned above, Indian companies gain where they are unable or unwilling to make the necessary investments for setting up the marketing infrastructure.

CRAMS provide a larger space of operations for the Indian companies but have an adverse impact on the market structure as MNCs and generic companies share profits at the cost of consumers.

Emerging Barriers to Exports: Equating generics with "counterfeits"

Certain policy initiatives and actions at the behest of MNCs and developed countries may also have an adverse effect on international trade in generic products not involving the MNCs. Alleging intellectual property violations, several consignments of Indian exports meant for Africa and Latin America have been confiscated at several European ports through which these consignments were routed for logistical reasons. This was done despite the fact that the products did not violate any intellectual property rights and were legal in both India and the importing countries. While in some cases the cargo was allowed to sail to the final destination, in others it was directed back to India (CUTS, 2009).

International bodies such as International Medical Products Anti-Counterfeiting Taskforce (IMPACT) of the WHO and the proposed Anti Counterfeiting Trade Agreement (ACTA) initiated by the United States Trade Representative (USTR) have been trying to redefine the term "counterfeit" in a manner which might create barriers to exporting of generic medicines from India.[52] These definitions and initiatives often confuse generic medicines with sub-standard or fake medicines. In line with such interpretations, Kenya has passed an anti-counterfeiting law in December 2008. Under this law, if a patent holder objects on the basis of a patent held in any country, Kenya shall consider the drug as counterfeit even if the product is not patented in Kenya or in the country of manufacture.[53] If more countries adopt such definitions, generic trade will be seriously hampered.

IV R&D Strategies

As noted in the Introduction, strong patent protection is argued as being beneficial for India as it will stimulate investment for research for innovation to suit local needs.

In the underdeveloped Indian pharmaceutical industry before 1972, the capacity to conduct R&D was limited. But has the situation changed following the rapid growth of the industry since the 1970s to justify stronger patent protection in India? Is it that product patent protection may have adverse impact on access by making prices dearer but can be good for the R&D-based pharmaceutical industry in India? What has been the nature of R&D activities and innovation in the Indian pharmaceutical industry? Does India's experience support the claims of MNCs and their supporters that strong patent protection is needed in India for R&D and innovation?[54]

51 "Recent MNC Alliances: Signaling Paradigm Shift?", *IDFC-SSKI India Research*, 30 June 2009.

52 "WHO's new definition of counterfeit drugs intended to hurt Indian cos: IPA", *Pharmabiz*, 19 November 2008 (*www.pharmabiz.com)*.

53 Lynne Taylor, "India urges African nations over anti-generic laws", *PharmaTimes*, 25 May 2009 (*www.pharmatimes.com*).

54 Such claims have re-surfaced after an Indian court rejected Novartis' challenge of India's patent law (see, for example the editorial of the *Wall Street Journal*, "Drug Patents in India", 14 August 2007).

During the TRIPS negotiations, it was specifically claimed that TRIPS-compliant patent protection will prompt developing country companies to conduct more R&D for the development of new drugs more suited to local needs.[55] Have those claims been borne out in India? This section focuses on these issues.[56]

Traditionally, the Indian pharmaceutical industry spent very little on R&D. In the early 1990s, its R&D expenditures amounted to only about 1.5 percent of sales (Grace 2004, p.37). Even larger companies such as Ranbaxy and Dr. Reddy's Laboratories spent only 2 to 3 percent of their sales on R&D in 1992/93.[57] Since then, however, and particularly since the early 2000s, there has been a substantial increase in research spending in a segment of the industry. Our sample of 166 CMIE Indian companies (see Annex I) can be divided into two sets of companies — (i) 37 major R&D spenders each with R&D expenditure of more than INR 100 million (around 22,3571 million USD) in 2007/08 and (ii) the remaining 129 companies. For the latter group, R&D expenditure as a percentage of sales continues to fluctuate around 1 percent. In 2007/08, the proportion was only 1.1 percent. But for the group of 37 major spenders, R&D expenditure has increased steadily from 1.39 percent of sales in 1992/93 to 3.89 percent in 2001/02, and then sharply to 7.65 percent in 2004/05 and 8.35 percent in 2005/06. Thereafter, a decline is observed to 7.04 percent in 2007/08.[58] Here we focus on the more dynamic segment of the Indian pharmaceutical industry for which R&D expenditures have substantially increased (see Table 5).

The objectives of R&D conducted by Indian companies can be broadly classified as follows:

- Development of NCEs
- Modifications of existing chemical entities to develop new formulations, compositions, combinations (also known as incrementally modified drugs)
- Development of generics (that is, development of processes for manufacturing active pharmaceutical ingredients (APIs) and development of formulations to satisfy quality and regulatory requirements for marketing patent-expired drugs)

The development of NCEs is not yet a significant part of the R&D activities of Indian companies constituting less than a quarter of the total R&D expenditure by the major companies.[59] Nor are most of the large R&D spenders involved in NCE development; Cipla, for example, is the third largest spender on R&D but has no NCE portfolio (see Table 5).

As seen above, the Indian pharmaceutical industry is highly export oriented. Significant R&D efforts are directed towards developing processes and products to get regulatory approvals for entry and growth in patent-expired generic markets in developed countries. Development of processes for manufacturing APIs and product development of formulations, process validation, bio-equivalence testing and generation of other

55 See Velasquez and Boulet (1999, p.37) for a reference to such views.

56 This section is a condensed and updated version of Chaudhuri, 2008.

57 CMIE Prowess database.

58 Calculated from the CMIE Prowess database. See also Table 5.

59 Ranbaxy, Dr. Reddy's Laboratories and Cadila Healthcare spend about one-third of their R&D budget on NCE R&D (Singh 2006, p. 198); Dr. Reddy's Laboratories, *Annual Report, 2005-06*, p. 75; Cadila Healthcare, Investor Presentation, October 2006, accessed from company website. *www.zyduscadila.com*. Assuming that other Indian pharmaceutical companies involved in NCE R&D, maintain a similar proportion (and this may be an overestimate for the smaller companies), total R&D expenditure for NCE is about INR 5531 million in India in 2005/06. This constitutes only 23 percent of the total R&D expenditure by the 28 major companies.

data required for DMFs and ANDAs for getting international regulatory approvals are specifically highlighted as areas where R&D is undertaken by the companies active in the regulated markets.[60] Also, as noted above, apart from DMFs and ANDAs, patenting is increasingly becoming important for generic companies desiring to move up the value chain.

Thus much of R&D by Indian pharmaceutical companies has nothing to do with TRIPS. It is the result of increasing export orientation of Indian pharmaceutical companies and diversification to the regulated markets, particularly to the US.

R&D for new chemical entities begins

A remarkable feature of pharmaceutical R&D in India is that, though it is a relatively smaller share than other forms of R&D, the Indian private sector has started investing in R&D for new chemical entities. This began around the time TRIPS came into effect in the mid-1990s.[61] R&D investments were initiated by Dr. Reddy's Laboratories followed by Ranbaxy Laboratories. Since then eleven other companies — Sun, Cadila Healthcare, Lupin, Nicholas Piramal, Dabur Pharma, Torrent, Wockhardt, Orchid, Glenmark, Biocon and Seven Lifesciences have also joined in.[62] These companies are among the major pharmaceutical R&D spenders.[63] Together they invested INR 18264.6 million (USD 454 million) (8.18 percent of net sales) on R&D in 2007/08 (Table 5).

None of these companies is engaged in the entire process of drug development. The reason is simple: Indian pharmaceutical companies are not yet ready for a start-to-finish model in NCE research because of the lack of the skills and funds necessary to develop a drug and put it to the market.[64] Whereas the 13 Indian companies together spent USD 454 million in 2007/08, Pfizer, the largest MNC, alone spent USD 8.1 billion in 2007 (*Pharmaceutical Executive*, May 2008). The model that the Indian companies have adopted, rather, is to develop new molecules up to a certain stage and then license them out to partners from developed countries, primarily MNCs. This has been a marriage of interests. It is the development of biotechnology companies which has encouraged specialization according to stages of the drug development process. The MNCs seek and contract out specific activities (Nwaka and Ridley, 2003, p. 920). As the NCE pipeline of the MNCs started drying up, they in fact have intensified efforts to license promising compounds developed by others and most of the major MNCs have opened compound acquisition departments in their companies. There are also specialized companies which keep track of promising compounds, maintain libraries, catalogue them and offer them for sale to prospective clients.[65]

Even at the pre-clinical stage, Indian companies are not engaged with all elements of the R&D involved. Indian companies are not involved in basic research of target identification for new drugs. They rely on the basic research of others and adopt an approach called 'analogue research.' This entails working on certain pre-identified targets for specific diseases to develop molecules that alter the target's mechanism in the diseased

60 See, for example, Dr Reddy's Laboratories, *Annual Report, 2005-06*, p. 85; Ranbaxy, *Annual Report, 2005*, p. 46.

61 In the Indian private sector, Sarabhai Research Centre was the first one to be set up in the 1960s for developing new drugs. But it was wound up in the 1980s.

62 Among the large Indian companies, a notable absentee is Cipla.

63 Some other companies are also involved in NCE R&D. Advinus Therapeutics, for example is involved in new drug discovery services.

64 See, Chaudhuri, 2005, chapter 5.

65 Interview with B Gopalan, then with Glenmark Research Centre, Navi Mumbai, 11 February 2005.

person.[66] But even this requires medicinal chemistry and biology skills that are still scarce in the Indian pharmaceutical industry. In the pre-TRIPS era, Indian pharmaceutical industry scientists primarily acquired and developed organic chemistry skills required for process development. Indian companies are now filling up this gap primarily by hiring Indian scientists who worked in MNC laboratories in India and abroad and in the Indian public sector laboratories.[67]

Dr. Reddy's commenced drug discovery R&D in 1993. It filed its first patent in the US in 1995 for an anti-diabetic compound. This was out-licensed to Novo Nordisk in 1997. It developed two more anti-diabetic compounds and out-licensed these to Novo Nordisk in 1998 and Novartis in 2001. The deal with Novartis involved upfront and milestone payments up to USD 55 million depending on the progress and the company received USD 5 million to begin with, in 2002/03. These deals were major news and generated tremendous optimism and lured other smaller companies, such as Glenmark, into new drug R&D.

The initial optimism is reflected in what the chairman of Dr. Reddy's Laboratories said in the company's *Annual Report 2002-03* after signing the Novartis licensing agreement:

> "When we started our drug discovery program in 1993, industry pundits viewed it with skepticism. This ambition, they said, would not be within the reach of an Indian company. The challenge was to prove them wrong. And in this last decade, we have done just that."[68]

Table 5: R&D expenditure of major Indian pharmaceutical companies

CMIE companies	INR million, 2005/06	Percentage of net sales, 2005/06	INR million, 2007/08	Percentage of net sales, 2007/08	USD million, 2007/08
Ranbaxy Laboratories Ltd*	6393.3	17.78	4605.1	11.29	114.4
Dr. Reddy's Laboratories Ltd*	2539.5	11.35	3334.5	8.82	82.9
Cipla Ltd.	1554	5.23	2323	5.54	57.7
Lupin Ltd*	1080.2	6.55	1933.7	7.52	48.1
Cadila Healthcare Ltd*	1187	9.3	1618	9.43	40.2
Sun Pharmaceutical Inds. Ltd*	1614.9	12.91	1443.9	6.27	35.9
Wockhardt Ltd*	810.8	9.26	1267.4	10.81	31.5

66 Glenmark Pharmaceuticals Ltd, *Annual Report, 2003-04*.

67 In the pre-TRIPS regime too some R&D for new drug development were undertaken in India primarily by Central Drug Research Institute (CDRI) (public sector), Ciba Geigy, Hoechst and Boots (all MNCs). As a result of these efforts not many drugs have come to the market, but it generated skills (see Chaudhuri, 2005).

68 Similarly, the Chairman said in the *Annual Report 2000-01* that "Our achievements in drug discovery are testimony to our belief that there is little correlation between innovation and size" and in its *Annual Report 2001-02* that "Even today, I am often inundated by various 'facts and figures' … Our response to such data has been that in the area of discovery research we cannot be a prisoner of averages. The test of successful R&D driven pharmaceutical company should be its ability to consistently beat these so-called averages. Your Company exemplifies this tenet."

Table 5: R&D expenditure of major Indian pharmaceutical companies (contd.)

CMIE companies	INR million, 2005/06	Percentage of net sales, 2005/06	INR million, 2007/08	Percentage of net sales, 2007/08	USD million, 2007/08
Matrix Laboratories Ltd.	599	7.75	1197	12.59	29.7
Aurobindo Pharma Ltd.	647.9	4.64	1175.1	5.17	29.2
Torrent Pharmaceuticals Ltd*	873.6	12.6	1131.7	11.37	28.1
Panacea Biotec Ltd.	543.8	10.08	1076.7	12.85	26.8
Orchid Chemicals & Pharmaceuticals Ltd*	613.6	7.08	709	5.73	17.6
Jubilant Organosys Ltd	393.8	2.8	708.6	3.54	17.6
Glenmark Pharmaceuticals Ltd*	330.2	6.14	659.1	4.89	16.4
Biocon Ltd*	400.8	5.8	646.5	7.36	16.1
U S V Ltd.	624.6	11.44	590.2	8.71	14.7
Alembic Ltd.	266.7	4.24	462.4	4.67	11.5
Ind-Swift Laboratories Ltd.	458.6	14.61	446.9	10.05	11.1
Ipca Laboratories Ltd.	378.8	5.02	429.2	3.94	10.7
Strides Arcolab Ltd.	401.9	12.2	375	9.52	9.3
Piramal Healthcare Ltd*	911.5	6.55	352.8	1.86	8.8
Unichem Laboratories Ltd.	123.2	2.71	327.1	5.66	8.1
Ajanta Pharma Ltd.	NA	NA	314.1	11.02	7.8
Suven Life Sciences Ltd*	218.5	27.27	300.6	25.64	7.5
Emcure Pharmaceuticals Ltd.	NA	4.02	286.3	6.69	7.1
Plethico Pharmaceuticals Ltd.	NA	NA	279	6.32	6.9
Venus Remedies Ltd.	38.9	4.58	264.4	12.43	6.6
Fresenius Kabi Oncology Ltd*	268.9	10.91	262.3	10.96	6.5
Neuland Laboratories Ltd.	43.4	2.66	259.8	11.9	6.5
Shasun Chemicals & Drugs Ltd.	263.6	7.39	207	4.77	5.1
S M S Pharmaceuticals Ltd.	30.2	2.52	203.3	9.7	5.1
Arch Pharmalabs Ltd.	NA	NA	155.3	3.02	3.9
F D C Ltd.	64.1	1.89	117.6	2.41	2.9
Ind-Swift Ltd.	34.2	1.25	116.3	2.27	2.9
Divi's Laboratories Ltd.	100.6	2.6	114.7	1.11	2.9
J B Chemicals & Pharmaceuticals Ltd.	121.8	2.64	107.8	1.94	2.7
Indoco Remedies Ltd.	45.7	2.35	101.4	2.9	2.5
TOTAL 37 companies above	**24113.9**	**8.35**	**29902.8**	**7.04**	**743.1**
TOTAL 13 NCE R&D companies	**17242.8**	**11.2**	**18264.6**	**8.18**	**453.9**

Source: Author's calculation based on CMIE Prowess data base (see Annex I).

Note: The 13 Companies marked * are involved in NCE R&D.

Setbacks and changing strategies

Ranbaxy and Dr. Reddy's, the two Indian companies that have invested most heavily in R&D (Table 5) and served as prime advocates for new drug R&D in India, have each suffered several setbacks. Novo Nordisk and Novartis discontinued further development of the three compounds in-licensed from Dr. Reddy's. Similarly, Schwartz Pharma discontinued the clinical trials of a compound licensed from Ranbaxy. No success at the clinical trial stages have yet been reported from the much publicized Ranbaxy-GSK R&D collaboration.[69] Given that drug development did not progress as anticipated, the prospect of huge licensing revenue through milestone and other payments failed to materialize. This is true for other companies also involved in R&D for NCEs except for Glenmark, which has been able to out-license molecules in each of the years 2004-2007 and has earned a total of USD117 million as licensing revenue. But Glenmark too has been facing problems. Merck KGaA has returned to the company a molecule and the development of a molecule it out-licensed to Eli Lilly has been stalled.[70]

What the Indian companies initially did not understand is that while their objectives are to earn license fees and royalties from successful commercialization, the MNCs do not necessarily aim to develop the in-licensed compounds for commercialization. In fact where the compound may compete with the MNC's existing or planned products, the MNC's objective may actually be to 'kill' the compound.

Indian companies are now aware of this potential conflict. In some cases they are attempting to develop drugs further despite the lack of interest on the part of the MNCs who initially licensed them. Torrent, for example, entered into an agreement with Novartis in 2002 for the development of the Advanced Glycation End product (AGE) breaker compound for the treatment of heart disease and diabetes. In 2004 the compound was out-licensed to Novartis. The agreement was terminated in 2005 when Novartis decided not to proceed further with the compound. Torrent is now trying to develop it on its own and explore other options. Torrent received only USD 0.5 million initially and then USD 3 million from Novartis.[71] This was too small an amount for a large MNC such as Novartis to have any stake in the project. Dr. Reddy's has suffered several similar setbacks.

The later the stage at which a compound is licensed out, the higher the license revenues. The licensor is also in a better position to select a licensee who is actually interested in developing the drug for commercializing and may therefore provide a genuine possibility of earning royalties. But Indian companies face the predicament that the unilateral development of a drug to such a later stage entails considerable cost and risk.

For companies involved in the development of NCEs, R&D expenditure has risen at the Compound Annual Rate of Growth (CARG) of 38.25 percent between 1996/97 and 2005/06, with proportion of sales spent on R&D increasing from 3.14 percent to 11.47 percent in 2005/06 (Table 6). The rising R&D expenditure but lack of adequate returns has put strains on the profitability of these companies. From a peak of INR 2977.9 million (17.95 percent) in 2004/05, Dr. Reddy's R&D expenditure declined by about 15 percent in 2005/06 to INR

69 Unlike the other product specific licensing deals, the second largest MNC in the world, GSK and the largest pharmaceutical company in India, Ranbaxy, announced on October 2003 that they had entered into an R&D collaboration agreement covering a wide range of therapeutic areas. The agreement has been revised and the scope enlarged in February 2006 (see press releases in company website, *www.ranbaxy.com*).

70 Glenmark Pharmaceuticals, Corporate Presentation, August 2009 (*www.glenmarkpharma.com*).

71 "Novartis Acquires Rights in Torrent's AGE Compound", Media Release, Torrent Pharmaceuticals Ltd. 31 October 2002 and "Torrent Licenses AGE Compound to Novartis, " Media Release, Torrent Pharmaceuticals Ltd , 29 July 2004 (accessed from *www.torrent-india.com*).

2,539.5 million (11.35 percent). The expenditure has since recovered but the proportion is lower (8.8 percent of net sales in 2007/08) (see Table 11).

Dr. Reddy's has changed its R&D strategy. Rather than licensing out the molecules to MNCs, Dr. Reddy's is experimenting with a number of alternative business models. One is joint development and sharing of costs with smaller specialized research companies, such as Rheoscience and ClinTec. Dr. Reddy's entered into an agreement with the former in September 2005 to co-develop an anti-diabetic compound (DRF 2593) and with the latter in September 2006 to co-develop an anti-cancer compound (DRF 1042). It also has an agreement with Argenta for joint development of drugs for treatment of chronic obstructive pulmonary disease or COPD. Dr. Reddy's has also sought to de-risk R&D investment by setting up a separate drug development company with equity investment from two leading venture capital companies in India — Citicorp Venture Capital and ICICI Venture Fund. Dr. Reddy's transferred to the new company four NCEs that it had already developed. The new company will be responsible for the clinical development and out-licensing, co-development or joint commercialization of those NCEs.

Table 6: R&D expenditure of NCE R&D companies

	R&D expenditure INR million	Growth rate	As percent of net sales
1996/97	940.7		3.14
1997/98	1076.9	14.48	2.98
1998/99	1573.7	46.13	3.72
1999/2000	1659.1	5.43	3.29
2000/01	3356.3	102.3	5.15
2001/02	4231.7	26.08	5.15
2002/03	6598.8	55.94	6.23
2003/04	9778.6	48.19	7.81
2004/05	13475.8	37.81	10.53
2005/06	16573.1	22.98	11.47
2006/07	17518.2	5.7	9.36
2007/08	17355.8	-0.93	8.18

Source: Author's calculation based on CMIE Prowess data base (see Annex I).

Note: Data in this table are for 11 companies involved in NCE R&D (except Biocon and Fresenius Kabi) (see Table 4) for which data are available for each of these years.

De-risking and reduction of R&D expenditure on NCEs

For Ranbaxy too R&D expenditure declined by about 25 percent from INR 6,393.3 million (17.78 percent) to INR 4,838.2 million (12.18 percent) in 2006/07 (Table 11). Ranbaxy has de-merged its NCE business with the result that expenditure has further declined in 2007/08. The other companies which have de-merged their NCE R&D part include Sun Pharmaceuticals and Piramal Health Care with both showing decline in expenditure in 2006/07. Such de-risking and reduction of R&D expenditure is an indirect admission that NCE R&D has not been working as expected. By separating NCE R&D from the main business, the companies are able to protect the finances from disappointing results. But standalone R&D companies are unlikely to be viable unless there is a stream of prospective molecules bringing in some returns to sustain the activity. And if that were the case, then in it would not have been necessary to 'de-risk' the first place.

No NCE developed by Indian companies has yet been approved for marketing in any country. But as shown in Table 7, 30 NCEs developed by Indian companies are at various stages of clinical trials. Dr. Reddy's and Ranbaxy the largest R&D spenders and which have been very active in NCE R&D have only 2 NCEs each under clinical trials. Some smaller companies have a larger NCE pipeline. Glenmark and Cadila Healthcare have 5 molecules under clinical trials followed by Lupin and Piramal Healthcare with four each.

Indian NCE research and development and neglected diseases

As shown in Table 7, the NCEs being developed by Indian companies are related primarily to 'global diseases' such as diabetes, cancer, heart diseases, asthma, and obesity. These are the diseases that offer much larger and more lucrative market in developed countries (though they are also prevalent in developing countries). The 'neglected diseases' which primarily or exclusively effect developing countries and promise much less financial returns are absent from the list except for malaria and TB. In both these cases, public sector or philanthropic funding is involved. Ranbaxy is participating in an international project sponsored and funded by the Medicines for Malaria Venture (MMV), a public-private partnership to develop a synthetic anti-malarial drug. Lupin is involved in developing an anti-TB drug in partnership with some publicly funded research institutions in India (CIPIH 2006, p. 101). The trend towards R&D for drugs for global diseases is unlikely to change in future. A survey on the R&D plans of Indian companies found that only about 10 percent of the R&D funds are aimed at diseases principally affecting developing countries (CIPIH, 2006, p. 101).

In short, the anticipated benefit of TRIPS that the product patent incentive will prompt local companies to put resources in developing drugs more suited to developing countries has not materialized. In any case even for MNCs research has shown that TRIPS has provided little incentive for R&D in neglected diseases (CIPIH). Indeed the positive impact of patents on R&D in general is being increasingly questioned and alternatives are being talked about (see Baker 2004 for a review of some of the proposals).

In any case, strong patent protection has traditionally been seen as unnecessary until relatively late in a country's development process. Developing countries are net users, not net developers of R&D intensive products. Penrose (1951) and some later studies, including Vaitsos (1972) and Greer (1973) have argued that developing countries lose by granting patent protection. For such countries, these studies contend, the costs of patent protection actually outweigh the benefits. Developing countries suffer from higher prices resulting from patent monopolies. And the benefits of technological progress which are supposed to follow from patent protection take place in developed countries, not in developing countries.

V Financial Performance and Business Strategies

The Indian pharmaceutical industry has performed well since the beginning of the TRIPS regime, not only in terms of growth in the domestic and export markets and R&D expenditure but also financially. The profit margin of the entire industry based on our sample of 166 CMIE companies (see Annex I) has increased from 16.13 percent to 17.65 percent between 1994/95 and 2007/08 and the return on equity from 16.85 percent to 20.23 percent during the same period. Return on assets has gone down marginally from 12.21 percent to 11.22 percent. The profitability of the Indian pharmaceutical industry in fact has been substantially higher than in other industries such as textiles, food and beverages, transport equipment, machinery (Dhar and Gopakumar

Table 7: NCEs under Clinical Trials, Indian Pharmaceutical Companies

Company	NCE	Indication	Development stage
Cadila Healthcare	ZY11	Pain	Phase II
Cadila Healthcare	ZYH2	Diabetes	Phase I
Cadila Healthcare	ZYH1	Dyslipidemia	Phase II
Cadila Healthcare	ZYH7	Dyslipidemia	Phase I
Cadila Healthcare	ZYO1	Obesity/diabetes	Phase I
Dabur	DRF 7295	Anti-cancer	Phase II
Dr. Reddy's Labs	DRF2593	Diabetes	Phase III (partner Rheoscience, Denmark)
Dr. Reddy's Labs	DRF1042	Anti-cancer	Phase I (partner Clintec International. UK)
Glenmark	GRC8200	Diabetes	Phase II
Glenmark	GRC6211	Osteoarthritis, pain	Phase II
Glenmark	GRC3886	Asthma/COPD	Phase II
Glenmark	GRC10693	Neuropathic pain	Phase I completed
Glenmark	GRC 4039	Rheumatoid Arthritis	Phase I
Lupin	LL3348	Anti-psoriasis	Phase II
Lupin	LL3858	Anti-TB	Phase I
Lupin	LL2011	Anti-migraine	Phase III
Lupin	LL4218	Anti-psoriasis	Phase II
Nicholas Piramal	P276	Anti-cancer	Phase II
Nicholas Piramal	P 1448	Anti-cancer	Phase I
Nicholas Piramal	P 1736	Diabetes	Phase I
Nicholas Piramal	P 1201	Diabetes	Phase I
Orchid	BLX1002	Diabetes	Phase II
Ranbaxy Labs (jointly with MMV)	RBx11160	Antimalarial	Phase II
Ranbaxy	RBx10558	Statin	Phase I
Sun Pharmaceutical Industries	SUN 1334H	Anti-allergy	Phase II
Wockhardt	WCK771	MRSA, resistant infection	Phase II
Wockhardt	WCK1152	Respiratory infections	Phase I
Biocon	IN-105	Diabetes (oral insulin)	Phase II
Biocon	T1h	Oncology inflammation	Phase II
Suven	SUVN 502	Neurodegenerative	Phase I

Source: Company annual reports and websites, accessed April, 2009.

2006, p. 33). But the Indian pharmaceutical industry is very heterogeneous. In Annex I, we have tried to classify the industry into different groups in terms of size of sales, size of exports, size of R&D expenditure and whether they are domestic market oriented or export market oriented. Whether we take the net profit margin or return on equity or return on assets as indicators of financial performance, a similar trend is observed. The larger and export oriented companies have done much better than the smaller and domestic market oriented companies.

Net profit margin

The net profit margin of the top 50 companies was 18.39 percent and that of the remaining 116 companies, 10.65 percent during the period 2006/07 and 2007/08. The profit margin of the smallest 50 companies is in even lower at 9.15 percent and that of the top 10 companies higher at 20.07 percent (see Table 8).

For the domestic market oriented companies, the net profit margin is 12.81 percent. This is lower than the margin of export oriented companies, which is 18.45 percent. The profit margin of the major exporters is higher at 19.09 percent. The exporters to the US, i.e. the ANDA and DMF groups, have similar profit margins at 18 to 19 percent.

The profit margin of the major R&D spenders is 18.92 percent which is higher than the remaining group which stands at 12.22 percent.

Between 1994/95 and 2007/08, we observe substantial fluctuations for all groups. If we compare the annual average of 1994/95 and 1995/96 with that of 2006/07 and 2007/08, we see that profit margin has improved from 16.13 percent to 17.65 percent, i.e., by 9.45 percent for the industry as a whole. The profit margin has improved also for the top 50 companies, domestically oriented companies, top exporters and top R&D spenders (Table 8). But while the profit margin of the top 50 companies has increased by 8.02 percent, there has been a significant deterioration for the remaining 116 companies — with profit margins declining by 23.66 percent. For the smallest 50 companies, the decline is even more severe (-46.28 percent). Similarly there has been a decline

Table 8: Profit Margin of groups of Indian pharmaceutical companies

	Average, 1994/95 and 1995/96	Average, 2006/07 and 2007/08	Growth rate
All CMIE companies (166 companies)	16.13	17.65	9.45
Top 10 CMIE companies	20.48	20.07	-1.99
All CMIE companies other than top 10	13.57	15.21	12.13
Top 50 CMIE companies	17.03	18.39	8.02
All CMIE companies other than top 50	13.95	10.65	-23.66
Smallest 50 CMIE companies	17.03	9.15	-46.28
Domestic market oriented	11.89	12.81	7.71
Export market oriented	17.75	18.45	3.94
Major R&D spenders	17.57	18.92	7.69
Other R&D spenders	13.61	12.22	-10.24
Major exporters	17.79	19.09	7.33
Other exporters	13.47	12.45	-7.53

Source: Calculated from CMIE Prowess data base as explained in Annex I.

Table 9: Return on equity of groups of Indian pharmaceutical companies

	Average, 1994/95 and 1995/96	Average, 2006/07 and 2007/08	Growth rate
All CMIE companies (166 companies)	16.85	20.23	20.05
Top 10 CMIE companies	17.20	22.72	32.13
All CMIE companies other than top 10	16.51	17.22	4.27
Top 50 CMIE companies	17.65	21.07	19.43
All CMIE companies other than top 50	14.67	9.95	-32.17
Smallest 50 CMIE companies	13.41	2.21	-83.50
Domestic market oriented	13.61	17.51	28.67
Export market oriented	17.66	20.54	16.29
Major R&D spenders	17.87	21.03	17.66
Other R&D spenders	14.66	15.14	3.27
Major exporters	17.79	21.20	19.14
Other exporters	14.95	15.27	2.15

Source: Calculated from CMIE Prowess data base as explained in Annex I.

Table 10: Return on assets of groups of Indian pharmaceutical companies

	Average, 1994/95 and 1995/96	Average, 2006/07 and 2007/08	Growth rate
All CMIE companies (166 companies)	16.85	20.23	20.05
Top 10 CMIE companies	17.20	22.72	32.13
All CMIE companies other than top 10	16.51	17.22	4.27
Top 50 CMIE companies	17.65	21.07	19.43
All CMIE companies other than top 50	14.67	9.95	-32.17
Smallest 50 CMIE companies	13.41	2.21	-83.50
Domestic market oriented	13.61	17.51	28.67
Export market oriented	17.66	20.54	16.29
Major R&D spenders	17.87	21.03	17.66
Other R&D spenders	14.66	15.14	3.27
Major exporters	17.79	21.20	19.14
Other exporters	14.95	15.27	2.15

Source: Calculated from CMIE Prowess data base as explained in Annex I.

though less severe for the smaller exporters (-10.24 percent) and smaller R&D spenders (-7.53 percent). Profit margin has declined also for the top 10 companies, though marginally by 1.99 percent.

Return on Equity and Return on Assets

In Tables 9 and 10, we have analyzed these two ratios. The results as we have said are basically the same — the larger companies and the export oriented companies have done much better. Not only is the return on equity higher (21.07 percent) for the top 50 companies compared to the remaining companies (9.95 percent) during 2006/07 and 2007/08. Whereas the ratio declined for the latter by 32.17 percent between 1994/95–1995/96 and 2006/07–2007/08, it increased by 19.43 percent for the former. Similar trends are noted for export oriented and R&D intensive companies.

But the large and the export oriented companies are of diverse types and involved in different activities. Aggregate figures hide some important differences in the strategies adopted by different companies. The next section highlights these different strategies through case studies of key companies.

VI CASE STUDIES

While examining the different strategies and outcomes for key companies in the Indian pharmaceutical industry, one can think of a value chain as below in terms of risks and returns:[72]

1. NCEs
2. New Drug Discovery Systems
3. Patent challenges
4. Technology intensive drugs
5. Contract manufacturing and partnerships
6. Vanilla (simple) generics
7. Branded formulations in semi-regulated markets
8. Perfectly competitive semi-regulated API markets

The development of NCEs is at the top of the value chain, promising the highest return but also involving high investments and risks. Perfectly competitive API markets in semi-regulated markets would be at the other extreme providing least returns. In between there are different types of markets and opportunities depending on the entry barriers and the investments.

Indian pharmaceutical companies can be differentiated not only in terms of the development of NCEs as done in Section IV above, but also in terms of the importance accorded to and the extent of involvement in different stages in the value chain. As companies try to move up the value chain, higher returns are expected, but so are higher investments and greater risks. Ranbaxy and Dr. Reddy's have pursued a 'high-risk-high-gain' strategy, while Cipla, the other company in the group of "Big three", has opted for a 'safer' strategy. Ranbaxy, Dr. Reddy's and Cipla are respectively the 9th 10th and 11th largest generics companies in the world.[73] These companies have dominated the Indian pharmaceutical industry in almost every respect. They have greatly influenced the strategies adopted by other companies. This section discusses the differences in strategies and outcomes for each of these three companies.

Ranbaxy

Ranbaxy is the largest pharmaceutical company in India (in terms of consolidated sales). Overseas markets account for 80 percent of its total sales. It has 23 subsidiaries in 13 countries including India and 15 manufacturing plants spread over eight countries, including India.[74]

Formulations and bulk drugs: The beginning

Ranbaxy started with formulations manufacturing and diversified to bulk drugs in the 1970s. It set up an API plant in 1973 immediately after the abolition of product patents in India in pharmaceuticals and became one of the early Indian companies to take full advantage of the Patents Act, 1970 to develop processes for

72 This is a slightly modified version of the value chain discussed in "India Pharmaceuticals: Formula for Growth", *SSKI India Research*, 3 March 2004., p. 5.

73 *The World Generic Market Report 2009, Volume 1: Global Overview and Company Profiles*, Espicom Business Intelligence, p. 56.

74 Unless otherwise indicated, information has been obtained from Ranbaxy Ltd.'s Annual Reports and official website (*www.ranbaxy.com*).

manufacturing drugs and marketing them. Its major successes at the time included the development of a new process for manufacturing *doxycycline* in 1978 and *ranitidine* in 1985. *Ranitidine* was the world's largest selling drug at that time. But the breakthrough which earned Ranbaxy international recognition was the development of a non-infringing process for manufacturing *cefaclor*.[75] *Cefaclor* is a complex molecule and Eli Lilly protected it through 32 processes. Ranbaxy managed to develop a new and superior process in 1992.[76]

After consolidating its position in the domestic market, Ranbaxy started exploring export opportunities in the 1980s. In 1985, exports constituted only 7.4 percent of total sales. Throughout the 1980s and the early 1990s, the focus was on the semi-regulated markets of South East Asia, West Africa and Eastern Europe, particularly the erstwhile Union of Soviet Socialist Republics (USSR) and China. Exports expanded rapidly growing at an annual rate of more than 30 percent. It was not before the mid-1990s when exports (mainly to semi-regulated markets) had already contributed to about 40 percent of its sales that Ranbaxy ventured to enter the US market seriously.[77]

Transitioning to a "research-based" company

In 1993, Ranbaxy announced its mission of becoming a "research based international pharmaceutical company" and steps were initiated to reposition the company along three important dimensions:

- From developing markets to developed markets
- From bulk drugs and intermediates towards formulations
- From reverse engineering products towards original research[78]

As a senior official of Ranbaxy explained, the restructuring exercise undertaken was a conscious response to the General Agreement on Tariffs and Trade (GATT) Uruguay round of multilateral negotiations. It was clear by then that a product patent regime would soon be introduced in India and elsewhere and the global trading rules would change.[79]

In line with this mission, a new research centre was established in 1994 and R&D expenditure was increased significantly and steadily from INR 365.8 million in 1994/95 to INR 771.2 million in 2001/02. Thereafter there was a quantum jump to INR 1,921.7 million (5.71 percent of net sales) in 2002/03 and to INR 6,393.3 million (17.78 percent) in 2005/06 (see Table 11). Ranbaxy's first successful NDDS product was an oral once-a-day formulation of *ciprofloxacin*, the marketing rights of which it licensed out in 1999 to the innovator company, Bayer. Other than this, however, there were hardly any other returns from the huge R&D investments Ranbaxy was making.

Setting up regional headquarters

To push its growth in regulated markets, Ranbaxy established regional headquarters in the mid-1990s in the UK and US. It acquired a manufacturing unit (Ohm Laboratories) in the US in 1995, started marketing

75 Raizada 2002.

76 Ranbaxy Laboratories Ltd and Management Development Institute n.d., "Ranbaxy Laboratories Ltd: On its way to becoming a Research-based International Pharmaceutical Company."

77 Raizada 2002; Ghemawat and Kothavala 1996.

78 Ghemawat and Kothavala 1996.

79 Raizada 2002.

products in the US under its own name in 1998 and started filing DMFs and ANDAs. The most significant was the ANDA related to *cefuroxime axetil* which has two physical forms — amorphous and crystalline. Ranbaxy challenged GSK's patent on the amorphous form by developing an innovative crystalline product. GSK filed an infringement suit but Ranbaxy was able to demonstrate that its version of the product was different from the product patented by GSK and became the first generic company to received manufacturing and marketing approval for the product in February 2002 from the USFDA.[80] This became the first USD 100 million product of Ranbaxy in the US in 2002.[81]

Challenging patents in the US

Enthused by this success and also the success of Dr. Reddy's in getting 180-day exclusive marketing rights for *fluoxetine*, 40 mg capsules in 2001, Ranbaxy started pursuing the strategy of aggressively challenging patents. By 2006 it had filed 197 ANDAs with 76 ANDAs pending, of which 20 were first to file Para IV ANDAs. It challenged the patents of several big MNCs such as Pfizer, Abbott, AstraZeneca, Wyeth, GSK and Astella. This increased its litigation costs tremendously but the rewards have been disproportionately less (Care Research n.d., p. 36). It tasted success only in the case of *Simvastatin* 80 mg tablets for which it obtained 180-day exclusivity in 2006 while for some of the others the company reached out of court settlements with innovator companies. In 2007, it reached settlements with GSK for *valacyclovir* (marketed by GSK as Valtrex) and with Boehringer Ingelheim/Astellas for *tamsulosin* (marketed by Boehringer Ingelheim as Flomax). In 2008 it reached settlements with Pfizer for *atorvastatin* (marketed by Pfizer as Lipitor) and AstraZeneca for *esomeprazole* (marketed by AstraZeneca as Nexium). While *valacyclovir* and *tamsulosin* could be marketed in 2009 and 2010 respectively under the agreements, the company will have to wait till November 2011 for *atorvastatin* and May 2014 for *esomeprazole*.[82]

Ranbaxy led the trend among some of the larger Indian companies to set up their own selling and distribution networks primarily in semi-regulated markets but also in some regulated markets. Perhaps they were prompted to do so in view of their marketing success in the domestic market. But Ranbaxy was not able to develop the scale to justify the high entry costs in marketing.[83]

Acquiring generic companies

To grow more rapidly and increase its geographical presence, Ranbaxy also started acquiring companies abroad. In 2004, it took over RPG (Aventis) in France and the following year acquired the generic product portfolio from EFARMES in Spain. In 2006 this inorganic growth accelerated with the acquisition of the unbranded generic business of GSK in Italy and Spain, of Be-Tabs Pharmaceuticals, the 5th largest generic company in South Africa for USD 70 million and of Teraparia, the largest independent generic company in Romania for USD 324 million.[84]

80 "US Federal Circuit vacates injunction against Ranbaxy Laboratories in patent infringement matter", in *www.wptn.com*.

81 The product was instrumental in the increase of 162 percent of sales of Ranbaxy in USA from USD 113 in 2001 to USD 296 in 2003. Ranbaxy became among the top 10 generic companies in the US (See Ranbaxy Laboratories Ltd, *Annual Report, 2002*).

82 Annual Reports, 2007 and 2008.

83 "Recent MNC Alliances: Signaling Paradigm Shift?", *IDFC-SSKI India Research*, 30 June 2009.

84 "Milestones", *www.ranbaxy.com*.

Financial troubles begin

Eventually, the increasing expenditure on risky R&D, patent challenges with inadequate returns and high entry costs in foreign markets took its toll on the financial health of the company. It reduced its R&D expenditure by 24 percent in 2006/07 and another 5 percent in 2007/08. R&D expenditure as a percentage of net sales reduced as a result from 17.78 percent in 2005/06 to 11.29 percent in 2007/08 (see Table 11). Its net sales declined from INR 41,577.7 million in 2003/04 to INR 40,799.6 million in 2007/08 (see Table 12). Its profits after tax or PAT in 2007/08 (INR 6177.2 million) is still below the level of INR 7,947.7 million in 2003/04 (see Table 13).

The Buy-out

The inability to cope up with these financial troubles is believed to be an important factor behind the decision of the Indian promoters of Ranbaxy, the Singh family, to relinquish their control to Daiichi Sankyo. This may have been good for Ranbaxy which needed an influx of funds but whether this has a positive impact from the point of view of access to medicines is questionable. Ranbaxy's activities may be re-oriented to suit the interests of the MNC that acquired it rather than the generic requirements of developing countries (Ministry of Commerce & Industry, 2008, pp. 42-43).

Table 11: R&D Expenditure of Ranbaxy, Dr. Reddy's and Cipla

	Ranbaxy		Dr. Reddy's		Cipla	
	INR million	Percentage of net sales	INR million	Percentage of net sales	INR million	Percentage of net sales
1994/95	365.8	4.92	39.8	2.2	NA	NA
1995/96	457.9	4.94	53.4	2.74	NA	NA
1996/97	498.7	4.58	78.3	3.47	163	3.83
1997/98	522.8	4.06	70.7	2.37	206.8	4.26
1998/99	456.4	2.85	94	2.49	240	4.02
1999/2000	553.9	3.1	132.7	3.04	300.2	4.26
2000/01	733.9	3.91	415.4	4.53	409.2	4.17
2001/02	771.2	3.73	1017.6	6.25	467.6	3.64
2002/03	1921.7	5.71	1634.9	10.11	NA	NA
2003/04	2761.3	6.64	2260.5	12.86	565	2.94
2004/05	3996.6	9.58	2977.9	17.95	983.8	4.37
2005/06	6393.3	17.78	2539.5	11.35	1554	5.23
2006/07	4838.2	12.18	2928	6.71	1757.3	4.94
2007/08	4605.1	11.29	3334.5	8.82	2323	5.54

Source: Author's calculation based on CMIE Prowess data base.

Dr. Reddy's Laboratories

A remarkable similarity is observed between the strategy followed by Ranbaxy and Dr. Reddy's. Dr. Reddy's was set up in 1984.[85] It started with bulk drugs and made a quick transition from the domestic market to European markets and then to the US and Japan. It started formulations in 1987 and again diversified to semi-regulated markets, such as Russia, very soon. Like Ranbaxy, Dr. Reddy's too opted for an aggressive growth strategy. The development of NCEs started in 1993 and work on a generics facility dedicated to the US market began the following year. It filed the first ANDA for *ranitidine* in 1997 and in 2001 became the first Indian company to get 180-day exclusivity for *fluoxetine* 40 mg capsules.

This was a major success as noted above and net sales for the company more than doubled from INR 4,360.1 million in 1999/2000 to INR 9,172.2 million in 2000/01 (see Table 12). As of 31 March 2005, Dr. Reddy's had 49 ANDAs pending with 29 para IV ANDAs. During 2006/07, it had 7 para IV ANDAs out of the 33 ANDAs pending and during 2007/08, 10 para IV ANDAs out of the 19 ANDAs pending. But like Ranbaxy, it suffered several setbacks in the patent litigations that ensued. Among the major patent challenges it lost were against AstraZeneca's patent on *omeprazole* and Pfizer's patent on *amlodipine maleate*.

It received its second success of 180-day exclusivity in 2006 for *ondenesetron hydrochloride* tablets which increased its sales by 94.98 percent in 2006/07 making it India's largest company (on a consolidated basis). But sales again dropped next year by 13.27 percent (see Table 12).

Dr. Reddy's first overseas acquisition was BMS Laboratories and its subsidiary, Meridian Helthcare in UK in 2002. In the last few years mergers and acquisitions have accelerated. Dr. Reddy's acquired Roche's API Business at the state-of-the-art manufacturing site in Mexico with a total investment of USD 59 million in November 2005 (Espicom 2009, p. 101). This was done during the year (2004/05) when its sales declined by 5.64 percent (Table 12) and the chairman of the company justified it (in the *Annual Report, 2005-06*) by saying that was part of their conscious strategy and in fact attributed its recovery in 2005/06 partially to it. But perhaps the company went too far. In March 2006, it acquired Betapharm- the fourth-largest generics company in Germany for a total enterprise value of €480 million in March 2006, the biggest acquisition ever in the pharmaceutical industry in India. But since the Betapharm acquisition, Germany has witnessed severe generic price cuts due to some regulatory initiatives putting the company in a very difficult financial situation.

As in the case of Ranbaxy, huge investments in R&D, patent challenges and acquisitions but inadequate return led to severe decline in profitability. Its R&D expenditure increased moderately from INR 39.8 million in 1994/95 (2.2 percent of net sales) to INR 132.7 million (3.04 percent) in 1999/2000. Since then, the expenditure accelerated to INR 1,634.9 million (10.11 percent) in 2002/03 and then to INR 2977.9 million (17.95 percent) in 2004/05. Thereafter the R&D expenditure declined in absolute terms in 2005/06 and in 2007/08 it is only 8.82 percent of net sales (Table 11). Its profits after tax declined from INR 4,596.5 million in 2001/02 to INR 654.6 million in 2004/05. Since then there has been some improvements. But its profit after tax (PAT) continues to fluctuate — it declined in 2007/08 after showing a dramatic increase the previous year (see Table 13).

Unlike Ranbaxy, however, the company has not been bought out. The company has re-worked its strategy. As discussed, it has opted for a collaborative R&D model reducing its investments and risks. It has also tied

85 This account of Dr Reddy's is primarily based on information obtained from its Annual Reports and website (*www.drreddys.com*).

Table 12: Net Sales of Ranbaxy, Dr. Reddy's and Cipla

	Ranbaxy		Dr. Reddy's		Cipla	
	INR million	Growth Rate	INR million	Growth Rate	INR million	Growth Rate
1994/95	7431.8	13.61	1811.9	12.76	2788.4	21.54
1995/96	9260.7	24.61	92607	7.68	92607	20.78
1996/97	10880.5	17.49	108805	15.79	108805	26.21
1997/98	12877.8	18.36	128778	31.78	128778	14.18
1998/99	15988.4	24.15	159884	26.81	159884	22.88
1999/2000	17847.2	11.63	178472	15.49	178472	18.17
2000/01	18790.3	5.28	187903	110.37	187903	39.21
2001/02	20679.7	10.06	206797	77.52	206797	30.98
2002/03	33647.1	62.71	336471	-0.71	336471	13.52
2003/04	41577.7	23.57	415777	8.75	415777	31.65
2004/05	41725.5	0.36	417255	-5.64	417255	17.26
2005/06	35956	-13.83	359560	34.81	359560	31.88
2006/07	39729.3	10.49	397293	94.98	397293	19.72
2007/08	40799.6	2.69	407996	-13.27	407996	18.04

Source: Author's calculation based on CMIE Prowess data base.

up with innovator companies in both US and non-US markets. Quite in contrast to its aggressive patent challenges model, it has acted as an authorized generic partner of innovator companies and has opted for out-of-court settlements.

Cipla

In contrast to Ranbaxy and Dr. Reddy's, Cipla has been pursuing a very safe model. Like Ranbaxy and Dr. Reddy's, Cipla is;

- A large integrated company manufacturing both APIs and formulations;
- A strong player in the domestic formulations market; but is also
- Export oriented

But unlike Ranbaxy and Dr. Reddy's, it has opted for a safe business model. Cipla:

- Has not acquired any foreign enterprises;
- Has no manufacturing plants abroad (except for some joint ventures in Africa);
- Undertakes no investments in setting up its own sales and distribution networks abroad; and
- Undertakes no R&D for NCE

Cipla has avoided huge investments in acquiring companies abroad or setting up its own marketing infrastructure or fighting patent cases. The main component of its strategy has been to serve export markets

Table 13: Profit after tax of Ranbaxy, Dr. Reddy's and Cipla

	Ranbaxy		Dr. Reddy's		Cipla	
	INR million	Growth Rate	INR million	Growth Rate	INR million	Growth Rate
1994/95	1100.6		400.1		285.4	
1995/96	1404.8	27.64	501.7	25.39	289.6	1.47
1996/97	1605.3	14.27	337	-32.83	707.5	144.3
1997/98	1741.7	8.5	488.4	44.93	1019.7	44.13
1998/99	1498.7	-13.95	517.6	5.98	1149.5	12.73
1999/2000	1935.8	29.17	603.2	16.54	1330.6	15.75
2000/01	1806.1	-6.7	1444.7	139.51	1790.7	34.58
2001/02	2624.3	45.3	4596.5	218.16	2076.3	15.95
2002/03	4784.7	82.32	3920.9	-14.7	2477.4	19.32
2003/04	7947.7	66.11	2832	-27.77	2955.9	19.31
2004/05	5275.2	-33.63	654.6	-76.89	4096.1	38.57
2005/06	2120.4	-59.8	2111.2	222.52	6076.4	48.35
2006/07	3951.2	86.34	11768.6	457.44	6680.3	9.94
2007/08	6177.2	56.34	4752.2	-59.62	7014.3	5

Source: Author's calculation based on CMIE Prowess data base.

through partnerships and alliances mainly with foreign generic companies.[86] In the US, for example, Cipla has typically concentrated on developing processes and manufacturing, leaving regulatory filings, marketing and legal matters to foreign partners. Its filings have typically been only for DMFs with ANDA filings being more recent. And as can be seen from Table 14, it has only 12 ANDAs compared to Ranbaxy's 244 and Dr. Reddy's 140 ANDAs. Of course in such cases, margins would be much lower as profits would be shared between the partners. Cipla, in fact never achieved spectacular successes as Ranbaxy and Dr. Reddy's did in patent challenges. But it also did not experience failures the way the other two companies did. In fact Cipla's growth path has been much more stable. Cipla's R&D budget is much less than that Ranbaxy and Dr. Reddy's. It has been slow in increasing its R&D budget from 3.83 percent of net sales in 1996/97 to 5.54 percent in 2007/08. But it did not face the disruptions that Ranbaxy and Dr. Reddy's witnessed in their R&D spending in recent years (see Table 11). Its sales growth too has fluctuated less than the other two companies. Sales never declined in absolute terms the way they did for Ranbaxy and Dr. Reddy's (see Table 12). It also never experienced any fall in its PAT as the other two (see Table 13).

As shown in Table 14, in terms of profitability ratios (profit margin, return on equity and return on assets), Cipla's performance has been more stable but no less rewarding overall and it has been able to prevent any sharp fall in profit margins. Its average profit margin during the last three years (2005/06 to 2007/08) is also higher than that of Ranbaxy and Dr. Reddy's.

86 Espicom 2009, pp. 81-4; "Recent MNC Alliances: Signaling Paradigm Shift?", IDFC-SSKI India Research, 30 June 2009.

Table 14: Net profit margin, return on equity and return on assets of Ranbaxy, Dr. Reddy's and Cipla

	Ranbaxy			Dr. Reddy's			Cipla		
	P-m	R-e	R-a	P-m	R-e	R-a	R-m	R-e	R-a
1994/95	21.14	17.12	12.56	24.25	16.38	15.1	14.71	29.81	15.69
1995/96	20.1	17.32	12.71	29.27	17.07	15.54	13.87	13.66	12.13
1996/97	20.93	13.96	12.01	19.3	11.2	10.71	19.92	25.76	20.64
1997/98	19.95	13.54	12.26	19.89	14.33	13.02	21.8	27.99	19.29
1998/99	14.62	10.7	10.72	17.11	13.48	11.08	20.04	24.86	16.91
1999/2000	15.4	12.92	12.29	17.58	13.86	11.31	19.27	23.12	16.35
2000/01	12.99	11.41	10.22	20.48	26.11	17.62	18.52	24.71	17.4
2001/02	14.99	16.33	12.29	29.1	31.53	25.99	16.47	23.33	14.96
2002/03	14.98	25.54	17.62	24.63	21.7	17.24	17.29	23.15	13.88
2003/04	19.31	34.26	21.94	16.35	13.83	10.71	16.09	23.38	13.92
2004/05	12.91	21.04	12.71	4.71	3.16	2.62	18.71	26.36	16.13
2005/06	6.63	8.92	4.92	10.54	9.33	6.05	21	30.64	18.03
2006/07	11.42	16.82	6.39	28.39	26.91	21.35	19.1	20.64	15.39
2007/08	17.43	24.35	8.93	13.25	9.88	7.69	17.14	18.68	12.55

Source: Author's calculation based on CMIE Prowess data base.

Notes: P-m: Net profit margin; R-e: Return on equity; R-a: Return on assets

There seems to be a difference between Ranbaxy and Dr. Reddy's on the one hand and Cipla on the other regarding the attitude towards intellectual property rights. The former have accepted the new patent regime passively and have been exploring aggressively opportunities in generic exports and new drug R&D to compensate for the loss of the domestic market. Cipla has consciously avoided new drug R&D. It has successfully expanded its exports. But Cipla has consistently maintained that product patent protection will have negative consequences both for the industry and the consumers. Its Chairman and Managing Director, Y. K. Hamied has argued that in the long run with the full implementation of TRIPS, the loss of domestic markets will put severe strain on the Indian generic companies and exports will not be able to compensate for this loss. In fact the lack of dynamism in the domestic market will adversely affect exports.[87]

In line with such an outlook, Cipla has continued to challenge MNC patents in India for a larger domestic space. Cipla has not only filed pre-grant oppositions against patent applications but is also opposing granted patents. Roche has filed infringement suits against Cipla for alleged infringement of its patents relating to *erlotinib* and both are involved in protracted legal proceedings over the patent on *valganciclovir*. While the court decisions have not been unfavourable to Cipla, if Roche is granted the patents, Cipla shall have to pay damages. This is the risk Cipla has undertaken in India unlike in the export markets such as the US.

87 See the interview given by Hamied to India Knowledge@Wharton as late as 7 May 2009 (accessed from *www.cipla.com*).

Interestingly enough, in the post-TRIPS situation, Cipla, which is more critical about the benefits of TRIPS, has done much better than Ranbaxy or Dr. Reddy's.

Other companies

In Tables 15 and 16, we have considered a few other companies. Of these, Sun Pharmaceuticals has done exceedingly well with its net sales expanding more than 30 percent per annum in the last three years (Table 15) and even faster profit growth (Table 16). Like Cipla, it has pursued the domestic market very aggressively but like Ranbaxy and Dr. Reddy's it has also taken some risks though its approach to both the scale and nature of these risks has been much more measured. Glenmark is another interesting case study. In terms of strategy it is very similar to Ranbaxy and Dr. Reddy's and is the only Indian company which has made some gains by licensing out molecules developed by it. Such returns were used for expansion abroad but, unlike Ranbaxy or Dr. Reddy's, it has avoided costly litigations with the MNCs. Its strategy has been 'small-gain-small-risks'. It has acquired companies abroad but in countries such as Brazil and Poland where the cost of acquisitions are much less. It has targeted markets which may be small now but have prospects for growth in the future. In the US market it has gone for para IV ANDAs but not those with high stakes.[88] Until 2007/08, it has been able to avoid the type of financial difficulties which these two companies faced. In fact it did extremely well with sales and profits increasing at hyper rates (Tables 15 and 16). In 2007/08, net sales increased by 72 percent and profits after tax by 189 percent. But in 2008/09, sales declined by 38 percent and profits after tax by 44 percent. It also could not sustain its growth of R&D expenditure. It has declined by about 6 percent in 2008/09.[89]

Among the other larger companies that have faced financial difficulties are Wockhardt and Matrix. As shown in Table 16, PAT of both these companies have been decreasing since 2005/06. Matrix incurred a loss in 2007/08 and Wockhardt the next year (INR 3487 million[90]). In both the cases, the problem is largely the fallout of costly foreign acquisitions. Wockhardt has been the worst affected. It went for costly foreign acquisitions primarily funded through foreign currency loans. Rising interest costs, depreciation of the Indian rupee and pricing pressures in the regulated European markets (which account for more than half of its revenue) have put the company in a severe financial crisis. It has not only suffered losses but has been finding it difficult to service its debts and is now undergoing a major corporate re-structuring.[91]

Elder Pharmaceuticals belongs to a different league. It is one of the larger pharmaceutical companies in India with a CMIE rank of 31 (See Annex I). But unlike the general trend in the industry, it is amongst neither the major R&D spenders nor the major exporters. In 2007/08 its exports amounted to only 4.26 percent of its sales. But it has one of the best growth and profitability records. It sales increased by 23 percent in 2007/08 and its profits after tax by 42 percent (Tables 15 and 16). It is basically a domestic formulations company — about one-fourth of turnover comes from in-licensed products. Its strategy has been to first develop in the domestic market and then explore exports. It is only now that the company feels confident of catering to exports market that it is aiming to target the branded generics segment in semi-regulated markets where entry costs are

88 Interview with Achin Gupta, Vice President, Corporate Strategy, Glenmark Pharmaceuticals, Mumbai, 11 May 2009.

89 Glenmark Pharmceuticals, *Annual Report, 2008-09*.

90 Wockhardt, *Annual Report, 2008*.

91 "High interest cost eating into profit of Wockhardt", *Economic Times*, 4 January 2009; "Wockhardt takes a hit on expansion", *Business Standard*, 2 February 2009.

lower. It is consciously avoiding the US market.[92] Elder's example shows that even with a domestic orientation a company can do quite well.

The general picture that comes out from the case studies is that companies which have been able to expand in the domestic market and, at the same time,have avoided high risks in foreign markets and in R&D, have done well.

VII Conclusions and Policy Implications

Our study shows that little has changed to dispute the conventional wisdom that developing countries should not grant product patent protection in pharmaceuticals. They are already paying the cost of high prices of patent protected products without having seen the expected concomitant technological benefits. While R&D activities have diversified, efforts in the full development of NCEs are yet to succeed. There have been several setbacks and the partnership model has not always worked properly. What Indian companies have really demonstrated is the ability to develop generics — an ability acquired and improved during the pre-TRIPS period.

Contrary to what was claimed during the TRIPS negotiations, the product patent regime has not prompted Indian companies to devote more resources to developing drugs for neglected diseases that exclusively or predominantly affect developing countries. The large Indian pharmaceutical companies, who are the major R&D spenders in the country, have been focusing on the larger and the more lucrative developed country markets, particularly the US. In that regard, the primary incentive to invest in R&D, whether for NCEs, for modifications, or for the development of generics, has not been the new TRIPS-compliant product patent regime but the product patent regime in developed countries (and the size of their markets) that was in place well before TRIPS. TRIPS may have accelerated the trend toward such R&D because of the anticipated shrinkage of domestic opportunities. But in the absence of TRIPS, such R&D activities would still have been undertaken. With the larger domestic operations, Indian companies, in fact, would have had access to larger resources and would have been better placed to undertake R&D.

The capacity and capability of Indian generic companies to manufacture drugs has not yet weakened. In the post-TRIPS environment what has been adversely affected is the opportunity for manufacturing new patented drugs. This has made drugs more expensive. Also, the shrinkage of space of operations of Indian generic companies will make their growth tougher and more challenging. The post-TRIPS environment seems to have provided Indian companies enough opportunities to grow. The larger companies which dominate the industry have, in general, been able to improve their financial conditions. But the true impact of TRIPS is yet to be faced. Most of the large companies that have done well have a strong presence in the domestic market. The latter has been expanding very rapidly. Indian companies have been able to enlarge their product baskets aggressively. As of now only a few new patented drugs have been introduced by the MNCs. In the future, depending on the rate of introduction of new drugs, the shrinkage of the domestic space of operations can have a negative impact on Indian companies.

92 Interview with Himanshoo Nayak, General Manager, Business Development, Elder Pharmaceuticals, Mumbai, 12 May 2009.

Exports have expanded rapidly. But the prospect of huge gains in the patent expired markets in developed countries, particularly in the US, have not materialized — significant price erosions have taken place even in the value-added segments of the markets. Some companies which have aggressively pursued growth in foreign markets with high costs and stakes have landed themselves in trouble. Some Indian companies including the largest one, Ranbaxy, have been sold out to foreign companies. Is this the beginning of a trend? Perhaps it is too early for a categorical answer to this question. But one hardly heard of such takeovers in the pre-TRIPS environment when a space was guaranteed for the generic companies to grow. Depending on the shrinkage in domestic operations, more and more companies may experience difficulties and the sellout to MNCs may not be exceptions unless public policies are adopted within or without TRIPS to improve the environment. Smaller or less ambitious companies may be content with whatever space is available including outsourcing deals with MNCs. But as in the case of Ranbaxy, if a good bargain can be struck for the price of the shares, an outright sale may turn out to be a preferred option for several players in the industry (Chaudhuri, 2008(b)). The amount that may satisfy Indian promoters would be quite small compared to the massive resources of the MNCs. A few more Ranbaxy-type takeovers can shatter the confidence of the Indian generic industry and "neutralize the sting out of India's generics revolution" (Ministry of Commerce & Industry 2008, pp. 42-44).

Previously Indian generic companies had what was essentially an antagonistic relationship with MNCs. But competitors have been turning into allies. Collaborative arrangements between them have been on the rise and encompass the entire range of activities — manufacturing, marketing and R&D. The extent of the CRAMS market is still small but the prospects are considered huge for a segment of the industry. If these prospects materialize, they will have a positive impact on the Indian pharmaceutical industry, but an adverse impact on the market structure. In the pre-TRIPS situation, companies could enjoy a larger space through competition with MNCs leading to lower prices. Effectively what Indian companies will be doing now is to help foreign companies economize on costs and contribute to their profits in return for some manufacturing space. It is often argued that the prospects of CRAMS are linked to TRIPS — MNCs will not be keen on partnerships unless the country provides for proper intellectual property rights. This is contestable. The main motivation for MNCs to outsource their requirements is reduction of costs for their global operations. If costs are considered to be important then, even if product patent protection is not provided, MNCs are unlikely to deprive themselves of such low-cost sources. However, the gains of Indian companies would be incomparably small compared to the costs that developing countries would be incurring for the high prices resulting from product patent rights granted to the MNCs. From a public health perspective, such industry gains can hardly be a justification for a country such as India to grant such patent protection.

Policy Implications

The Indian government has played a very important role in the development of the pharmaceutical industry in the country. Not only were product patents abolished in 1972, other aspects of public policy also contributed to the success of the indigenous pharmaceutical sector. Before TRIPS, about 47 other countries also did not provide product patent protection in pharmaceuticals (Nogues, 1990, p. 83), yet the pharmaceutical industry remained under-developed in many of these countries, such as in Ghana, Malawi, Uruguay and Vietnam. These countries lacked the entrepreneurial and technological skills to take advantage of the absence of product patent protection. India is different not only because of the long tradition of drug manufacturing. The entrepreneurial spirit of the indigenous private sector was actively supported through public investments in R&D and manufacturing after India's independence in 1947. The Indian pharmaceutical industry has now

gained maturity. They have demonstrated the capacity and the capability to manufacture proper quality drugs at affordable prices. They may no longer require the type of government support which was necessary, in fact vital, for their early development. But state intervention is still important. Opportunities must be available for utilizing the competencies which Indian generic companies possess.

In the post-TRIPS environment, a proper compulsory licensing system as elaborated below is essential to provide a larger space of operations to generic companies which will in turn drive down prices. As a result both the health policy objective and the industry policy objective will be simultaneously satisfied. A larger space is required not only for the large Indian companies but also the smaller ones. The small scale industry has played a very important role in the Indian pharmaceutical industry. But as discussed above, many small companies are finding it difficult to survive and grow in the changed business environment. An active industrial policy must be pursued for the promotion of the small scale sector.

Preserving generic competition

In the immediate context the stress of the Indian government must be on utilizing fully the flexibilities provided under TRIPS and to also undertake measures which TRIPS does not forbid. Indian law provides for these flexibilities to be used. But India has been under pressure from MNCs and developed countries to dilute some of these flexibilities. It is very important for the Indian legislature not to make any changes in the law and for the Indian judiciary not to interpret the law in a manner which might deprive India from enjoying flexibilities such as section 3(d) which limits secondary patents. India also should not succumb to the demands of data exclusivity and linking patent status to drug regulatory approvals. In fact what should be done is to further tighten the patent law to prevent the tendency of the MNCs of resorting to multiple patenting of the same product. It is also important to minimize patent litigations.[93]

A key area of concern in this regard is the number of FTAs India is currently negotiating; in particular those under negotiation with the EU, the European Free Trade Association (EFTA)[94] and Japan. All these negotiations feature demands for TRIPS-plus provisions by developed partners. The EU, for instance, is demanding among other changes to India's IP system, data exclusivity, patent term extensions and border measures of the sort that led to the seizures of Indian generic medicines by the EU.[95] The negotiations with Japan will probably feature an investment chapter that is likely to place indirect restrictions on the imposition of compulsory licenses by India.[96] As discussed below this is a key safeguard that India must utilize in the coming years to ensure continued generic production. The capitulation by India in any of these agreements to TRIPS-plus measures will have a significant impact on the space for generic competition in India.

93 See 'Address by Dr. Y. K. Hamied, Chairman and Managing Director,' Seventy-Third Annual General Meeting, Cipla, 26 August 2009 (*www.cipla.com*).

94 This comprises the countries of Switzerland, Liechtenstein, Iceland and Norway.

95 See, Draft Chapter on IPR and Goods, EU-India FTA Negotiation Text (*www.bilaterals.org*), February 2009.

96 See, the Japan-Thailand Economic Partnership Agreement and the Japan-Philippines Economic Partnership Agreement for such provisions. The Investment chapters in these agreements recognize intellectual property as investments and provide for market rate compensation if any investment is 'expropriated'. This could include the issue of a compulsory license and if so, the requirement for market rate compensation in these Agreements would in effect nullify the very purpose for which a compulsory license may be issued.

Compulsory Licensing

The most important flexibility that developing countries can utilize is to introduce an easy to use compulsory licensing system. As different studies and reports have highlighted, in a product patent regime, a proper compulsory licensing system is of vital importance to deal with the negative implications of product patent protection on prices. If generic companies are given licenses to produce a patented drug on payment of royalty, then competition among manufacturers would drive down prices, but the royalty paid to the innovators would continue to provide funds and the incentive for R&D (CIPR 2002; Correa 2000). In fact as WHO and WTO (2001, p. 99) point out, compulsory licensing is one of the ways in which TRIPS attempts to strike a balance between promoting access to existing drugs and promoting R&D in new drugs. Compulsory licensing can also be used to take care of the abuse of dominance under competition laws. As CUTS (2006, p. 119) has pointed out, proper coordination is required between the competition authority and the patent office.

As discussed above, the legislative history of the compulsory licensing provisions in India's patent law have resulted in overly procedural provisions for applying for and using compulsory licenses. But as CIPR (2002, p. 44) has stressed, what is often crucial for an effective compulsory licensing system is to have straightforward, transparent and fast procedures. A patent holder will naturally be opposed to any compulsory licenses. The pre-1993 Canadian experience (Box 2) shows how the practice and the procedures can be such that the patentees have no opportunity to delay or prevent the grant of compulsory licenses. But in India that has not been the case. The entire process is excessively legalistic and provides the patentees the opportunity to buy time through litigation. The huge legal expenses involved in fighting the MNCs holding the patents may dissuade generic companies from applying for licenses in the first place. These are not mere theoretical possibilities. This is precisely what happened in India under the Patent and Designs Act of 1911 and what India has inherited after TRIPS. It is important to note that despite the high drug prices in India those days and the urgent need to use compulsory licenses, these could be granted in only two cases before 1972 (Chaudhuri, 2005, chapter 3).

It is important to note that where India's law has what should have been an easy to use compulsory licensing procedure for exports. Indeed, protracted proceedings by the MNC patent holder and the application of this procedure by India's patent office has complicated matters. In any case a review of the August 2003 decision to make the system more user friendly is important to ensure that India's competencies can be utilized for developing countries which lag behind in manufacturing capacities.

Two important TRIPS conditions which are often considered to stand in the way of the fast use of compulsory licenses are that any grant of compulsory licenses must be (i) considered on individual merits (Article 31 (a)) and (ii) subject to review by higher authorities (Article 31(h and j)). As Watal (2001, p. 322) has clarified, consideration of individual merits does not mean patent-by-patent consideration. In fact, while TRIPS was being negotiated, the US did not want the phrase, "each case" to be mentioned because that would have gone against its own law and practice. The procedure can be such that the merits of each case would be the consideration of the royalty rates payable. Again the requirement that any compulsory licensing decision would be subject to review, does not mean that the actual use should be held up till all disputes are settled. TRIPS does not require governments to grant injunctive relief to patent holders (Article 44 (2) (Love, 2001, p. 1). The consideration of any opposition to the royalty rate proposed would satisfy the requirement of review of the compulsory licensing decision. It is also not difficult to issue guidelines about reasonable royalty

BOX 2: Compulsory Licensing for Pharmaceuticals in Canada, 1969–1992

One of the main reasons for the very successful compulsory licensing experience of Canada between 1969 and 1992 was the simple and easy to use procedure. The main features were:

(i) Anyone could apply for a compulsory license — the applicant was not required to prove that he or she was capable or competent to exploit the license and handle the pharmaceutical products.

(ii) To prevent delays, time limits were specified: The Commissioner of Patents would notify the patentee about the application and the latter would have two months to file a counterstatement and affidavit; the Commissioner would take at most 18 months after the date of notification to decide whether or not to grant a compulsory license. Six months after submitting the application, the applicant could petition the Commissioner for a six-month interim license pending the final decision. This was rarely denied.

(iii) The Commissioner had to check whether there was any good reason not to grant a compulsory license. But apart from bankruptcy and false statements, nearly all other arguments were rejected. The compulsory licenses were available almost by asking as a matter of right. The Commissioner seemed to take the view that a compulsory license enhanced competition and reduced prices, and that this formed the conclusive evidence of the fact that normally the grant of compulsory license was in the public's interest.

(iv) As in all laws, appeals against the decision of the Ccommissioner granting compulsory licenses were permitted. But the Federal Court of Appeal never set aside the Commissioner's decision and invariably took the view that it would not interfere with the compulsory licensing decisions of the Commissioner.

(v) In the very first case, the Commissioner fixed a royalty of 4 percent of the net selling price. This was routinely applied in virtually all subsequent cases.

Source: Torremans (1996, pp. 316-19); Reichman and Hasenzahl (2002, pp. 33-38).

payable. Countries such as Japan and Canada have done that and different proposals have also been made by organizations such as UNDP (see Love, 2008, for a review of the issues and some recommendations).

It is of fundamental importance to have a simple and easy way to administer a compulsory licensing system. TRIPS does not prohibit this and the Canadian experience (Box 2) shows how it is possible to have such a system. Under Section 11A(7), generic companies "which have made significant investment" and were manufacturing the product before 1 January 2005 can continue to do so on payment of 'reasonable royalty' even after a patent is granted for the product later. This is a type of compulsory licensing which does not involve case-by-case decision making (T'hoen, 2009, p. 58). Such a provision can be made more general.

The Indian government should also adopt a strategy to use effectively the 'government use' provisions of the Indian patent law. As the World Bank (2003, p. 39) has pointed out, even if the government recovers the cost of drugs fully or partially, such an arrangement will be consistent with TRIPS so long as the government does not seek to make a profit out of it. India has a number of public sector drug manufacturing units. The units, particularly Hindustan Antibiotics Ltd (HAL) and Indian Drugs and Pharmaceuticals Ltd (IDPL), have played a very important role in the development of the pharmaceutical industry in the country. But currently most

of these are in financial distress. A simple but very significant step that the government can take to improve access to essential medicines in the country without violating TRIPS is to utilize the capacities of these public sector units to manufacture patented drugs and supply these through public health care facilities on a no-profit basis. As a part of the Eleventh Five Year Plan (2007-11) initiative, a Working Group (2006, pp. 112-115) of the Planning Commission of India has in fact made a recommendation along similar lines. But no decision has yet been taken.

Addressing pricing

Another flexibility which India can utilize is to control the price of patented drugs. Price control is not forbidden under TRIPS or any other agreement of the WTO. The 'Draft National Pharmaceuticals Policy, 2006' (p. 15) recommended mandatory price negotiations of patented drugs before granting marketing approval and stressed the importance of studying the experiences of Canada, Australia, France and other countries believed to have a good system. In fact a 'Committee on Price Negotiations on Patented Drugs' has been set up in the Department of Pharmaceuticals within the Ministry of Chemicals and Fertilizers. This is an important initiative and efforts should be expedited to initiate measures to control the prices of patented drugs. One important difference between price control measures and compulsory licensing may be noted. The former, if properly implemented, makes drugs more affordable but does not provide any room for generic companies. The latter not only makes the prices more affordable through competition. It also ensures some space to generic companies, which is vital for their long term sustenance.

For drugs to be accessible, however, it is not enough that prices are lower than the patent protected monopoly prices. If those who need the drugs cannot afford even these prices, proper finances should be available to pay for the drugs. Publicly funded healthcare and/or subsidized insurance can both influence prices and shift the financial burden from the poor who are unable to afford the cost themselves, thereby improving accessibility. In India the involvement of government in health care is low and the scope of insurance is grossly inadequate. That is one of the main reasons that access to medicines is among the lowest in India despite the remarkable progress of the pharmaceutical industry (Chaudhuri, 2007a). If the vast majority of the Indian population is to benefit from the capacities and capabilities of the Indian pharmaceutical industry, it is of vital importance that public healthcare and insurance facilities are improved.

TRIPS review

The experience of the Indian pharmaceutical industry also clearly demonstrates that TRIPS has not delivered the benefits that were claimed at the time it was negotiated, as well as \the need for a review of the TRIPS Agreement. The first step towards such a review took place through the WHO's Commission on Intellectual Property, Innovation and Public Health (CIPIH). The CIPIH report recognized clearly that "there is no evidence that the implementation of the TRIPS agreement in developing countries will significantly boost R&D in pharmaceuticals on" diseases predominantly affecting developing and LDCs as well the need for developing countries to utilize TRIPS-flexibilities to ensure access.

This recognition is reflected in the Global Strategy and Plan of Action on Intellectual Property, Innovation and Public Health adopted by the World Health Assembly which mandates WHO members to explore alternative mechanisms and collaborative frameworks for R&D as well as options to ensure access to medicines, including through the use of TRIPS flexibilities and public health oriented models for the collective management of

patent rights. Based on this resolution, steps are underway to establish a patent pool, the success of which depends on the extent to which the MNCs holding the patents will voluntarily want to be a part of the pool. Of course generic companies too must be willing to use the patents on payment of royalties. Collaborative R&D models, such as the Indian Government's Open Source Drug Discovery (OSDD) project for TB and the establishment of prize funds, are also underway.

The WHO process is only the first step in addressing the distortions caused by TRIPS. The enforcement not only of TRIPS but of TRIPS-plus measures through FTAs continues to exert pressures across the developing world. The Indian experience as evidenced in this study, along with that of several other developing countries and LDCs, provides sufficient fodder for a proper review and renegotiation of TRIPS. Indeed with fifteen years of experience with the TRIPS regime, such a review is overdue. UNDP *et. al.* (2003) have urged countries to start negotiations for replacing or fundamentally altering TRIPS. This in fact should be the long term policy objective of developing countries.

CHAPTER 2A:
THE IMPLEMENTATION OF INDIA'S PATENT LAW: A REVIEW OF PATENTS GRANTED BY THE INDIAN PATENT OFFICE

Chan Park ◊

I. Introduction

In 2005, India amended its Patents Act, 1970 to come into full compliance with its obligations under the TRIPS Agreement. As a developing country that did not recognize product patent protection on pharmaceuticals prior to the entry into force of TRIPS on 1 January 1995, India had made full use of the 10-year transition period available under TRIPS to delay the introduction of product patent protection on pharmaceuticals until 2005.[97] Due to the central role that the Indian pharmaceutical industry plays in the supply of affordable generic medicines throughout much of the developing world, grave concerns were raised from both within and without India about the effects that product patent protection on pharmaceuticals would have on continued access to affordable essential medicines.

One of the chief concerns at the time was the growing prevalence of what are known as 'secondary' patents i.e., patents covering various ancillary features of existing medicines. Such secondary patents, often of questionable validity, had been known to be strategically used by patent-holding pharmaceutical companies to 'evergreen' their patent monopoly periods and thus unduly delay the entry of generic competition.[98] Since then, there has been even further confirmation that patent-holding pharmaceutical companies regularly engage in such practices. A recent inquiry into the pharmaceutical sector by the European Commission's Competition authority, for instance, concluded: "Filing numerous patent applications for the same medicine (forming so called 'patent clusters' or 'patent thickets') is a common practice. Documents gathered in the course of the inquiry confirm that an important objective of this approach is to delay or block the market entry of generic medicines" (EC, 2009).

Partly in response to these concerns, the Indian Parliament included some unique provisions in its patent legislation that were designed to ensure that the most common types of such secondary patents are not granted in India. In this respect, India in many ways pioneered the exercise of what had been a largely overlooked TRIPS 'flexibility' — that of setting strict criteria for patentability. Among these provisions was section 3(d) of the Act, which set a showing of a higher level of inventiveness for patent applications relating to "new forms" of already known substances. Despite this and other safeguards in the amended patents law, questions remained about how this and other provisions would be interpreted and implemented by the Indian Patent Office, and how

◊ The author acknowledges with thanks the guidance and assistance of Cecilia Oh, Tenu Avafia, Savita Mullapudi and Luciana Mermet in this study. Mythili Venkatesh of Majumdar & Co. assisted in obtaining the relevant documents from the Patent Offices.

97 See TRIPS, Art. 65.4.

98 See, e.g., USFTC (2002).

effective these provisions would be in preventing the grant of secondary patents.[99] The Indian Patent Office comprises separate offices in four Indian cities, Delhi, Mumbai, Chennai and Kolkata and questions also arose as to the uniform application and interpretation of the new law across these offices.[100]

In the four years since the Patents (Amendment) Act, 2005 ushered in the era of pharmaceutical product patent protection in India, there have been several significant developments that may now allow us to begin to address some of these unanswered questions. For one, the Indian Patent Office has granted a large number of pharmaceutical patents — well over 2000 such patents from 2005 to 2008, according to this study (see below). Second, a significant number of patent disputes — both in the various Patent Offices and in the courts — have been concluded, and the reported decisions have begun to lay out both legally binding and persuasive precedent on how these provisions should be interpreted. Lastly, although much more needs to be done, the Indian Patent Office has finally embarked on the process of increasing the transparency in its functioning, including making some patent office decisions available online.[101]

This chapter presents and discusses the findings of a study of four years of the implementation of the product patent regime in India by the Indian Patent Office. Specifically, the study focused on (1) an analysis of the published 'mailbox' patent applications relating to pharmaceutical products that were filed during the 10-year transition period from 1995 to2005; and (2) a closer examination into how the provisions included in Indian law designed to prevent evergreening have, in practice, been interpreted and implemented by the Indian Patent Office.

II. A brief background of Indian patent law

Prior to the entry into force of TRIPS in 1995, India, like several other developing countries at the time, did not recognize product patent protection on pharmaceuticals. The substance of the original Patents Act, 1970, was largely based on the recommendations of a report of a commission chaired by the jurist Rajagopala Ayyangar in 1959. The Report, which came to be known as the 'Ayyangar Report', recommended a vast overhaul of the Indian patent system, observing that the system in place at the time "has failed in its main purpose, namely, to stimulate invention among Indians and to encourage the development and exploitation of new inventions for industrial purposes in the country so as to secure the benefits thereof to the largest section of the public" (Ayyangar, 1959). That system was the patent law India inherited from the British which provided strong patent protection and rights including product patent protection.

In discussing the costs and benefits of a patent system, Ayyangar observed that simply having a patent system in place is insufficient to promote innovation and economic development:

99 For instance, a question left unresolved in Parliament when the 2005 Act was passed was to what extent India, in compliance with its TRIPS obligations, could limit the grant of pharmaceutical patents to "new chemical entities." This question was referred to the Technical Expert Group (TEG) on Patent Law Issues for further consideration.

100 For the purposes of this chapter, specific patent offices are referred to in relation to specific decisions given by them or to highlight differences and trends across the different offices.

101 See *https://www.ipindiaonline.gov.in/patentdecisionsearch/patentsearch.aspx*, where one is able to search Patent Office decisions according to various fields. As will be discussed in detail in this chapter, however, there remain many aspects of the Patent Office that render it extremely difficult, if not impossible, to access what is legally required to be publicly available information.

> "The advantages accruing to a nation's economy from rewarding inventors with the grant of [patents] are dependent on two main factors: (1) The country must be technologically advanced to maintain the rate of invention which is brought forth by the promise of the reward… (2) The patented invention must be worked in the country which grants the patents…
>
> From the above it will be seen that the monopoly created by the patent…offer advantages which have been claimed for the system, only in the highly industrialized countries which have a large capital available for investment in industries and a high degree of scientific and technological education.
>
> It is further obvious however that the system would not yield the same results when applied to under-developed countries." (Ibid.)

Ayyangar recognized that laws "have to be designed, with special reference to the economic conditions of the country, the state of its scientific and technological advance, its future needs and other relevant factors…so as to minimize if not eliminate the abuses to which a system of patent monopoly is capable of being put." Of particular importance to Ayyangar was the need to ensure the easy availability of affordable medicines. As such, he recommended that Indian law not provide patent protection for pharmaceutical products, in order to ensure that food and medicines are available to the public at reasonable prices.

Interestingly, this recommendation was based largely on Ayyangar's observation that this was the accepted practice at the time in virtually every European country. Of course, most countries today (with the exception of a handful of LDCs[102] and non-WTO members) are legally prohibited from emulating what was near universal European practice just a few decades ago.

As a result of the recommendations in the Ayyangar Report, under the Patents Act, 1970, claims covering a pharmaceutical product itself were deemed to be non-patentable, and only processes patents were made available.[103] In addition, the patent term for even these process patents was shortened, to the shorter of five years from grant or seven years of filing, and automatic 'licenses of right' were made available three years after the grant of the patent (Dhar & Rao, 2004). As such, a competitor would be able to obtain an automatic license to practice the patent three years after grant on terms as agreed to by the parties, or failing agreement, on terms as set by the Patent Controller (Patents Act, 1970, Sections 87, 88). As Dhar and Rao have noted, these amendments effectively eliminated patent barriers on pharmaceuticals (Dhar & Rao, 2004).

This legal framework of not recognizing product patent protection on pharmaceuticals, along with a number of other industrial policies designed to foster the growth of the domestic pharmaceutical industry, resulted in a

102 LDCs that are members of the WTO (and thus bound by the TRIPS agreement) are permitted to exclude pharmaceutical products from patent protection until at least 2016 (WTO, 2001).

103 A "product" patent is distinguished from a "process" patent in that a product patent covers the final product itself (and thereby precludes others from manufacturing the product), whereas a process patent only covers the method by which one makes the product. Thus, the latter form of protection is decidedly narrower: the patenting of a particular process of manufacturing a medicine does not preclude competitors from entering the market with the same product, as long as the competitor is able to devise an alternative means of manufacture. Indeed, Ayyangar specifically recommended that India provide process patent protection for medicines, as he was of the view that doing so "would accelerate research in developing other processes by offering an economic inducement to the discovery of alternative processes leading again to a larger volume of manufacture at competitive prices (Ayyangar, 1959).

dramatic growth of domestic manufacturing capacity, such that by "1999, the Indian pharmaceutical industry supplied 70 percent of the bulk drugs (active pharmaceutical ingredients) and 80 percent of formulations in the country. This would make India one of the few countries, and possibly the only developing country in the world, that has come this close to achieving so-called self-sufficiency in medicines" (Musungu & Oh, 2006).

As a result of the lack of patent protection on pharmaceuticals in India, its generic manufacturers were able to offer triple-combination ARVs at a fraction of the cost of what was then being offered by patent-holding multinational pharmaceutical companies in the developed world. The lack of patent barriers also allowed Indian generic companies to manufacture fixed dose combinations of ARVs that have become the weapon of choice in the global scale up of ARV treatment throughout the developing world. Today, the importance of Indian generic manufacturers in supplying affordable medicines throughout the developing world is hard to overstate. In Sub-Saharan Africa, Indian generic ARVs account for 85 percent of the total volume of generic ARVs supplied (Avafia et al, 2006). And when compulsory licenses on several essential medicines for the treatment of various diseases, including AIDS, heart disease and cancer, were recently issued in places such as Brazil, Thailand, Malaysia and Indonesia, these governments looked to India in order to import affordably priced generic versions (Khor, 2009).

Understandably, for these and other reasons, grave concerns were voiced from within and without India as Parliament debated the modalities of fulfilling India's TRIPS obligations. In reviewing the transcripts of the Parliamentary debates leading up to the passage of the Patents (Amendment) Act, 2005, it becomes clear that the effects of patent protection on access to affordable medicines was foremost on many parliamentarians' minds. A few representative quotes are worth reproducing here:

> Suresh Kurup: "…Sir, ever since this Patents (Amendment) Ordinance was promulgated, widespread apprehensions were expressed by groups concerned in India and also outside the country about the provisions of the Bill. The concern was due to the fact that it will prevent the common man in our country and also of the other developing and least developed countries having access to the life-saving medicines…One major area where all of us have raised our criticism was the provision which helps the patent holder multinational companies for ever greening of patents. Sir, a company which obtains a patent by changing their chemicals, before the expiry of the patent, they will again apply for a patent and again get a patent. So, in this way, they will continue to get a patent for the same medicine."
>
> Uday Singh: "We all accept the fact that this Bill is perhaps one of the most important pieces of legislation that this Parliament is considering. I say this because it directly concerns the lives of billions of people and the livelihood of millions of people not only in India but in the lesser developed countries which are dependent on India for medical treatment from where medicines go [sic]."
>
> Rupchand Pal: "Now, our main concern is as to what will happen to our countrymen, our poor and common people…Even yesterday, we have been getting telephone calls from South Africa. Today, in the morning, when we were discussing things with them, the President of New Zealand made us a telephone call. South Africa, New Zealand and other developing countries are making telephone calls throughout the whole night that as to what stand we

> are going to take…[Indira Gandhi] said in 1981…that my idea of a better world order is one in which medical discoveries would be free of patent, and there would be no profiteering…"

Responding to these and other concerns, Kamal Nath, the then Minster of Commerce stated:

> Kamal Nath: "In regard to evergreening, I just want to read out section 3(d) which says that a mere discovery of a new property or a new use for a known substance or the mere use of a known process in a new product — these are exceptions, these will not be granted any patent — and substances obtained by a mere ad-mixture resulting only in aggregation of properties of the components thereof or, processes of producing such substances will not be given patents. There is no question of evergreening." (Lok Sabha Debates, 22 March 2005).

As these excerpts indicate, the Indian Parliament was well aware of India's central role in the provision of affordable medicines throughout the developing world, and was particularly concerned about the pernicious effects of evergreening on access to medicines. Some of the provisions that are of potential application in the pharmaceuticals context will be described later in this chapter.

III. Overview of Indian provisions relating to patentability of pharmaceutical substances

Section 3 of the Indian Patents Act, 1970 lists 15 broad categories of knowledge as "not inventions within the meaning of this Act." Particularly relevant in the pharmaceutical context are the following exclusions:

- New uses of known substances (section 3(d));
- New forms of known substances, without significant enhancement in efficacy (section 3(d));
- "Mere admixtures" (section 3(e));
- "Any process for the medicinal…therapeutic or other treatment of human beings" (section 3(i)).[104]

As will be explained below, the cumulative effect of these provisions, if robustly interpreted and applied, could potentially prevent the most common types of secondary pharmaceutical patents from being granted in India.

New uses/new forms

Section 3(d) of the Patents Act provides as follows:

> **Sec.3. What are not inventions.**
>
> The following are not inventions within the meaning of the Act:
>
> ... (d) the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant.

104 Other exclusions of potential relevance include: the "discovery of any living thing or non-living substance occurring in nature" (section 3(c)); and an "invention which, in effect, is traditional knowledge" (section 3(p)).

> Explanation: For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy.

As a close reading of this provision will reveal, section 3(d) contains three separate and independent exclusions: (1) The discovery of a new form of a known substance; (2) the discovery of a new property or new use of a known substance; and (3) the use of a known process. Both the "new form" and "new use" exclusions could potentially have a far-reaching effect in preventing questionable secondary patents from being granted.

New uses of known substances

Many 'new' drugs that are approved for human use are in fact not new. In some cases, the active ingredient has been known to science for years, if not decades. For instance, the active substance in the ARV drug *zidovudine* (AZT) had been known since the 1960s, and was initially investigated as a cancer drug (Horwitz, 1964). Then, in 1985, researchers, with the aid of public sector funding from the US National Institutes of Health and informed by earlier research on the use of AZT against retroviruses generally, discovered that AZT could also be used in the treatment of HIV.[105]

Although the novelty requirement prevented the patenting of the active substance per se, patent laws in the US, Europe and other jurisdictions allowed the researchers to obtain a patent by drafting their claims as "the method of treating" HIV/AIDS by administering AZT or "the use of AZT" to treat HIV/AIDS. Thus, Burroughs Wellcome (now incorporated into GSK) was able to obtain a 20-year patent which only recently expired in 2005, on this decades-old molecule.

BOX 1: Novelty and Inventive Step

Although Article 27.1 of TRIPS requires that patents be made available for "any inventions, whether products or processes, in all fields of technology, provided that they are new, involve and inventive step and are capable of industrial application," the key terms, including "new" and "inventive step" are left undefined, and countries have considerable flexibility in defining these criteria (CIPR, 2002).

Novelty, for instance, can be interpreted broadly or narrowly, and a distinction can be made as between "relative" novelty and "absolute" novelty. The former refers to a determination of whether an alleged invention had been disclosed only within the country in which the patent is being sought, while an "absolute" novelty standard holds that an alleged invention fails for lack of novelty if it has been previously disclosed anywhere in the world.

The rationale behind the **inventive step** requirement is that a patent applicant should not be granted exclusive rights to an idea that was so obvious that the "innovation" would have happened anyway. Carlos Correa has observed that "the best policy form the perspective of public health would seem to be the application of a strict standard of inventiveness so as to promote genuine innovations and prevent unwarranted limitations to competition and access to existing drugs (Correa, 2007).

105 See, e.g., US Patent No. 472432.

In 2002, however, the CIPR warned developing countries against allowing patents on new uses of known substances:

> "…we caution against developing countries simply taking over from the comparatively recent European jurisprudence the counter-intuitive notion that a product may be regarded as new, if a new use is identified for it. Such an approach is not required by TRIPS and different views can reasonably be taken of whether it is desirable to extend protection in this way, which developing countries will wish to consider with care" (CIPR, 2002)

Correa has also cautioned developing countries from adopting such a practice, stating:

> "…the patenting of a new use of a known product including, in particular, second indications, expands the scope of protection inconsistently with the novelty requirement. In addition to the lack of novelty, there are other possible objections to the patentability of second indications:
>
> - there is no industrial applicability, since what is new is an identified effect on the body, not the product as such or its method of manufacture;
>
> - a patent covering the second medical indication of a known product is substantially equivalent to a patent over a method of therapeutic treatment."[106] (Correa, 2007).

On its face, the Indian provision excluding from patentability the discovery of "any new property or new use of a known substance" would appear to preclude the patenting of new use claims. What is less clear, however, is how robustly this new use exclusion is being interpreted and implemented by the Patent Offices. For instance, while it would presumably exclude patent claims that are formulated as 'the use of compound X (with X being a known substance) for the treatment of disease Y,' what remains less clear is whether and to what extent patent agents can 'draft around' this objection.

The EPO, for instance, expressly recognizes the patentability of second use claims. A common means of 'drafting around' novelty objections are to formulate such a claim as a "Swiss" claim, generally in the form of: "the use of compound X for the manufacture of a medicament for the treatment of disease Y". However, the European Patent Convention (EPC), unlike Indian law, does not contain a specific provision excluding new uses of known substances from patentability. In fact, to the contrary, the EPC expressly includes an exception to its novelty requirement to make new uses of known substances patentable.[107] Given these differences, it would be reasonable to expect that the Indian provision could not simply be bypassed through the clever drafting of patent claims. As will be seen below, however, this may not always be the case.

106 Method of treatment claims will be further discussed below.

107 See EPC, Arts. 54 (4) and 54(5), which provide as follows: "(4) Paragraphs 2 and 3 shall not exclude the patentability of any substance or composition, comprised in the state of the art, for use in a method [of treatment] provided that its use for any such method is not comprised in the state of the art. (5) Paragraphs 2 and 3 shall also not exclude the patentability of any substance or composition referred to in paragraph 4 for any specific use in a method [of treatment], provided that such use is not comprised in the state of the art."

New forms of known substances

Many secondary pharmaceutical patents cover 'improvements' to a known drug that are often routinely practiced throughout the industry. It is routine, for instance, to develop a pharmaceutically acceptable salt form of a given medical compound (Bastin et al, 2000, Gould; 1986). A particular salt form of a drug may result in improvements along a number of important parameters, including bioavailability, stability, ease of manufacture, and other solid-state properties (Berge et al, 1977). However, the fact that these improvements are **useful** need not lead to the conclusion that they are particularly inventive, as there are a finite number of known acids that are used in the industry to produce pharmaceutically acceptable salts, and the desirability of converting base molecules into a salt form is well known.[108]

Other secondary patents that cover 'new forms' of known substances are subject to a similar analysis. For instance, polymorphism is a known phenomenon among a wide range of substances (both pharmaceutical and non-pharmaceutical). In a pharmaceutical substance that expresses itself in one or more polymorphic forms, it may be the case that a particular form exhibits beneficial qualities, such as improved stability or solubility. However, "polymorphism is a natural property; polymorphs are not 'created' or 'invented'; they are discovered normally as part of the routine experimentation related to drug formulation" (Correa, 2007). For instance, one of the patents relating to the antifungal drug *posaconazole* (US Patent No. 6,958,337) states, "[w]e have discovered that the compound of formula I can exist in the form of three crystalline polymorphs, each having distinctly different form [sic] each other and from the amorphous form in their physio-chemical data, their physical properties, and their methods of preparation… Of the three forms, Form I is the most stable." As this disclosure indicates, the existence and properties of different polymorphic forms are discovered, not invented.

Other examples in the pharmaceutical context could include the discovery that a previously known compound exists in various stereoisomeric configurations (e.g., as enantiomers) and that one or more of these are more pharmaceutically active, or the discovery that a specific metabolite of a known compound exhibits valuable pharmaceutical properties (Park, 2008). For example, Indian Patent No. 218923 claims the (R) and (S) enantiomers of a known class of *thiophene hydoxamic acid* derivatives. Despite the fact that the parent compounds had been known in the art, these particular enantiomers were patented for their "improved physiochemical and pharmacokinetical properties such as better solubility and improved plasma stability."

Many such "new forms" of already existing substances are the subject matter of a proliferation of secondary patents on pharmaceuticals. And, as mentioned, such secondary patents are the primary tools by which patent holding companies engage in strategic behaviour to artificially extend their periods of market exclusivity. In an unprecedented effort to address these concerns, India amended section 3(d) of the Act to specifically target these sorts of patents. The exclusion of "new forms" of known substances does not eliminate such patents altogether, but makes them patentable only where the patent applicant can demonstrate that the new form makes the drug significantly more effective. The Explanation to this clause demonstrates its broad applicability, expressly including within its ambit "salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes [and] combinations," as well as a catch-all provision that includes all "other derivatives".

108 See, e.g., *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348 (Fed. Cir. 2007), holding that the claims covering the besylate salt of amlodipine was invalid for obviousness. The court observed: "given the range of 53 anions disclosed by Berge, one skilled in the art would expect those anions to provide salts having a range of properties, some of which would be superior, some of which would be inferior … Pfizer has simply failed to prove that the results were unexpected".

One of the central disputes over this provision is precisely what the term 'efficacy' means, and what types of evidence would be sufficient to establish that a new form demonstrates a significant enhancement in efficacy. Depending on how this question is answered by the Indian Patent Office and eventually the courts, section 3(d) could either serve as an effective bulwark against many forms of secondary patents or be rendered largely toothless in preventing many forms of potential patent abuse. For instance, some have argued that any beneficial modification to a drug should be sufficient to meet the efficacy requirement (see, e.g., Basheer and Reddy, 2008). Thus, for instance, this 'loose' definition of efficacy would mean that any improvement to an existing drug that makes it, say, easier to store, or more convenient to manufacture, could potentially satisfy the efficacy requirement. Others, however, have countered that adopting such a loose standard of efficacy could defeat the central legislative intent of the provision — i.e., preventing evergreening (see, e.g., Park and Jayadev, 2009). As will be discussed in further detail below, there have been recent decisions and judgments interpreting section 3(d) that have direct bearing on this question.

Mere admixtures

Of the most common types of secondary patents on pharmaceuticals are those covering the final composition or formulation of a finished product. Thus, for instance, a drug designed to be administered as a tablet form will often have associated with it a patent that covers the composition of the active ingredient with a number of commonly used excipients, fillers, binding agents and the like (EC 2009). For example, US Patent No. 6,113,920 claims the combination of two AIDS drugs, *lamivudine* and *zidovudine*, each known both individually and in combination, with a glidant in order to easily manufacture the combination in tablet form. However, as Correa has observed, "in most cases, it is likely that the claimed inventions in this field [of compositions and formulations] lack inventive step." Moreover, "it should be noted that processes to prepare formulations or compositions are generally well known and routinely applied. Hence, claims over such processes would rarely be inventive" (Correa, 2007).

Indian patent law contains a provision that could potentially reduce the number of such compositions/formulations that are patented in India. Section 3(e) of the Patents Act, 1970 provides as follows:

> **Sec. 3. What are not inventions.**
>
> The following are not inventions within the meaning of the Act:
>
> ... (e) a substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof or a process for producing such substance.

As the provision suggests, both the substance obtained through a 'mere admixture' and the process for producing such a substance are considered non-patentable under Indian law. Patent laws in a few other jurisdictions also contain similar provisions.[109] The Indian Patent Office, in its yet-to-be finalized Draft Manual of Patent Practice and Procedure, 2008, has indicated that in order to be patentable under section 3(e), a composition or formulation must demonstrate synergistic effects:

109 Australian law, for instance, states: "The Commissioner may refuse to accept a request and specification relating to a standard patent, or to grant a standard patent: …
(b) on the ground that the specification claims as an invention:
(i) a substance that is capable of being used as a food or medicine (whether for human beings or animals and whether for internal or external use) and is a mere admixture of known ingredients; or
(ii) a process producing such a substance by mere admixture. Australia Patents Act, section 50(1)(b)(i)-(ii).

> "In general all the substances which are produced by mere admixing, or a process of producing such substances should satisfy the requirements of synergistic effect in order to be patentable. The synergistic effect should be clearly brought out in the description and examples by way of comparison at the time of filing of the application and should be stressed in the principal claim." (Patent Office, 2008).

However, it is important to note that the existence of a synergistic effect alone is not sufficient to make the admixture patentable, as the invention would still have to independently satisfy the novelty, inventive step and industrial applicability requirements. As will be discussed further below, there has been some useful precedent from the Patent Offices in how section 3(e), as relating to 'mere admixtures' ought to be understood.

Methods of treatment

As mentioned, one of the most common ways to "draft around" the novelty objection for a new use of a known substance is to formulate the claims as "A method of treating disease X by administering compound Y." However, TRIPS, in Article 27.2, expressly allows countries to exclude "diagnostic, therapeutic and surgical methods for the treatment of humans or animals." As such, many jurisdictions' patent laws contain provisions stating that method of treatment claims are excluded, as such claims do not fulfill the requirement of industrial applicability.[110] However, many of these same jurisdictions provide a further exception to this exclusion, expressly providing that products for use in such methods do not fall under this exclusion.[111] Thus, such jurisdictions expressly allow for method or use claims relating to treatment using a medicinal product. However, there is no requirement under TRIPS to make this exception (CIPR, 2002).

The Indian law, for instance, contains no such qualifications, and is unusually broad in that it explicitly excludes claims covering even the *medicinal* treatment of humans and animals. section 3(i) of the Patents Act provides as follows:

> **Sec. 3. What are not inventions.**
>
> The following are not inventions within the meaning of the Act:
>
> ... (i) any process for the medicinal, surgical, curative, prophylactic, diagnostic, therapeutic or other treatment of human beings or any process for a similar treatment of animals to render them free of disease or to increase their economic value or that of their products

Thus, presumably, under Indian law, any method or use claim that purported to utilize a medicinal product for the treatment of human beings would be excluded from patentability. However, as Correa notes, patent offices must be vigilant in closely examining claims to detect method of treatment claims in disguise: "In many cases, a method of treatment claim is not apparent at first sight since reference may be made, for instance, to compositions which are not characterized by their chemical structure or intrinsic characteristics but by

110 See, e.g., European Patent Office Guidelines for examination: "Methods of treatment for the human or animal body by surgery or therapy or diagnostic methods shall not be regarded as inventions which are susceptible to industrial application."

111 See, e.g., EPC Art 53(c), which excludes: "methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body; *this provision shall not apply to products, in particular substances or compositions, for use in any of these methods* (emphasis added).

their dosage or form of administration" (Correa 2007). A few examples of method of treatment claims 'in disguise' that have been granted by the Indian Patent Office will be examined below.

The potential impact of a robust application of Indian exclusions from patentability

As the foregoing indicates, the public health safeguards included in Indian law, if properly interpreted and rigorously applied, can prevent many of the most common types of secondary patents from being granted. Recent evidence indicates that preventing the grant of secondary patents will be very effective in removing many of the patent barriers that exist to generic competition.

For instance, as mentioned, the EC recently released a report on the pharmaceutical sector that concluded that patent holding companies strategically create "patent thickets" around a successful drug, in order to prevent generic competition (EC, 2009). In coming to this conclusion, the EC performed a comprehensive analysis of the patenting practices of the major patent holding pharmaceutical companies. The EC requested patent information from the pharmaceutical companies on over 200 "blockbuster" medicines, and observed that "for the 219 INNs nearly 40,000 patents had been granted or patent applications (as defined above) were still pending…Of the nearly 40,000 cases, some 87 percent were classified by the companies as involving secondary patents, giving a primary:secondary ratio of approximately 1:7. Of the applications still pending, 93 percent were classified as secondary (a primary:secondary ratio of approximately 1:13), whilst 84 percent of the patents granted were classified as secondary (a primary:secondary ratio of approximately 1:5)" (EC, 2009).

Table 1: Subject-matter of secondary patents or patent applications in EC Pharmaceutical Sector Inquiry

Subject-matter claimed	% with at least one claimn to subject-matter
Products	81%
Processes	38%
Second/further medical uses	24%
First medical uses	6%

Source: Pharmaceutical Sector Inquiry.

Table 2: Break-down of product claims in secondary applications in EC Pharmaceutical Sector Inquiry

Category of product claim	% of all prduct claims
Formulations	57%
Devices	7%
Combinations	7%
Polymorphic forms	5%
Salts	4%
Intermediates	4%
Substances	4%
Product by-process	4%
Unspecified	3%
Hydrates	2%
Particles	1%
Solvates	1%
Others	1%

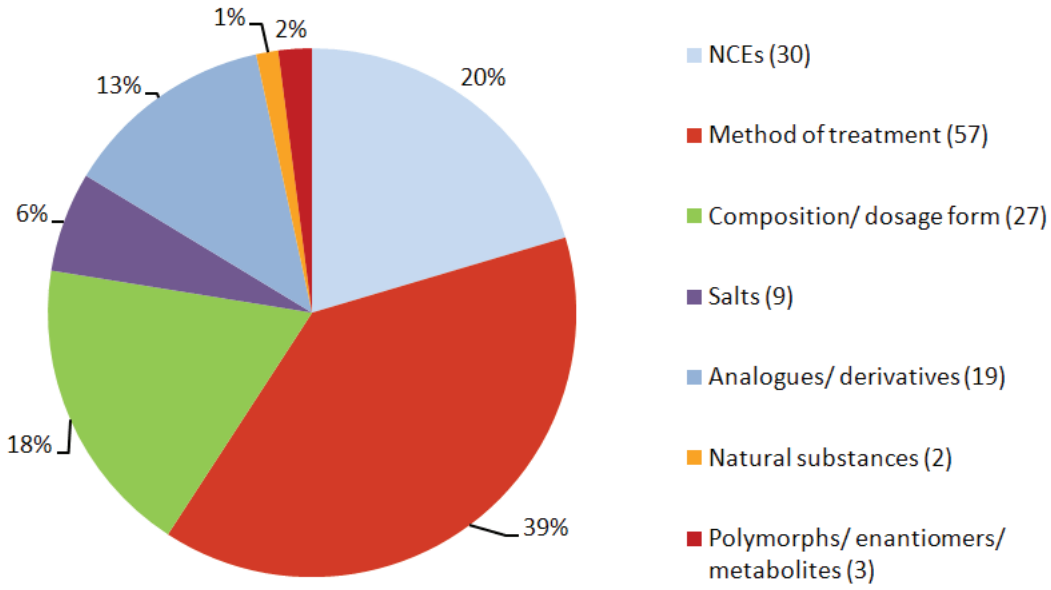
Source: Pharmaceutical Sector Inquiry.

In short, it appears that the vast majority of patents relating to particularly successful medicines are precisely the types of patents that Indian law has the potential to prevent. As the EC observed, "The subject-matter of the secondary patent applications filed in respect of the 219 INNs was largely concerned with claims to products, processes and second/further medical uses" (EC, 2009). Reproduced below are tables detailing the EC's analysis of the subject matter of secondary patents.

As the table above demonstrates, the most common types of secondary pharmaceutical patents filed in relation to the 'blockbuster' drugs include formulations, combinations, polymorphs, salts, and first and second use patent claims. As detailed above, the various provisions of Indian law could be utilized to prevent precisely these types of claims from being patented.

Additionally, a recent analysis of the patents listed in the *Orange Book*[112] for new drug approvals over a 40-month span from January 2005 to April 2008 revealed that a large majority of the patents listed in relation to these drugs were secondary patents, such as method of treatment, compositions, and salts (see chart) (Park, 2008).

Chart 1: Types of patents listed in the Orange Book associates with USFDA NCE approvals (Jan. 2005–April 2008)

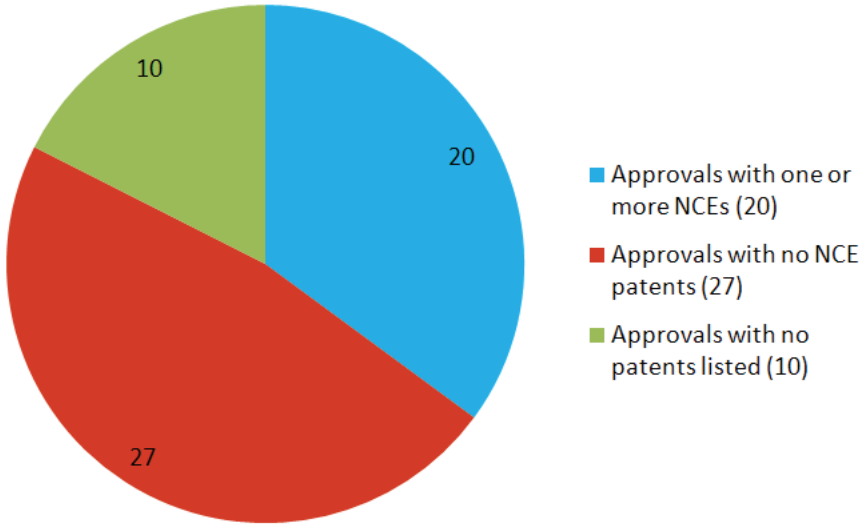


Source: Park (2008).

Indeed of the 57 "new chemical entity" (NCE) drugs approved by the USFDA during this time period, the study found that only 20 (35 percent) of such NCE approvals in fact had associated with them patents covering the actual active compound itself (see chart below). The remainder either had no patents listed, or had only various types of secondary patents listed in relation (Park, 2008).

112 Under the US drug regulation laws, the USFDA requires originator companies to list many of the patents protecting a particular drug. When a generic competitor wants to enter the market with a competing product, the generic competitor must 'certify' that its competing product either does not infringe the patents listed, or that the patents listed are invalid. See generally United States Code of Federal Regulations, 21 CFR 314 (2008), *et seq.* The publication that contains all of the information relating to the patents listed for approved drugs has become known as the "*Orange Book*." The online version of the *Orange Book* can be accessed at: *www.fda.gov/cder/ob/*.

Chart 2: Analysis of USFDA NCE approvals and corresponding patents listed in Orange Book (Jan. 2005–April 2008)



Source: Park (2008).

Again, this demonstrates the potential impact of a robust application of India's patentability safeguards in removing patent barriers to access to affordable medicines. If vigorously applied, these provisions have the potential to make a substantial portion of "new" drugs open to generic competition without fear of liability. Of course, the extent to which this will be the case will depend largely on how the various provisions are interpreted by the courts, and applied by the Patent Offices. A review of some of the more notable patent cases will be discussed below.

IV. Review of selected Indian court and patent office decisions

Once the Patents (Amendment) Act, 2005 was enacted in March 2005, it did not take long for disputes to arise as to the meaning and scope of its provisions. Shortly after the Act's passage, the patent application relating to Novartis' anti-cancer drug *imatinib mesylate* came up for examination in the Chennai Patent Office. Taking advantage of the pre-grant opposition provisions included in the Act, which allowed "any person" to oppose a patent application at any time before grant,[113] the Cancer Patients Aid Association, a non-governmental organization working for the welfare of cancer patients, opposed the patent application. Several generic companies also filed oppositions to Novartis' patent application. The opponents claimed, among other things, that this particular application, which related to a specific polymorphic form of *imatinib mesylate*, was merely a "new form" of a known substance and was thus not patentable under Section 3(d).

Interestingly, the drug to which this patent application pertained, *imatinib* (marketed by Novartis as Gleevec/Glivec), was a key subject of concern among parliamentarians while the Patents (Amendment) Act 2005 was being debated. As noted above, Suresh Kurup (then Member of Parliament representing the Kottayam

113 See Patents Act, 1970, Section 25(1).

constituency of Kerala) was one of the key parliamentarians who discussed issues related to the affordability of medicines in light of the amendments; in his remarks he specifically referred to the un-affordability of this particular medicine in arguing for the necessity of Section 3(d):

"One major area where all of us have raised our criticism was the provision which helps the patent holder multinational companies for ever greening of patents. Sir, a company which obtains a patent by changing their chemicals, before the expiry of the patent, they will again apply for a patent and again get a patent. So, in this way, they will continue to get a patent for the same medicine. For example, the drug called [Glivec] is used for the treatment of leukemia. It is patented by Novartis. This was originally patented in 1993. The cost of the drug for the treatment of this disease comes to about INR 1,20,000 per month in India. At the same time, the generic versions are available in the country which cost only INR 8000 to INR 10,000" (Lok Sabha Debates, 22 March 2005).

Indeed, because India did not recognize patent protection on pharmaceuticals prior to the entry into force of TRIPS on 1 January 1995, it was not under an obligation to provide retroactive patent protection to products before this date. As such, the original compound patent for *imatinib*, disclosed in 1993, was ineligible for patent protection in India. The application that was the subject of dispute in 2005 was over a particular "beta" polymorphic form of the *mesylate* salt of *imatinib*, and thus fell squarely within Section 3(d)'s ambit. At issue, then, was whether the claimed "benefits" of the beta-crystalline form (i.e., greater stability, less hygroscopicity, and greater bio-availability of the salt form over the free base) were sufficient to constitute enhanced efficacy. The Chennai Patent Office, in January 2006, found in favor of the opponents, finding that the claimed benefits of the beta-crystalline form failed to satisfy the 'enhanced efficacy' requirement of section 3(d).[114]

Novartis v Union of India, Madras High Court

Subsequent to the Chennai Patent Office's rejection of the patent application for *imatinib mesylate*, Novartis appealed the matter before the Madras High Court.[115] However, in addition to appealing the rejection itself, Novartis went a step further and challenged the validity of section 3(d) itself, claiming that it was inconsistent with India's obligations under the TRIPS Agreement and that it was unconstitutional under Indian law.[116] The Madras High Court dismissed Novartis' challenge on all counts. In upholding the validity of Section 3(d) against constitutional challenge, the Court noted:

> "We have borne in mind the object which the Amending Act wanted to achieve namely, to prevent evergreening; to provide easy access to the citizens of this country to life saving drugs and to discharge their Constitutional obligation of providing good health care to its citizens."[117]

114 *In the matter of an application for patent No. 1602/MAS/1998 filed on 17 July, 1998*, Chennai Patent Office, 25 January 2006.

115 India is a federation of States and each state has its own High Court. Under India's Patents Act, appeals from decisions of the Patent Office should be heard by an Intellectual Property Appellate Board. However at the time of Novartis' appeal, this Board had not been constituted and the jurisdiction to hear the appeal went to the High Court. The Madras High Court is the high court of the state of Tamil Nadu where the Chennai Patent Office is located. Moreover, as Novartis also challenged a provision of the amendments to the patent law on Constitutional grounds, this matter had to be heard by the High Court. The High Courts of the various States are sub-ordinate only to the Indian Supreme Court which is the highest court of the country.

116 See *Novartis v Union of India*, (2007) 4 MLJ 1153.

117 Ibid at ¶ 19.

Moreover, in the process, the Court had the opportunity to begin to address the meaning of "efficacy" contained in section 3(d):

> "The position therefore is, if the discovery of a new form of a known substance must be treated as an invention, then the patent applicant should show that the substance so discovered has a better therapeutic effect. Darland's Medical Dictionary defines the expression "efficacy" in the field of pharmacology as "the ability of a drug to produce the desired therapeutic effect," and "efficacy" is independent of potency of the drug. Dictionary meaning of "Therapeutic" is the healing of disease — having a good effect on the body." Going by the meaning for the word "efficacy" and "therapeutic" extracted above, what the patent applicant is expected to show is, how effective the new discovery made would be in healing a disease/having a good effect on the body?
>
> In other words, the patent applicant is definitely aware as to what is the "therapeutic effect" of the [known substance] and what is the difference between the therapeutic effect of the [known substance] and the drug in respect of which patent is asked for. Therefore it is a simple exercise…for any patent applicant to place on record what is the therapeutic effect/ efficacy of a known substance and what is the enhancement in that known efficacy."[118]

Thus, in defining 'efficacy' as 'therapeutic efficacy,' and distinguishing such a property from a drug's 'potency,' the Madras High Court clearly indicated a very high threshold that would have to met before the 'efficacy' requirement in section 3(d) was satisfied. This standard would be further explained by the Intellectual Property Appellate Board (IPAB), which subsequently heard the appeal of the Chennai Patent Office's rejection of Novartis' application.

Novartis v. Union of India, Intellectual Property Appellate Board

Although Novartis initially challenged both the Chennai Patent Office's rejection of its patent application and the validity of section 3(d) in court, the Madras High Court decided only on the matter of section 3(d)'s validity. During the pendency of the appeal, the IPAB was notified and created, which had exclusive jurisdiction to hear appeals from all patent office decisions. As such, the actual appeal of the Chennai Patent Office's rejection of the patent application was decided only recently by the IPAB. In June of 2009 (after lengthy procedural appeals not germane to the present discussion), the IPAB upheld the Chennai Patent Office's rejection of the product claims contained in the application as unpatentable over Section 3(d).[119] In doing so, the IPAB agreed with the Madras High Court's definition of efficacy, and explained it further. It is worth quoting the IPAB decision at some length, as it provides significant guidance as to how Section 3(d) is to be interpreted by the Patent Offices:

> "The term "efficacy" has already been defined by the Madras High Court…as "therapeutic effect in healing a disease or having a good effect on the body" taking into consideration the legislative intent for introduction of this provision in the patent law amended in such

118 Ibid at ¶ 13.

119 See *Novartis v. Union of India*, M.P. Nos 1 to 5/2007 in TA/1 to 5/2007/PT/CH, IPAB, 26 June 2009. The IPAB reversed the Chennai Patent Office's rejection of the process claims. Novartis recently filed an appeal against the IPAB's decision in the Supreme Court of India. See "Novartis moves SC in Glivec patent case," *Economic Times*, 29 August 2009.

> a fashion so as to avoid proliferation of patents around existing pharmaceutical…We also respectfully agree with the observation of the Hon'ble Court.
>
> ...
>
> We have already observed that bio-availability is not the same as therapeutic efficacy… Therapeutic efficacy is different form advantageous property of a drug…Imatinib *mesylate* as such and its beta form are therapeutically same substances…and also beta form of *imatinib mesylate* and *imatinib* are same substances with regard to efficacy…From our above observations we have convincingly come to the conclusion that by demonstrating enhanced bio-availability of 30 percent…the Appellant could not show any actual enhancement of known efficacy for its subject compound with respect to either *imatinib* or *imatinib mesylate* as the known substance."
>
> ...
>
> [Novartis] has discovered the new crystalline form with improved thermodynamic stability, improved flow properties and lower hygroscopicity. These physical properties in a drug are important to formulate the active ingredients in solid dosage forms such as capsules, tablets, etc. but has no contribution to actual therapeutic effectiveness of the drug. We have already observed…that advantageous properties such as thermodynamic stability, and lower hygroscopicity and better flow properties of a drug substance cannot be equated with the therapeutic efficacy of a drug. We also have observed…that the Appellant cannot also make out a case by adducing new information at a later date…The patentability would have to be based on the original disclosure as available in the specification and disclosed on the date of filing.[120]

Thus, the IPAB specifically endorsed the Madras High Court's interpretation of the meaning of 'efficacy,' and made a clear distinction between "advantageous properties" and "therapeutic efficacy" (with only the latter satisfying the requirements of section 3(d)). Among the "advantageous properties" specifically excluded by the IPAB are: improved bio-availability; better stability; improved flow properties; and lower hygroscopicity.

Moreover, the IPAB laid down an extremely significant procedural rule towards establishing enhanced efficacy: the evidence for such improved efficacy must be clearly laid out in the original disclosure, and not supplied at a later date during opposition proceedings. Thus, unless a patent specification, on its face, establishes a clear link between the "new form" and enhanced efficacy, it would not be patentable under the reasoning of the IPAB.

Boehringer Ingelheim v. Indian Network for People Living with HIV/AIDS (INP+) and Positive Womens Network (PWN), Delhi Patent Office

In the wake of the Madras High Court's judgment in the *Novartis* matter, patent opponents — particularly civil society groups involved in the opposition process — sought to have the *Novartis* precedent applied and extended in a number of other cases. For instance, INP+ and PWN, in successfully opposing Boehringer Ingelheim's patent application for a pediatric formulation of the ARV *nevirapine*, stressed to the Delhi Patent Office the need to realize the legislative intent of Parliament in enacting section 3(d) to promote access to medicines. Thus, in rejecting the application, the Delhi Patent Office agreed with INP+ and PWN that it "should

120 See IPAB, ibid, at pp. 187-190.

give a strict interpretation of patentability criteria as decision thereof shall affect the fate of people suffering from HIV/AIDS for want of essential medicine."[121]

At issue in the *nevirapine* patent opposition were claims purporting to cover the pharmaceutical composition containing *nevirapine hemihydrate* along with a number of inactive pharmaceutical components to produce a syrup dosage form which is suitable for the administration of the medicine to children. INP+ and PWN argued, and the Delhi Patent Office agreed, that such claims were excluded from patentability under both sections 3(d) and 3(e) of the Patents Act, 1970. Although the word "composition" does not appear expressly in the Explanation to section 3(d), the 'catch-all' phrase "and other derivatives" was broad enough to include compositions and formulations in section 3(d)'s ambit. Thus, the Delhi Patent Office concluded, "the therapeutic effect of *nevirapine*, whether in *hemihydrate* form or anhydrous form, or whether administered in aqueous, tablet, parenteral, or any other dosage form would remain unchanged. The applicant has failed to place on record any evidence to show that the therapeutic effect of *nevirapine hemihydrate* in aqueous solution is significantly enhanced over other known forms of *nevirapine*."[122]

Moreover, with regard to section 3(e)'s exclusion of "mere admixtures" from patentability, the Delhi Patent Office concluded that it agreed, "with the opponent that the applicant failed to show either in the specification or through the submissions that the novel pharmaceutical composition claimed exhibits any of the properties above and beyond the aggregation of the constituent parts. So the claims fall under section 3(e) of the Act and are non-patentable."[123]

Gilead Sciences' Tenofovir patent applications, Delhi Patent Office

Amongst key decisions of the Indian Patent Office on section 3(d) are those by the Delhi Patent Office on the multiple patent applications of Gilead Sciences related to the ARV, *tenofovir*. As noted in chapter 1, Gilead's patent applications were originally opposed by several generic companies which then withdrew their oppositions as a result of the voluntary licenses they signed with Gilead Sciences for the manufacture of *tenofovir*. Ultimately only those companies that did not take the license continued with their oppositions. Several oppositions were also filed by civil society groups. In 2009, the Delhi Patent Office rejected two of these patent applications[124] including an application by Gilead Sciences claiming the ester prodrug of the active compound, *tenofovir*. In rejecting the claims as non-patentable under section 3(d) of the Act, the Delhi Patent Office explained, "The intention of the legislation encompassed in section 3(d) of the Patent Act is very clear…pharmaceutical product [patents] in India should be granted with utmost care and should be granted only to very genuine cases."[125]

Thus, echoing its earlier decision in rejecting Boehringer Ingelheim's application for *nevirapine*, the Delhi Patent Office once again expressly recognized the need to give particular scrutiny to pharmaceutical patent applications in India.

121 *In the matter of an application for patent having no. 2485/DEL1998*, 11 Delhi Patent Office, June 2008, at p. 3.

122 Ibid at p. 13.

123 Ibid at p. 14.

124 Indian patent application nos. 896/DEL/2002 and 2076/DEL/1997; see *In the matter of patent application No. 896/DEL/2002 filed on 4/9/2002, and In the matter of patent application No. 2076/DEL1997, filed on 25-7-1997*, Delhi Patent Office.

125 *In the matter of patent application No. 2076/DEL1997, filed on 25-7-1997*, Delhi Patent Office, 30 July 2009.

Novartis v Torrent, Chennai Patent Office

A decision from the Chennai Patent Office is representative of how a broad interpretation and application of the "new use" exclusion of Section 3(d) could be applied in the pharmaceutical context. In this matter, Novartis had filed an application claiming (among other things) the "use of *valsartan*" "for producing a pharmaceutical preparation for the treatment" of various conditions, including lung and breast cancer.[126] Initially, as filed, Novartis had laid stake to 15 claims, including such "use claims," as well as a number of composition claims, such as "A solid oral dosage form comprising *valsartan* in free form and more than 30 percent of microcrystalline cellulose by weight based on the total weight of the core components of said form."[127]

However, in response to repeated objections raised by the Chennai Patent Office, the applicant narrowed its application to a single claim, as follows:

> "A pharmaceutical composition for the treatment of invasive lung cancer comprising a therapeutically effective amount of *valsartan*… or pharmaceutically acceptable salt thereof and comprising auxiliary microcrystalline cellulose."

Thus, all of the "use" claims were deleted by Novartis, and reformulated as a composition claim. The Chennai Patent Office was not convinced. "The said pharmaceutical composition comprises *valsartan* as active drug. There is no dispute that *valsartan* is known before the date of filing the present application... According to the Indian patent law new use of a known substance is not allowable under Section 3(d). Since *valsartan* is only the ingredient in the said composition used to cure invasive lung cancer [but not microcrystalline cellulose, which has other purpose]… it appears that the sole aim of the applicant is to have [a] patent for the new use of *valsartan*."[128]

A summary of some further Indian Patent Office decisions as they pertain to the interpretation and application of Sections 3(d) and 3(e) of the Patents Act, 1970 are in Table 3 below.

From the precedents described in Table 3, the following positions begin to emerge:

- The legislative intent of Parliament in enacting section 3(d) was to protect public health and prevent evergreening;
- Thus, Patent Offices must recognize that "pharmaceutical product [patents] in India should be granted with utmost care and should be granted only to very genuine cases;"
- Specifically, in interpreting the meaning of 'efficacy,' an extremely high standard applies; an 'advantageous property' is not the same as efficacy. Thus 'new forms' that result in advantageous properties with respect to bioavailability, stability, etc., are not patentable;
- With respect to 'mere admixtures,' compositions, dosage forms, formulations, and combinations are not patentable unless there is a demonstrable synergistic effect between the components.

126 *In the matter of application for patent bearing the number IN/PCT/2001/00864/CHE filed on 21 January 2001*, Chennai Patent Office, 24 October 2007.

127 Ibid.

128 Ibid.

Table 3: Summary of Patent Office Decisions

Drug (opponents/applicants) Type of claim Application No.	Basis for rejection
Adefovir dipovoxil (Gilead v Ranbaxy) Crystal Form 712/DEL/2002	Section 3(d): cites Novartis; then concludes "I have analyzed the results as provided by the applicants regarding improved stability of the alleged compound. I have observed that the applicants have not provided a comparative data with respect to the amorphous/parent compound of the alleged invention. Also no improvement in the therapeutic efficacy of AD as compared to its parent compound (PMEA) has been provided. In fact both compounds (AD) are used to treat viral infections which is also the activity shown by the parent compound (PMEA). In view of the above I state that the subject matter for application no. 712/DEL/2002 is not patentable under section 3(d)." Section 3(e): "The invention claims a crystalline AD and its composition which is basically a mixture of crystalline AD and the excipient. The Agents for the opponents alleged that the applicant has stated that the 'composition of the invention comprises a synergistic admixture with improved efficacy and other enhanced and new properties which are not disclosed or taught in any of the prior art' but since they have failed to substantiate these arguments to prove the synergistic effect of the composition over the prior art cited documents, the composition claims should be rejected." *In the matter of Patent application no. 712/del/2002 filed on 03/07/2002*, Delhi Patent Office, 18 March 2009.
Rosiglitazone (Smithkline Beecham) Sulphonate Salt 295/DELNP/2003	Section 3(d): "The applicants could not establish that the compound as claimed in the instant Patent Application is better in terms of the efficacy with respect to the parent compound as known in prior art, hence in lack of the efficacy the instant Patent Application cannot (sic) be allowed. Accordingly the instant Patent Application No. 00295/DELNP/2003 is **refused**." *Patent Application No.00295/DELNP/2003 — Hearing U/S 14 read with 15 of the Patents Act*, 1970, Delhi Patent Office, 6 January 2009.
Crystalline Macrolides (Novarts v Ranbaxy) Crystal Form 1440/MAS/1998	Section 3(d): cites Novartis; "In continuation of their arguments the agent for the opponent while admitting at the utility of the crystalline forms in the preparation of galenical forms such as creams, emulsions and ointments provided by the applicant in page 12 [original numbering] stated that **utility is not the enhanced pharmaceutical efficacy** and hence the claims are not allowable under section 3(d) of the Patents Act…In the entire description of the invention the therapeutic effect of the crystalline forms is not disclosed. Hence it is concluded that the crystalline forms exhibit the same efficacy as the amorphous form." *In the matter of Application for Patent bearing the number as 1440/MAS/1998 filed on 29th June 1998 by Novertis AG of Schwarzwaldallee 215, 4058 Basel, Switzerland,, A Swiss Company*, Chennai Patent Office, 13 July 2007.

Table 3: Summary of Patent Office Decisions (contd.)

Drug (opponents/applicants) Type of claim Application No.	Basis for rejection
Atorvastatin (Warner-Lamber v Torrent) Crystal Form 1577/DEL/1996	Section 3(d): "By converting a compound to another form sometimes certain properties like stability or dissolution are improved, as it is evident from the affidavit of Stephen Byrin who has reviewed the expert opinion of Dr. Charles Edward Colson, which states that "crystalline form III Atorvastatin is more stable against degradation than the amorphous atorvastatin degradation under similar condition (4 weeks at 40o C/75 percent RH"). But in my opinion a mere enhancement in stability by way of lesser degradabilty by 1 to 2 percent only, does not entitles an applicant to a grant of patent. Moreover this amounts to improvement in the quality of the product rather than the therapeutic efficacy. The opponent has succeeded in proving the grounds of "insufficiency of description u/s 25(1)g "and " not patentable under section 25(1)(f) and section 3(d)." *In the matter of the Application for patent No.1577 /DEL/1996 filed on 19th April, 1998*, Delhi Patent Office, 12 June 2007.
Amlodipine-astorvastatin combination (Pfizer v Torrent) combination 2571/DEL/1998	3(d): A composition under section 3(d) cannot be patented unless any significant therapeutic efficacy over the parent substance is shown. There is not evidence in the body of specification any therapeutic efficacy of the said combination. The composition of claims 1 to 13 essentially a combination of atorvastatin calcium salt & amlodipine besylate which is already disclosed and no statement of enhanced efficacy. Therefore, composition of claim 1 to 13 are not patentable under section 3(d) of the Act. Section 3(e): "Given that the said combination does not result in any enhanced additive effect because not a single example in the entire specification demonstrates the said composition provides surprising result. Therefore the composition/combination claimed in claim 1-13 is a mere collocation of the properties of the individual ingredients. The applicant has submitted in their reply statement an annexure II which provides certain in vitro data and tried to demonstrate that the composition as claimed in synergistic. Para 7 to 9 clearly states that the stock solutions individually of amlodipine or atorvastin have been prepared and used for their purposes of the experiment & there is no indication in the annexure that the said combination is synergistic. Also the opponent argued that such further data submitted in annexure II in the reply statement, even if is relevant, cannot be taken on record as of now. They referred to Cipla vs Glaxo Case wherein it was held that "…unexpected bonus effects not described in the specification cannot form the basis for a valid claim of this kind … If a synergistic effort is to be relied on, it must be possessed by everything covered by the claim and it must be described in the specification…" Therefore the claim 1 to 13 are not patentable under section 3(e) of the Patent Act." *In the matter of the application for Patent No. 2571/del/1998 filed on 28th Aug. 1998*, Delhi Patent Office, 3 February 2009.

Table 3: Summary of Patent Office Decisions (contd.)

Drug (opponents/applicants) Type of claim Application No.	Basis for rejection
Erlotinib polymorph (OSI v Cipla) Crystal Form IN/PCT/2002/507/DEL	Section 3(d): cites Novartis; "It is well recognized in the pharmaceutical field that many solids exhibits polymorphism which is frequently defined as the ability of the substance to exist as two or more crystalline phases that have different arrangement or conformation of the molecule in the crystal lattice (US pharmacopoeia). It is also well recognized in the art that the different polymorph will display different physical properties such as X-Ray diffraction, melting point, solubilites etc. The present invention are drawn to the same pure substance as the prior art and that the only difference is the different arrangements and/or different conformations of the molecule. A mere difference in physical property is a well known conventional variation of the same pure substance not showing any unobvious properties. Therefore the changes alleged by the applicant is in the physical properties are not in the therapeutic efficacy. I therefore conclude that the instant invention claim 1&2 are not patentable under section 3(d) of the Patent (Amendment) Act." *In the matter the application for patent No. IN/PCT/2002/507/DEL filed on 14th May,2002*, Delhi Patent Office, 15 December 2008.
Darunavir (Tibotec v Cipla) Polymorph 3598/DELNP/2004	Section 3(d): "Pseudo polymorphs, namely the ethanolate and the hydrate are merely different physical form which may be stable and due to higher bio availability may readily available at the site of action i.e. in blood plasma, but do not increase or improve the action of the drug in terms of mitigating the disease in general or improving protease inhibitory activity in particular. In other words, such improvement in stability and bio availability do not, contribute to the therapeutic nature of the drug or alter therapeutic profile of the drug compound as compared to the generic compound." *In the matter of Application for patent no 3598/ DELNP/ 2004*, Delhi Patent Office, 6 July 2009.

- With respect to both the 'enhanced efficacy' requirement of Section 3(d) and the 'synergistic effect' requirement of section 3(e); data sufficient to establish this must be clearly set out in the specification, and not proffered at a later date during the opposition hearing.
- With respect to the 'new use' exclusion of section 3(d), it is insufficient to merely reformulate a 'new use' claim as a composition claim for such use.

It is important to note that in several of the decisions discussed above, the patent applications were also unable to fulfill other patentability criteria.

V. Review of Granted Patents

Although these broad and potentially powerful guidelines can be gleaned from the decisions described above, what is less clear is whether and to what extent such principles are being consistently applied by the different Patent Offices across all pharmaceutical patent applications. The cases described above, for the most part, have been the outcome of patent oppositions, in which the Patent Offices were compelled to closely examine the merits of the applications by the very fact of that they were opposed. However, given the sheer volume of pharmaceutical patent applications that are filed and pending before the Indian Patent Office, it is simply impossible for civil society groups and/or generic companies to oppose every questionable application. As of 2006-2007 (the latest Indian Patent Office Annual Report publicly available), India reported having a total of only 198 patent examiners and controllers to deal with nearly 29,000 applications filed in 2006-2007 (not to mention the backlog of pending applications from previous years). Thus, the question arises, what are the types of pharmaceutical patent applications that are pending in the 'mailbox'? What happens to the large number of secondary pharmaceutical patent applications that do not go opposed? Are the Patent Offices consistently and rigorously applying the various safeguards in India's patent law? The review of patents granted by the Indian Patent Office conducted in this report attempts to begin to address this question.

Methodology

Inevitably, the methodology by which information was gathered from the different Patent Offices was constrained by the limited amount of information that they made available to the public at the time this study was conducted which, in respect to granted patents, was only made available through the Patent Office Journal. The Journal lists abstracts of published patent applications, as well as the granted patents on a weekly basis. These weekly publications are made available at the Indian patent office website, where they can be downloaded in pdf format, often running into thousands of pages. Moreover, the information regarding granted patents, at the time of this Study was extremely limited, providing only: (1) the Indian patent number; (2) the Indian application number; (3) date of application; (4) priority date; (5) title of invention; (6) name of patentee; (7) date of publication of the abstract; and (8) the granting office (see Table 4).

No further information regarding the granted patents was available through the Patent Office Journal, including such potentially important information such as Patent Co-operation Treaty (PCT) application number (if any), the abstract of the claimed invention, or the country in which the priority application was filed.

Moreover, copies of the granted patents themselves were not available on the Patent Office website, and had to be requested in hard copy from the Patent Office that issued the patent, and was unavailable at any of the other three patent offices. Copies of the granted patents were then made available, if at all, upon payment of INR 4 per page for photocopying fees.

Thus, as a practical matter, it was simply impossible to conduct anything more than a cursory review of the granted patents from the limited information available from the Patent Office Journal. This introduced a substantial amount of ambiguity when attempting to identify the pharmaceutical patents granted. While in many cases, the pharmaceutical nature of the patent was obvious from the title alone, (e.g., "A Pharmaceutical Composition for Topical Administration"), there were a substantial number of instances in which the nature of the invention was ambiguous. For instance, a patent bearing the title, "A Fungicidal Compound" could

Table 4: Publication Under Section 43(2) in respect of the Grant

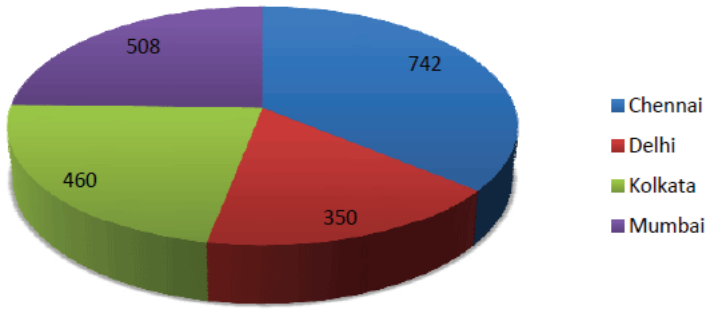
Following Paptents have been granted and any "person interested" in opposing these patents under Section 25(2) may at any time within one year from the date of this issue, give notice to the Controller of Patents at the appropriate office, on the prescribed form-7 along with written statement and evidence, if any.

Serial No.	Patent No.	Application No.	Date of Application (Date of Priority)	Title of Invention	Name of Patentee	Date of Publication of Abstract u/s 11(A)	Appropriate Office
1	221094	00170/ KOLNP/2006	22/06/2004 (28/03/2003)	A process for removing halide compunds adhering to finely divided metal oxide particles by means of steam	Degussa AG	15/12/2006	Kolkata
2	221095	00175/ KOLNP/2006	09/07/2004 (29/08/2003)	A subscriber unit (SU) that is sip enabled for facilitating a handoff of the SU from a sip-enabled wireless local area network (WLAN)	Motorola Inc.	22/06/2007	Kolkata
3	221096	00259/ KOLNP/2004	01/07/2002 (02/08/2001)	Highly anti-corrosive thin platelet like metal pigments	Merck Patent GMBH	07/04/2006	Kolkata
4	221097	00132/ KOLNP/2004	29/07/2002 (02/08/2001)	Process for the preparation of 5-substituted isobenzofurans	Infosint S.A.	07/04/2006	Kolkata
5	221098	00282/ KOLNP/2004	09/09/2002 (12/09/2001)	Method for controlling the position of foil strip edges	Aisapack Holding S.A.	31/03/2006	Kolkata

potentially be a patent relating to a pharmaceutical product. Equally as likely, however, the patent could relate to an agrochemical or veterinary product.

Oftentimes, the combination of the title of the invention and the patentee could resolve some ambiguity. For instance, a patent titled "Heterocyclic Compounds and Process for their Preparation Thereof," could potentially relate to any number of fields of use, but the fact that the patentee was Dr. Reddy's Laboratories, an Indian pharmaceutical company, allowed one to reasonably conclude that this particular heterocyclic compound was for pharmaceutical use. However, there were other instances in which even the combination of title and patentee did not resolve the ambiguity. Bayer, for instance, is a pharmaceutical company active in filing for pharmaceutical patents. However, Bayer also regularly files for patents relating to compounds for a wide number of other agricultural and industrial uses. Thus, for example, Indian Patent No. 206231, entitled "A Compound," to Bayer Corporation, was completely ambiguous from the limited information at hand, and was excluded from the analysis.

Chart 3: Pharmaceutical patents granted by each Patent Office, 2005–2008



Despite these ambiguities, best efforts were used to identify what appeared clearly to be pharmaceutical patents granted by the Indian Patent Office from 2005 to 2008. The weekly Patent Office Journals were reviewed from 28 January 2005 (the first Journal publication in 2005) to 26 December 2008. This review resulted in a total of 2,060 granted patents that appeared to relate to pharmaceutical products (Chart 3). Excluded from the analysis were pharmaceutical patents that were clearly process patents (e.g., a patent bearing the title, "A process for the manufacture of compound X"), as the focus of the study was to gauge the impact of the product patent regime introduced in 2005.

As the above chart illustrates, the Chennai Patent Office appears to have granted a significantly larger number of pharmaceutical patents than the other offices. Of the 2060 granted patents identified, 742, or 36 percent, of these patents were granted by the Chennai Patent Office. Conversely, the Delhi Patent Office appears to have granted less than half that number, accounting for less than 17 percent of the total number of patents granted.

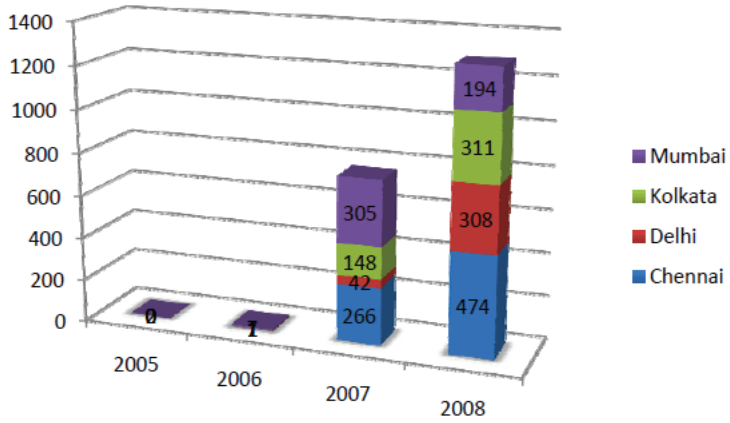
Moreover, the number of patents being granted appears to be increasing dramatically (see Chart 4, below). Very few patents that appeared to relate to pharmaceutical products were granted in 2005 and 2006. This stands to reason, as the examination of pharmaceutical product patent applications would have only begun in 2005, and the examination process would presumably take some time. However, the number of granted patents increased dramatically in 2007 (a total of 761 patents granted), and increased even more in 2008 (a total of 1287 patents granted).

Next, these patents were further categorized into 6 sub-categories: (1) compound patents; (2) secondary patents (i.e., salts, polymorphs, compositions, etc.); (3) biologics; (4) herbal/traditional/ayurvedic; (5) intermediates; and (6) undetermined. Again, because of the limited amount of information available from the Patent Office Journal, a fair bit of ambiguity in these categorizations was inevitable. However, for the most part, the categorization could be inferred from the title of the invention. Thus, for instance, patents bearing the word "compound" in the title were categorized as such. Also included in the compound category were those incorporating the word "substituted" in connection with a family of compounds — for example, "Substituted Indazole Derivatives" appeared to indicate that the patent relates to a new compound derived from indazole and were thus categorized as a compound patent.

The patents categorized as secondary patents generally included certain key words in the title to indicate that the patents related to various common secondary pharmaceutical patents. Thus, for example, all patents bearing the title, "A Pharmaceutical Composition…" were categorized as secondary patents. Also included were other telltale keywords, such as "preparation," "formulation," "dosage form," "combination," "crystalline form," "polymorph," "salt," and the like.

A significant number of the pharmaceutical patents granted appeared to be for biologics, and were thus categorized separately. Some keywords used to identify what appeared to be pharmaceutical patents for biologic drugs included: "antibody," "recombinant," "vaccine," "protein," and "enzyme."

Chart 4: Patents granted by year and office, 2005–2008



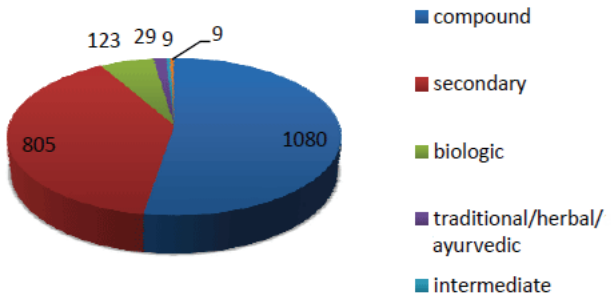
Perhaps a bit surprisingly, a significant number of pharmaceutical product patents granted in India since 2005 appeared to relate to traditional/herbal/ayurvedic pharmaceutical preparations. section 3(p) of the Patents Act, 1970 excludes from patentability "an invention which, in effect, is traditional knowledge or which is an aggregation or duplication of known properties of traditionally known component or components." Despite this, a small but significant number of patents appeared to have been granted in India for herbal and traditional remedies. Some examples of such titles include: "A Homeopathic Medicine" (Indian Patent No. 206461); "Herbal Ayurvedic Composition for Treatment of Psoriasis" (Indian Patent No. 208437); and "An Antipoison, Antiviral and Anti HIV Herbal Composition and Process for Preparation Thereof" (Indian Patent No. 209857).

A small number of patents expressly included the term "intermediate" in the title. An intermediate patent "claims a chemical compound that is used during the production of an active ingredient, but is not present in the final, marketed form of the drug product" (USFTC, 2002). As such, it is akin to a process patent, in that the patent relates to the process by which a drug substance is made, but is nevertheless a product patent, in that the patent covers the actual intermediate compound itself. Because of the hybrid nature of intermediate patents, the small number of patents that identified themselves as relating to intermediates were treated separately.

Finally, a small number of patents had titles so ambiguous that they were classified as indeterminate. These included patents bearing the title "A Pharmaceutical Product," (Indian patent nos. 224966 and 218075) and "Novel Pharmaceutical" (Indian patent no. 197370). The break-down of the different types of patents are described in Chart 5 below.

Of course, these broad classifications based largely on the title of the patent will inevitably be imprecise. Only by having access to the specification and the claims can one determine the exact nature of the patent, and the claims included therein. However, given the limited amount of information provided publicly by the Indian Patent Office at the time the study was conducted, there was simply no way to determine with any greater degree of accuracy the number, type and scope of the pharmaceutical product patents that have been granted since the introduction of the Patents (Amendment) Act of 2005.

Chart 5: Break-down of patents by type, based on title



Given that the primary focus of the study was to determine how the various provisions in the Indian patent law designed to prevent evergreening were being interpreted and implemented by the Indian Patent Office, particular attention was paid to the patents that fell under the classification of secondary patents. section 3(d), as it relates to "new forms" of "known substances," and section 3(e), as it relates to "mere admixtures," would have their primary application to the various types of the most common secondary pharmaceutical patent applications relating to compositions, salts, polymorphs and the like. Thus, in order to gain better insight into the effectiveness of such provisions in limiting the grant of such secondary patents, it was decided to examine more closely a selected number of secondary patents granted by the four Patent Offices in Mumbai, Delhi, Kolkata and Chennai. The number of what appeared to be secondary patents granted by each of the Patent Offices is represented in Chart 6, below.

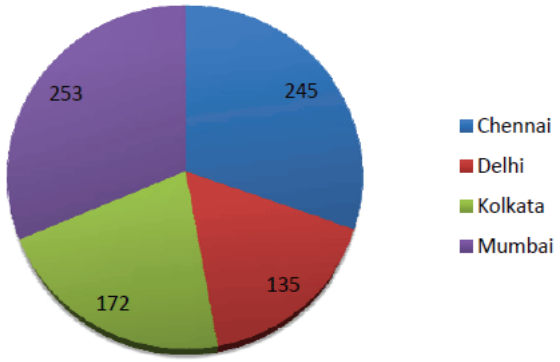
Of the 805 secondary patents initially identified, a decision was made to further narrow the potential pool of patents to be analyzed by limiting the analysis to those applications filed through the PCT. The primary reason for this decision was to have the possibility, if required, to examine how some of the equivalent patent applications were examined and disposed of in other jurisdictions. Under the Indian Patent Office's application numbering protocol, those applications filed through the PCT are easily identified by either an "NP" (national phase) or "PCT" in the application number. For example, the patent application number 5511/DELNP/2005 would indicate that this application was number 5511 filed in the Delhi Patent Office in the year 2005, and had entered the national phase of the PCT application process. Moreover, the application number: IN/PCT/2001/1093/KOL would indicate that this was the 1093rd PCT application filed in the Kolkata patent office filed in the year 2001.

Limiting the secondary patents in this manner resulted in a total of 564 secondary patents filed via the PCT; of these 183 were issued from Chennai, 78 from Delhi, 158 from Kolkata, and 145 from Mumbai. In order to obtain a reasonable sample of patents issued by each office, it was decided to select 30 patents at random from each office, for a total of 120 patents to be reviewed. The list of patents requested from the Patent Offices is attached as Annex II. In order to assist in requesting and obtaining the patents from the Indian Patent Office, the services of S. Majumdar & Co., a leading Indian Intellectual Property law firm, were retained. The list of 120 patents to be obtained was sent to S. Majumdar & Co. on 13 April 2009. As of 22 October 2009 — more than six months later — only 84 of the patents had been obtained from the different Patent Offices. A complete list of patents successfully obtained is listed in Annex III.

According to S. Majumdar & Co., these patents were requested from the various Patent Offices promptly after they received the list, and despite consistent follow-up with the patent offices, were only able to obtain

slightly more than two-thirds of the total number of patents requested within a six-month timeframe.[129] Given the time constraints in finishing the review for the study, it was decided to proceed with the analysis of the granted patents with this limited number, despite the fact that no patents were received from the Delhi Patent Office. Thus, the more detailed analysis of the granted patents were conducted on only 84 of the 120 patents, with 30 from the Chennai Patent Office, 26 from the Mumbai Patent Office, 27 from the Kolkata Patent Office, and only one from the Delhi Patent office.

Chart 6: Number of secondary patents granted by each Patent Office, 2005–2008



Results and Discussion

Transparency of patent offices

As the above difficulties demonstrate, one of the most striking findings of this review was an unexpected and a rather unfortunate one: the sheer difficulty of obtaining what should be publicly available information from the Patent Offices. One of the main justifications for the entire patent system is based on the notion that it represents a *quid pro quo* between the inventor and society — in exchange for public disclosure of technologically valuable information, society grants the inventor a limited monopoly on such information, after which the information becomes part of the public domain. Given how difficult it is to obtain even the most basic information from the Patent Offices, it appears that Indian society is not getting the benefit of this hypothetical bargain.

The difficulties that such a lack of transparency can cause are much more than theoretical — for potential generic competitors, it introduces a large amount of legal uncertainty. Although they may know, from the publication in the Patent Office Journal, that a patent relating to a specific technology has been granted, it will not be until after they can examine what claims have been granted that they can make any kind of determination with respect to their freedom to operate. And because Indian patent law is so different than what exists in other jurisdictions, studying the claims as granted in other jurisdictions with more transparent functioning (e.g., USPTO, EPO) would likely result in what are often mistaken conclusions with respect to their freedom to operate. The fact that it could take 6 months — *or more* — for a potential competitor to even obtain a copy of the granted patent from the Patent Office introduces a significant amount of delay and uncertainty.

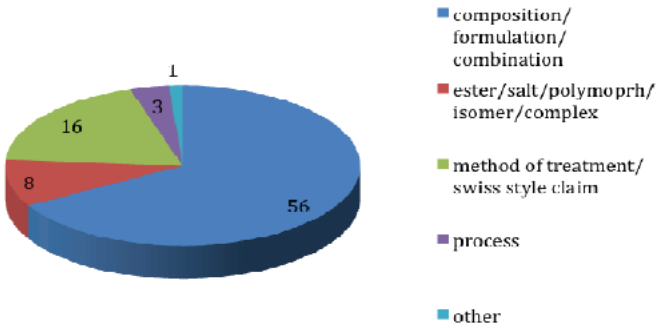
To be sure, the Indian Patent Office appears to be aware of the problem, and has made significant progress in improving the quantity and quality of information that is available from the Patent Office website. For instance, many Patent Office decisions are now available online (although not without its glitches).[130] And

129 Correspondence with S. Majumdar & Co., on file with the author.

130 For instance, although the site allows one to search according to any number of fields, including application number, opponent, applicant, controller, etc., as of the date of this writing, it was impossible to search Patent Office decisions by patent application number; any such search would result in the error message: "Error in bindGrid: An expression of non-boolean type specified in a context where a condition is expected, near".

whereas at the commencement of this study, no information at all was available online regarding any patents granted after 2005, the Patent Office website has recently managed to upload considerably more detailed information about granted patents including the specifications of the granted patents.

Chart 7: Analysis of granted patents collected from Patent Office



Unfortunately, for the purposes of the present review, the lack of success in obtaining the complete set of patents requested hindered the full extent of the intended analysis. For example, as there were no patents successfully collected from the Delhi patent office, it was impossible to make any observations with respect to how the Delhi Patent Office performed in relation to the other patent offices. The lack of information from the Delhi Patent Office is particularly unfortunate, as many of the more interesting decisions relating to pharmaceutical patents, as described above, came out of the Delhi Patent Office. Coincidentally or not, the Delhi Patent Office, as described above, appears to have granted a significantly smaller number of pharmaceutical patents as compared to the other three patent offices.[131]

Analysis of Claims

An analysis of the claims contained in the 84 patents that were obtained is depicted in Chart 7, below. Similar to the EC's findings, patents relating to composition/formulation constituted by far the largest proportion (67 percent) of secondary patents that were reviewed. Additionally, a significant number (16 patents, or 19 percent of the sample) of patents reviewed were formulated as composition claims but were in fact 'new use' or 'method of treatment' claims 'in disguise'. Some of these claims will be discussed in more detail below. A number of patents relating to other secondary features, such as the salt form, ester prodrug, enantiomer, etc., were also granted (8 patents, or 10 percent of the sample). Finally, because these patents were selected largely on the basis of Title and Patentee, some patents that appeared to be secondary product patents in fact turned out not to be so. For instance, the patent titled "A pharmaceutical composition for therapy of interstitial cystitis," turned out not to have any product claims, and only process claims relating to the process for manufacturing such composition. In addition, the patent titled "An isomer, enantiomer, diastereomer or tautomer of a compound," appeared from the title to be a secondary patent claiming an isomeric form of a known compound. However, upon reviewing the patent, it was concluded that this patent covered a new compound. Some of the more detailed findings will be described below.

131 Obviously, further information would be necessary before one could reasonably conclude that the Delhi Patent Office was granting fewer patents due to a more rigorous application of the patentability criteria. For instance, the Patent Office does not make public information regarding the total number and type of patent applications filed in each Patent Office. One would need, at the very least, baseline numbers of how many patent applications were filed, how many rejected, and how many granted before any sort of analysis could be undertaken.

Application of patent law safeguards

One of the findings from the review of the granted patents was the apparent inconsistency in how many of the safeguards discussed above were being applied to specific patent applications. For example, it appears that a number of patent applications relating to a specific polymorphic form of a known compound have been granted, despite the lack of any data provided in the application with respect to enhanced efficacy. Thus, Indian Patent No. 211338, granted from Application No. IN/PCT/2001/01478/MUM, claims a 'metastable polymorph' of what is admitted to be a known compound. Despite the Madras High Court's indication that efficacy means 'therapeutic efficacy,' and the IPAB's clarification that other 'beneficial properties' such as stability are insufficient to satisfy this requirement under section 3(d), this patent specification provides no indication that the polymorphic form exhibits significantly enhanced therapeutic efficacy. Rather, the only data that the specification provides is data relating to how stable the particular polymorphic form was after storage. Although this would appear to be a clear case of an application that should be rejected in India under the prevailing interpretation of section 3(d), it was granted by the Mumbai Patent Office.

Indian Patent No. 208357, granted from Application No. 512/MUMNP/2005, claims oxybutynin, a known compound, in gel formulation for topical application. Thus, given the "new form" of oxybutynin that is being claimed, the applicants presumably had the burden of establishing that there was an enhancement of "therapeutic efficacy" in this new form. However, the specification describes the therapeutic efficacy of the gel form in this manner: "…the number of incontinent episodes for those individuals treated by the non-oral method of the present invention is nearly identical to the number for those treated with the oral formulation." Thus, in establishing "therapeutic efficacy," the applicants showed that this new form was 'nearly identical'. Section 3(d), however, would appear to require a much higher showing of significant enhancement.

Patents granted in India, but rejected by US and/or European Patent Offices

More troublingly, however, are those instances where the patent application not only appeared to clearly fall under one or more of the exclusions contained in Indian patent law, but were also deemed to lack novelty or inventive step in jurisdictions that have much more liberal patentability criteria than India. For instance, Indian Patent No. 215154, granted from Application No. 362/MUMNP/2005 was granted for the γ-crystal polymorphic form of a known substance — *perinpodril* (a hypertension drug). Like the polymorphic patent discussed above, the specification provides no data relating to any alleged therapeutic efficacy arising from this new polymorphic form. Rather, the benefit that is suggested in the specification is that this new polymorphic form facilitates production on an 'industrial scale.' Again, such a beneficial property, even if real, would appear to clearly fall short of the therapeutic efficacy requirements discussed above. The patent, moreover, contains a claim covering a pharmaceutical composition comprising the γ-crystal form "in combination with one or more pharmaceutically inert nontoxic carriers." Again, in view of section 3(e) that excludes 'mere admixtures,' it is unclear what 'synergistic' effect was demonstrated that was deemed to overcome this exclusion.

Moreover, the equivalent application (filed via PCT — Publication No. WO/2001/083439) was deemed abandoned after a final rejection at the USPTO (US Application No. 10/811,727) as obvious.[132] The USPTO observed, "…absent a showing of unobvious and superior properties in terms of mechanic benefits, the

132 USPTO, Final Rejection of Application No. 10/811,727, 15 February 2007, *http://portal.uspto.gov/external/portal/pair*.

instant claimed crystalline forms and its compositions of known compounds would have been suggested to one skilled in the art."

Additionally, Indian Patent No. 211807, granted from Application No. 952/CHENP/2003, claims the combination of two known compounds, *amlodipine* and *benazepril*. This application, filed in 2003 and granted in 2007, contains 13 claims covering the combination of these two drugs. The equivalent US application (US Application No. 10/450,344), however, was abandoned after the USPTO issued a non-final rejection for lack of novelty.

The fact that a patent application that was deemed not to satisfy the significantly more lenient patentability criteria that prevails in the US was granted in India is puzzling. It is all the more so because the prosecution history of the equivalent US application is available online at the USPTO website. Indeed, Indian patent law requires the patent applicant to disclose details regarding the status of equivalent application in other jurisdictions, and confers power upon the Controller to require the applicant to keep such information updated.[133]

Method of treatment claims reformulated as composition claims; Swiss-style claims

As mentioned, Indian patent law contains two complementary provisions that could potentially exclude a large number of 'new use' and 'method of treatment' claims from patentability. Section 3(d) excludes the patentability of the discovery of any new use or property of a known substance, and section 3(i) prevents an applicant from reformulating such a 'new use' claim into a method of treatment claim in the form of 'the method of treating disease Y with substance X.' However, as Correa has noted, "in many cases, a method of treatment claim is not apparent at first sight since reference may be made, for instance, to compositions which are not characterized by their chemical structure or intrinsic characteristics but by their dosage or form of administration" (Correa, 2007). Such claims, which are essentially method of treatment claims 'in disguise,' would represent a significant loophole around the robust exclusions on new use and method of treatment. Thus, rather than formulating a patent claims as 'the use of (old substance X) for treating Y,' or 'the method of treating Y with substance X,' an applicant could simply re-formulate essentially the same claim in the form of 'a composition comprising (old substance X) for use in treating Y.'

As we have seen, the Chennai Patent Office, in the *Novartis v Torrent* matter, has rejected precisely such a claim as merely a reformulation of a new use claim. This, however, does not appear to be the consistent practice throughout the patent offices. There were several 'composition' claims that in fact appeared to be essentially 'new use' or 'method of treatment' claims.

For instance, Indian Patent No. 216832, granted from Application No. 221/KOLNP/2004 contains 35 claims relating to a certain class of *ogliopeptides* for use in bone marrow regeneration. Indeed, in the specification, the application admits that the invention relates, essentially, to the new use of a known compound: "…the present invention shows that previously known osteogenically active *ogliopeptides* can act as stimulants of the hemopoietic system." However, many of the claims, as granted, are formulated as composition claims, covering "a pharmaceutical composition comprising as an active ingredient an ogliopeptide…exhibiting enhancement of mobilization of multilineage hematopoietic stem cells to the peripheral blood…"

133 See Patents Act, 1970, Section 8.

Thus, the 'composition' claim is defined not in relation to what is contained in the composition, but the specific effect on the body that this composition will achieve. As such, it is unclear how this claim differs in any relevant legal aspect from the Chennai Patent Office's rejection of the Novartis application covering a 'new use' claim reformulated as a composition claim. Indeed, the equivalent application has been abandoned in both the USPTO and the EPO after a series of objections from both patent offices that the claimed invention lacked both novelty and inventive step.[134] With regard to novelty, the USPTO observed, "the discovery of a new use for an old structure based on unknown properties of the structure might be patentable to the discoverer as a process of using. However, when the claim recites using an old composition or structure and the "use" is directed to a result or property of that composition or structure, then the claim is anticipated."[135]

Likewise, the equivalent application was also abandoned in the EPO. The EPO recognized as well that the claims covered second medical use: "…the independent second medical use claims only define mechanisms of action of the active ingredients rather than representing different second medical uses, i.e., uses in the treatment of different pathologies."[136]

Similarly, Indian Patent No. 215514, granted from Application No. 97/KOLNP/2004, contains composition claims that are defined not in terms of the contents of the pharmaceutical composition, but in terms of how the composition can be administered: "A pharmaceutical composition comprising CCI-779 and EKB-569 capable of being used in the preparation of a medicament for the treatment of neoplasm in a mammal." Thus, this claim, similar to those rejected under *Novartis v Torrent* appear to be method of treatment claims reformulated as composition claims.

Thus, despite the broad exclusions of new use and method of treatment contained in the Indian patent law, the Patent Offices appear to be, at least in some cases, interpreting these exclusions in a more liberal manner than in the EPO and the USPTO, which expressly allow new use claims and method of treatment claims, respectively. If a patent application covering a new use of an old substance can be patented in India if it is simply reformulated as a composition claim, then the essential purpose of the safeguards in Indian law would appear to be quite easily circumvented.

VI. Conclusions and Recommendations

Indian patent law contains robust safeguards that, if strictly interpreted and applied, have the potential to eliminate a significant amount of patent barriers to affordable generic production. As the review of some of the more recent case law and other precedents from the Indian courts and Patent Offices indicate, many of these provisions are in fact being interpreted and applied in a robust manner.

However, it does not appear to be the case that such provisions, absent an opposition from a civil society group or generic competitor, are being applied in a consistent manner. Moreover, the rather extreme difficulties in obtaining what is legally required to be publicly available information hinders the ability of civil society

134 See File Wrapper for 10/766,527 at USPTO.

135 Ibid.

136 See File Wrapper for EP01961056 at EPO.

groups, generic competitors and other interested parties to participate to the fullest extent in preventing questionable patents from being granted.

Due to the difficulties in obtaining granted patent information that this review encountered, a more comprehensive review of how the various provisions have been interpreted and implemented in the Patent Offices may be appropriate, if and when such information becomes more easily accessible. Regardless, this initial analysis suggests a few policy reform options that the Government of India might consider undertaking immediately:

- **Expedite the process of making patent information online** and fully searchable, including published applications, granted patents, complete specifications, examination reports, patent office decisions, details of oppositions filed, and correspondence between the Applicant and the Patent Office;
- **Facilitate access to information at each of the Patent Offices**; decentralize information so that information about patent applications filed/granted in any of the Patent Offices are available at all of them;
- **Clarify through patent examination guidelines or through legislative change the robust exclusions** of new use claims, method of treatment claims, 'Swiss-style' claims, in order to ensure that applicants may not simply 'draft around' any such exclusions;
- **Strengthen the interpretation of section 3(e)** to clarify that composition, formulation and dosage form claims require a strong showing of synergy; clarify that this is independent of satisfying inventive step, and that as "a general rule, formulation techniques and the range of compounds that may be used for developing pharmaceutically viable products in different forms are well known to a person skilled in the art" (Correa, 2007);
- **Clarify**, through patent examination guidelines or through legislative change, that various common 'advantageous properties' arising from converting a known drug into a new form are not patentable under section 3(d), including (but not limited to): improvements in a drug's bioavailability, potency, stability, hygroscopicity, flow properties, ease of manufacture, etc.

CHAPTER 2B: THE LANDSCAPE OF PHARMACEUTICAL PATENT APPLICATIONS IN INDIA: IMPLICATIONS FOR ACCESS TO MEDICINES

K. M. Gopakumar ◊

I. Introduction

India is one of the few developing countries that decided to use the full ten-year transitional period (1995-2004) under the TRIPS Agreement. During this period from 1995 to 2004, India received numerous product patent applications that the Indian Patent Office started examining in 2005. These applications are at various stages of examination and whether they are granted or not will have a significant impact on continued access to generic medicines.

Transition periods under TRIPS

TRIPS allowed two types of transition periods for developing countries. The first transition period is with regard to general compliance with TRIPS. Thus, developing countries had five years from the date of entry into force of the Agreement to implement it.[137] The second transition period of an additional five years is available for the introduction of product patent protection for those areas of technology that the country in question did not grant patents for under its pre-TRIPS patent law. In the case of India this was in relation to pharmaceuticals, food and agrochemicals.[138]

The second transition period, however, came with additional obligations if the areas of technology not patentable under the developing country's laws related to pharmaceutical and agricultural chemical products, as was the case in India. In such cases, TRIPS, required member states to set up an institutional mechanism to provide, at the end of the first transition period, a means by which patent applications for such pharmaceutical and agricultural chemical products could be received. At the end of the second transition

◊ This study is the outcome of substantial assistance of many people. I express my deep gratitude and thanks for the following people who specifically assisted me in the elaboration of this study. Megha M. Mukund for helping to prepare the initial database, Reji K. Joseph for assisting in the statistical analysis, Dr. Visalakshi and Nidhi Singh for locating Indian patent applications corresponding to NMEs approved by the USFDA, Dr. Gopakumar Nair and Andreya Fernandes for the patent history analysis and Kajal Bhardwaj for the excellent editing. I would like to additionally thank Savita M. Narasimhan for her inputs and edits on earlier drafts and Tenu Avafia for his comments and inputs. However, the usual caveats apply.

137 See Article 65.2, TRIPS Agreement, "developing country member is entitled to delay for a further period of four years the date of application, as defined in paragraph 1, of the provisions of this agreement other than articles 3, 4 and 5".

138 See Article 65.4, TRIPS Agreement which reads, "to the extent that a developing country member is obliged by this agreement to extend product patent protection to areas of technology not so protectable in its territory on the general date of application of this agreement for that member, as defined in paragraph 2, it may delay the application of the provisions on product patents of section 5 of part ii to such areas of technology for an additional period of five years".

period, these applications would be opened and examined as if the examination were taking place on the date that they were filed.[139] Product patent applications received during the transition period are generally known as 'mailbox' applications. Where these 'mailbox' applications have been granted a patent and marketing approval in another member country, they are further eligible for exclusive marketing rights (EMR) for five years in the developing country.[140]

The first amendment to the Patents Act 1970, made in 1999, introduced the mailbox facility and EMR.[141] Then India carried out the second amendment in 2002 to comply with the other provisions of the TRIPS patent regime except the product patent protection. This second amendment focused on the introduction of TRIPS flexibilities related to the post-grant stage of patents, such as. compulsory license, parallel importation, Bolar provisions, etc. Finally, at the end of the transition period, i.e., 1 January 2005, India introduced product patent protection for pharmaceuticals and agrochemicals along with TRIPS flexibilities related to the pre-grant stage.

Flexibilities in India's patent law

India's use of the entire transition period offers an opportunity to examine the nature and trends in patent applications that were filed in the mailbox. It also provides an opportunity to examine the potential of key flexibilities contained in the patent law to create a viable space for continued generic production of medicines.

In 2005, when India was compelled to re-introduce the product patent regime, the Indian Parliament, aware of its responsibility not only to Indians but to patients across the world adopted the only pragmatic solution available — to utilize flexibilities available under TRIPS in an attempt to secure the availability, affordability and accessibility of medicines. According to this approach, TRIPS does not set any universal common standard for the substantial aspects of the patent law. Thus, as the Doha Declaration on the TRIPS Agreement and Public Health (Doha Declaration), clearly states every WTO member has the right "to use, to the full, the provisions in the TRIPS Agreement, which provide flexibility for this purpose".[142] Thus the TRIPS implementation strategy was "to find the means within the patent system and outside it, to generate the competitive environment that will help to offset the adverse price effect of patents on developing country consumers. The cautious approach suggests the implementation of TRIPS should be done with minimum damage".[143]

As noted above, the various amendments to India's patents law introduced flexibilities at both the pre- and post-grant stage of a patent application. This study explores the potential of three of these key flexibilities in allowing continued generic production of medicines.

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139 See Article 70.8, TRIPS Agreement which reads, "apply to these applications, as of the date of applications of this agreement, the criteria for patentability as laid down in the this agreement as if those criteria were being applied on the date of filing in that member or, where priority is available and claimed, the priority date of the application".

140 See Article 7.8, TRIPS Agreement which reads, "where a product is subject of a patent application in a member in accordance with paragraph 8 (a), exclusive marketing rights shall be granted, notwithstanding the provisions of part vi, for a period of five years after obtaining marketing approval n that member or until a product patent is granted or rejected in that member, whichever period is shorter, provided that, subsequent to the entry into force of the WTO agreement and a patent granted for that product in another member and marketing approval obtained in such other member."

141 This amendment was warranted by a WTO appellate body decision, which asked India to amend the Patents Act for the introduction of EMR and mailbox facility.

142 See Paragraph 4, WTO Doha Declaration on the TRIPS Agreement and Public Health.

143 CIPR (2003, p.38).

- The **first** relates to medicines invented prior to 1995. Under TRIPS there is no obligation to provide patent protection to products invented prior to 1 January 1995.[144]

- The **second** is one of the most important flexibilities employed by India which is the restriction of the scope of patentability in relation to known substances. Thus, section 3(d) of the Patents Act, 1970 prohibits the patenting of known medicines unless the patent applicant can demonstrate increased therapeutic efficacy. It must be borne in mind that section 3(d) is not a blanket prohibition on such patents. However, the Indian Patent Office is expected to apply this provision strictly while examining the applications before it. It is also expected to apply the provisions of section 3(e) that prohibits the patenting of mere admixtures and section 3(i) which excludes from patenting any process of "medical or surgical, curative, prophylactic or other treatment of human beings…"

- **Finally**, section 11A(7) of India's patents Act, 1970 provides that where a company was already producing and marketing a product before 1 January 2005 on which a patent application was made in the mailbox, should that patent be granted, the company may continue manufacturing that product on the payment of a reasonable royalty.

These are only some of the flexibilities available under the Indian law. However, if applied strictly they offer a significant space for generic production.

Objectives and methodology

As stated above, this study aims to examine the potential of the flexibilities contained in India's patent law and its implications for the continuation of generic competition. To this end, three key databases were created:

1. **Mailbox applications filed in India between 1995 and 2004:** The features of India's mailbox applications will indicate who the major players and countries are and the trends in patent applications filed during this period.

2. **The marketing approvals and patent history of NMEs approved by the USFDA between 1995 and 2004:** The lack of access to specifications of the patent applications filed in India makes it difficult to assess the true potential of the flexibilities in India's law. However, this information can be gleaned from the USFDA's *Orange Book* which provides detailed information not only of the NMEs[145] approved for marketing between 1995 and 2004 but also their patent history. Through a process of elimination such a database helps identify those medicines which are approved for marketing and therefore whose patent information should be examined as opposed to examining all patent applications many of which may not have resulted in an approved product. For this study the 2006 edition of the US *Orange Book* was used to create the database.

144 This is clear from article 70.3 which states that "there shall be no obligation to restore protection to subject matter which on the date of application of this agreement for the member in question has fallen into public domain".

145 New Molecular Entity (NME) is, according to the USFDA, a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the federal food, drug, and cosmetic act." an active moiety is a molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.

3. **The marketing approvals of NMEs given by India's drug regulator between 1995 and 2004:** This database was created to examine the potential of Section 11A and to enumerate those cases where even if there are patents, generic production can continue on the payment of a royalty. Based on the NMEs identified in the *Orange Book* database as having been approved between 1995 and 2004, information on the marketing status of these NMEs in India was collected from the CDSCO. The practice of the CDSCO in this regard varies with lists of approvals published at times on a monthly or yearly basis or as a consolidated list for a certain period of years.

The detailed methodology for analyzing these databases as well as the limitations of these databases is discussed below. The information from these three databases allows us to piece together the potential of the flexibilities in India's patent law. The patent history from the *Orange Book* helps us determine which of the medicines are pre-1995. This information matched with the applications in India's mailbox indicates whether patent applications on these pre-1995 medicines have been filed in the form of patents for known substances and how many would thus attract the provisions of section 3(d). Marketing approvals in India till 2004 indicate which medicines, even if patented would be eligible for continued generic production under section 11A of the Indian Patents Act.

II. Features of India's mailbox applications

In order to examine the patent applications received in the mailbox between 1995 and 2004, a database of patent applications published by the Indian Patent Office between 2005 and July 2006 was created. There were several reasons for compiling these particular applications for the Study. One, after 2005, the Indian Patent Office re-published all the applications it had received in the mailbox. Two, patent applications are to be published within 18 months of their receipt. To ensure that all applications filed in late 2003 and 2004 were captured in the database patent applications published up to July 2006 had to be included.

The limitations of this database are that they also include some patent applications filed after 2005 and that may have been published early within the 18-month period by the patent office. Further the Indian Patent Office does not distinguish between those applications received in the mailbox which would relate primarily to product patents and process patent applications received during this period. Thus, of the 9384 patent applications published between 2005 and July 2006, the titles of 1018 applications indicate that they are process patents. Nor does the database contain all the mailbox applications. As mentioned earlier, it captures patent applications published from January 2005 to July 2006. However the mailbox applications continued to be published by the Indian Patent Office till 30 November 2006 and again

Table 1: Country of Origin

Country	Total
US	2477
Germany	1266
Switzerland	527
Japan	468
UK	467
France	337
Sweden	323
Denmark	227
Belgium	154
Netherland	142
Italy	114
Canada	105
Other developed countries	333
Total	8426

Source: *Patent Office Journal*.

in the 17 March 2007 issue of the Patent Office Journal.[146] Nevertheless, it is safe to assume that the database of these applications comprises predominantly the mailbox applications and provides key information on trends in patent applications between 1995 and 2004.

Country of origin

The database reveals that 14 countries together accounted for 8426 applications in the database accounting for almost 90 percent of the applications. Of these 14 countries, except India, all are developed countries with the US leading in the list with 2477 patent applications (i.e., nearly 29 percent of the share of fourteen countries) followed by Germany with 1266 applications[147] (see Table 1).

Patent applicants

A closer look at the applications from the US, Germany and Switzerland, the three countries that account for the maximum applications among developed countries, indicates the level of concentration of applications with a few multinational companies (see Table 2). Thus, 22 entities in the US account for 44 percent of patent applications filed from the US with Pfizer making the maximum number of patent applications. In Germany, 14 entities hold 66.8 percent of the patent applications filed from Germany with Bayer leading the count. The level of

Table 2: Mail Box Applications from USA, Germany and Switzerland

	Patent applicant	USA	Germany	Switzerland
1	Abbott	22	1	0
2	American Cyanimide	39	0	0
3	Aventis	34	98	0
4	Bayer	27	258	0
5	Boehringer	8	98	0
6	Bristol Myers	78	1	0
7	Corixa	23	0	0
8	Dow	4	0	0
9	Eli Lilly	157	0	0
10	Gilead	7	0	0
11	Glaxo	125	10	8
12	Johnson & Johnson	32	2	0
13	Merck	21	173	0
14	Monsanto	9	0	0
15	Pfizer	297	0	0
16	Roche	1	3	219
17	Schering Corporation	67	37	3
18	Wyeth	48	0	0
19	Astra	0	33	0
20	Hoechest	4	117	0
21	Knoll	0	11	0
22	Novartis	3	4	150
23	Ciba Geigy	1	0	37
24	Universities	95	0	0
25	Total of the Above (1-24)	1102	846	417
26	Total Applications	2477	1266	527
27	Percentage of Total Applications	44.5	66.8	79.1

Source: *Patent Office Journal*.

146 Amit Sengupta et al, *Analyses of Mailbox Applications with Special Reference to Public Health*, WHO India, available at *www.whoindia.org/linkfiles/trade_agreement_part2_annexure.pdf*.

147 This number may go up further because the published data in the journal does not contain the information regarding the country of origin for 650 applications.

Table 3: Mail Box Applications from India

	Patent applicant	Applications
1	CSIR	146
2	Dr. Reddy's	110
3	Sun	63
4	Cipla	57
5	Ranbaxy	48
6	Hetero	39
7	Panacea	38
8	Orchid	37
9	Cadila	36
10	Dabur	33
11	Glenmark	26
12	Lupin	18
13	Natco	17
14	Wockhardt	11
15	University	5
16	Alembic	3
17	Aurobindo	2
18	**Total (1-17)**	**689**
19	**Grand Total of Indian applications**	**1486**
	Percent	**46.4**

Source: *Patent Office Journal*.

concentration is even higher in the case of Switzerland where just five entities together account for 79.1 percent of the patent applications filed from Switzerland. Roche has the largest share among the Swiss companies.

In the case of the patent applications from India, 17 firms together hold 46.4 percent of the patent applications filed from India during the transition period (see Table 3). The public sector research institution, Council of Scientific and Industrial Research (CSIR), has the maximum number of patent applications i.e. 146. In contrast to the US, Germany and Switzerland, the concentration of patent applications among Indian entities is low. Further, the largest generic pharmaceutical firms of Ranbaxy and Cipla have less than 100 patent applications. Dr. Reddy's Laboratories leads in the number of patent applications with over 100 applications.

The database also shows that 12 leading multinational companies account for 32 percent of the patent applications in the mailbox (see Table 4). Thus, of the 9384 patent applications in the database, these 12 companies together filed 2991 patent applications. GSK accounts for the maximum number of patent applications. However, these numbers may vary while taking into consideration the consolidation in the pharmaceutical industry that took place between 1995 and 2004. As a result several companies that filed patents no longer exist, for instance, Hoechst. Similarly in the initial years of mailbox applications GSK were three separate companies. Table 4 reflects these changes and the merged entities have been treated as such. The numbers may also not reflect several additional patent applications that these companies are likely to have filed through subsidiaries.

Trends in Patent Applications: Title Search

As noted above, one of the key concerns at the time that India changed its patents law in 2005 to re-introduce the product patent regime related to the patenting of known substances. Patent applications in this regard will usually claim compositions, formulations, salts, esters, ethers, polymorphs, pure forms, particle sizes, combinations, derivatives, crystalline forms, new uses, methods of treatment and formulations. Patents are also often claimed on drug delivery systems and routes of administration (e.g. sustained release, injectables, oral administration, etc.).

In order to ascertain whether a patent application relates to a product or a process or covers a known substance, the claims in the specifications of the application have to be examined. However, in the case of the Indian Patent Office, these specifications are not available in the public domain nor are they easy to obtain. In the absence of publicly available specifications, a word-based search of the titles of the patent applications in the database may provide some indication of the extent to which they relate to secondary patents. The word search was carried out using the terms used in section 3(d) of the Indian Patents Act 1970 (see Table 5).

There are several limitations to a title search. One, the title may not indicate that the application may, in fact, claim a new substance. Two, the results obtained may be overlapping as a title may use more than one term and may include, for instance, a formulation and a salt in the same application. However, the word search certainly provides an indication of the number of mailbox applications claiming patents on known substances. The search shows that the term composition is used over 1000 times, while the words salt, formulations, ester, combination and crystalline are used over a 100 times (Table 5).

The title search also reveals that patents have been claimed for new uses and methods of treatment which are explicitly excluded from patent protection in India.[148] Further applications have been filed for drug delivery mechanisms; thus 48 patent application titles include the words 'sustained release,' 15 contain the word 'injectable' and 226 contain the terms 'oral administration' or 'oral dosage form'. The strict application of patentability criteria may not allow the patenting of drug delivery systems as most such applications may fail to satisfy the strict scrutiny of the inventive step criterion.[149]

As noted in chapter 2A, such a title search helps identify patent applications that require greater scrutiny by the patent office. Applications for the patenting of known substances are unlikely to meet patentability criteria if strictly applied (see Correa, 2007); in India this takes the form of the provisions of Section 3(d).

148 Section 3(d) and 3(i), Indian Patents Act, 1970.

149 See Correa (2008).

Table 4: Mail Box Applications by Company

Patent applicant	Applications
Glaxo SmithKline Beecham	524
Astra Zeneca	384
Pfizer	358
Bayer	310
Sanofi Aventis	255
Merck	210
Novartis	187
Elli Lilly	166
Hoechest	142
Boehringer Ingelheim	123
Schering Plough	113
Roche	219
Total	2991

Source: *Patent Office Journal*.

Table 5: Nature of Claims (Title Search 1995–2004)

Nature of Claim	Applications
Compositions	1714
Formulation	410
Salt	179
Ester	135
Ether	47
Polymorph	72
Pure form	20
Particle	44
Combination	218
Derivatives	1393
Crystalline	135
Dosage	87
New use	13
Method of treatment	20

Source: *Patent Office Journal*.

Disease breakup

A title search of the patent applications also provides some interesting insights into what diseases companies and applicants apply their resources. The title search reveals a greater concentration of applications in certain disease areas. Thus, a large number of patent applications relate to cancer, HIV/AIDS, diabetes and cardiovascular diseases. Fewer applications have been filed related to TB and malaria.

Table 6: Disease Classification of Mail Box Applications

Type	Number
Cancer	136
Diabetes	120
HIV/AIDS	73
Antibiotics	53
Cardiovascular	19
Tuberculosis	24
Malaria	21
Hypertension	7
Influenza	6

Source: *Patent Office Journal*.

IV. Patent History of New Molecular Entities approved by the USFDA between 1995 and 2004

As noted above titles searches have several limitations. While an examination of the patent applications in India's mailbox clearly indicate the dominance of developed countries and certain multinational companies, the lack of publicly available specifications of these applications limits our ability to determine to what extent the flexibilities in India's patent law have the potential of allowing continued generic competition.

In this regard, one may turn to the *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations* published by the USFDA. The *Orange Book* details all medicines that have received marketing approval from the USFDA. Additionally, in light of requirements under various US laws, the *Orange Book* also provides several other details related to these medicines including classifying NMEs and the patent history of approved medicines. The advantage of examining the information in the *Orange Book* is that it helps focus on those medicines and the patents related to them that are actually being marketed. Several patent applications related to medicines may never finally result in a product for several reasons including lack of safety or efficacy. It must of course be noted that simply because a medicine has been approved for marketing by a drug regulatory authority is no indication of whether it is in fact of public health importance or

Table 7: Number of NMEs and Biologicals Approvals

Year	Approvals
1995	28
1996	53
1997	39
1998	30
1999	35
2000	27
2001	24
2002	17
2003	21
2004	31
Total	305

Source: *Patent Office Journal*.

that it is rational. The *Orange Book* also lists patent expiry dates related to a particular NME allowing us to track the history of these patents.

This Study uses the 2006 edition of the *Orange Book* to gather this data. Based on the information available in the *Orange Book*, a database of NMEs approved for marketing by the USFDA between 1995 and 2004 was created.

Table 8: Breakdown of NME Approval, 1995–2004

Company	NME Approvals
GSK	14
Sanofi Aventis	14
Novartis	13
Uppjohn	11
Pfizer	10
Merck	10
Astra Zeneca	9
Elli-Lilly	9
Abbott	9
Bayer	7
Bristol Myers Squibb	6
Boehringer Ingelheim	5
Wyeth	4
Roche	4
Johnson and Johnson	1
Total	126

Source: *Patent Office Journal*.

Table 9: Disease-wise classification

Name of the disease	Number
Hypertension	17
Cancer	33
HIV/AIDS	15
Cardiovascular	9
Diabetic	13
Skin diseaes	8
Throbosis	7
Antibiotic	7
Mental diaeses	7
Asthma	6
Epilepsy	6
Others	177
Total	305

Source: *Patent Office Journal*.

NME approvals by the USFDA (1995–2004)

The USFDA approved 305 NMEs and biologicals between 1995 and 2004 (see Table 7). Through further examination it was concluded that of these 301 NMEs would be the focus of this Study.[150] It should be noted that the focus on these 301 NMEs does not imply that all 301 NMEs are important from a public health perspective. Further, some of these NMEs were either banned or discontinued for human use at later dates as in the case of *valdecoxib* which has been banned in the US and many other countries since 2005. Of these

150 Even though the USFDA *Orange Book* gives the number of NMEs approved in 1997 as 39 once the name and approval date for NMEs approved in 1997 was recovered from the FDA Monthly Approval Database it gives only 36 NMEs instead of 39. Since the list also mentioned 'Urea' twice, for the purpose of this study this was counted only once. Thus the study focuses only on 301 NMEs. See *www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/ucm121102.html*.

Table 10: Number of NMEs with patent expiry dates on or after 2015

YEAR of Marketing Approval	Number of Patent Expiry on or After 2015					
	2015	2016	2017	2018	2019	2021
1995	0	0	1	0	0	0
1996	0	0	0	0	0	1
1997	0	0	0	0	0	0
1998	0	0	0	1	0	0
1999	0	1	0	0	1	0
2000	1	0	0	1	1	0
2001	5	0	0	0	1	0
2002	0	1	0	0	1	0
2003	2	2	1	1	0	0
2004	4	0	0	0	0	0
Total	12	4	2	3	4	1

Source: *Patent Office Journal*.

Table 11: Number of NMEs for which Patent Expiry Dates are not listed in the Orange Book

YEAR	Expiry Date not available
1995	5
1996	11
1997	7
1998	5
1999	5
2000	7
2001	3
2002	2
2003	1
2004	18
Total	64

Source: *Patent Office Journal*.

approvals, 137 or 46 percent are claimed by 15 companies (see Table 8). The maximum number of NMEs approvals relate to hypertension followed by cancer, HIV and cardiovascular diseases (see Table 9).

Patent History of NMEs approved by the USFDA (1995–2004)

As noted above, the *Orange Book* also details the patent expiry dates related to NMEs. An NME approved between 1995 and 2004 may have patents associated with it that are far older. It must be kept in mind that from the time of making a patent application related to a medicine to when it is approved for marketing, a substantial amount of time may elapse. An examination of the data reveals that a single NME can also have multiple patents with multiple expiry dates. Patent expiry data reveals the date and year of patent filing. Among the multiple patent expiry dates, the earliest expiry date reveals the oldest patent in force on that particular NME according to the Orange book. The limitations of relying on the *Orange Book* include the fact that companies may not list the latest patent there to suppress the expiry date of original patents on the substance in question. Further, there may be considerable delay in the listing of the patent expiry date. Still the *Orange Book* provides some of the most detailed information on approved medicines and the patents associated with them.

Hence, if the patent expiry date is on or after 2015 it can be concluded that such particular patent is filed on or after 1995 — the year that TRIPS came into force. If the earliest patent expiry date of an NME is prior to 2015, this means that the patent application was filed 20 years ago, i.e., prior to 1995. In India such patent applications being pre-1995 would be liable to be rejected.

An examination of the earliest patent expiry date of the 301 NMEs approved for marketing between 1995 and 2004, reveals that only 26 of the 301 NMEs have an original patent duration that expires on or after 2015 (see Table 10). However, the *Orange Book* does not list

the earliest patent expiry date for 64 NMEs (see Table 11). The patent history of these NMEs as well as of the 26 NMEs with expiry dates on or after 2015 were further examined.

The further examination of the patent history of the 26 NMEs using the Merck Index, the EPO's database and scientific journals revealed that with the exception of 6, all NMEs are pre-1995. The same methodology was used to examine the patent history of the 64 NMEs for which the *Orange Book* does not list patent expiry dates, revealing that except 4, all other 61 NMEs have been invented prior to 1995.

This examination thus shows that of the 301 NMEs approved for marketing by the USFDA during the period of this study, only 10 were invented after 1995. However, as noted above, there are 9384 applications in India's mailbox. It is evident after comparing these different sets of data that applications related to the other 291 NMEs relate to patents on known substances.

Indeed, a search of the patent applications on the Indian Patent Office website and the mailbox database reveals that patent applications claiming both process and product applications on 278 pre-1995 NMEs have been filed (see Annex IV for examples). The product patent applications clearly relate to the patenting of known substances and should attract the scrutiny of sections 3(d), (e)[151] and (i)[152] of the Indian Patents Act 1970.

Assuming that the Indian Patent Office is successful in the strict application of the patentability criteria under India's patent law, the primary concerns in terms of access to treatment relate to ten NMEs. The ten NMEs are for the treatment of cancer, HIV/AIDS, osteoarthritis, epilepsy, hyperactivity disorder, erectile dysfunction and for the imaging of appendicitis (Table 12).

Table 12: Post 1995 NMEs

No.	Name of NME	Year of Approval	Therapeutic Use
1	Oxcarbazepine	2000	Anti-epilepsy
2	Valdecoxib	2001	Osteoarthritis
3	Atomoxetine Hydrochloride	2002	Hyperactivity Disorder
4	Atazanavir	2003	HIV/AIDS
5	Vardenafil	2003	Erectile dysfunction
6	Abarelix	2003	Antineoplastic (hormonal)
7	Erolotinib Hydrochloride	2004	Cancer
8	Bevacizumab	2004	Cancer
9	Technetium 99m Tc fanolesomab	2004	Imaging of appendicitis
10	Ramelteon	2004	Sedative & hypnotic

Source: *Patent Office Journal*.

151 Section 3(e) prohibits patents on "a substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof or a process for producing such substance;"

152 Section 3(i) prohibits patents on "any process for the medicinal, surgical, curative, prophylactic or other treatment of human beings or any process for a similar treatment of animals or plants to render them free of disease or to increase their economic value or that of their products."

V. Marketing Approval for NMEs in India from 1995–2004

The marketing approval data from India's CDSCO shows that out of the 301 NMEs approved by the USFDA for marketing between 1995 and 2004, 161 are available in India. Between 1995 and 2004, the CDSCO gave marketing approval for 128 generic versions of the 301 NMEs approved by the USFDA during the same time period. Since the marketing approval for these 128 generic versions was given before the introduction of product patents in 2005, generic companies manufacturing these NMEs may continue to manufacture them on the payment of a reasonable royalty under section 11A of the Patents Act, 1970.[153] Annex VI provides the details of all 301 NMEs, their therapeutic uses, patent expiry dates, and marketing approval dates in the US and in India. The important point to keep in mind is that a strict application of section 3(d) can secure the generic production of most of the NMEs introduced between 1995 and 2004.

Of the post-1995 NMEs, three have received marketing approval in India prior to 2005 while one, *erlotinib hydrochloride*, is the subject of a patent battle between Roche and the Indian companies, Cipla and NATCO. During the course of this battle, the Delhi High Court refused to pass an injunction against Cipla from producing this medicine, in part due to concerns related to public interest and access to medicines. Although Roche appealed this decision, the Indian Supreme Court refused to interfere with this order of the Delhi High Court.[154]

VI. The Patent Application Landscape in India and Implications for Access to Medicines: A Case Study of NMEs for five Major Diseases

The three databases created from the Indian mailbox applications, the USFDA *Orange Book* and the CDSCO provide the information sufficient to determine the potential for generic competition to continue if the flexibilities in India's patent law are applied strictly and correctly. This is demonstrated through a case study of five key therapeutic areas such as diabetes, hypertension, cardiovascular diseases, cancer and HIV/AIDS. For a a detailed analysis of these case studies see Annex V.

Treatment for diabetes

There are 13 NMEs that received marketing approval from the USFDA between 1995 and 2004 for the treatment of diabetes. Of these, 9 are currently available in India. The patent expiry dates for 12 of these NMEs are listed in the *Orange Book* and clearly show that all 12 NMEs are invented prior to 1995. An examination of the patent history of the one NME not listed in the *Orange Book* also shows that it is a pre-1995 medicine. Thus, all the NMEs introduced for the treatment of diabetes during the transition period are pre-1995. Therefore patent applications on these molecules in the Indian mailbox should attract the safeguards against the patenting of known substances contained in India's patent law. Further, the generic versions of the nine NMEs available in

153 Section 11A(7) "…a patent is granted in respect of applications made under sub-section (2) of section 5, the patent holder shall only be entitled to receive reasonable royalty from such enterprises which have made significant investment and were producing and marketing the concerned product prior to 1-1-2005 and which continue to manufacture the product covered by the patent on the date of grant of the patent and no infringement proceedings shall be instituted against such enterprises".

154 'Roche's SLP against Cipla order quashed', *Business Standard*, 29 August 2009, available at *www.business-standard.com/india/news/roches-slp-against-cipla-order-quashed/368446/* (consulted on 14 October 2009).

India were introduced prior to 2004 and are eligible for immunity under section 11A (7) of the Patents Act (see Table E.1, Annex V).

Treatment for hypertension

During the transition period, 17 NMEs obtained marketing approval from USFDA for the treatment of hypertension. Of these generic versions of 13 NMEs are currently available in India. However, only six of these generic versions are eligible for the Section 11A immunity. The patent expiry data of the *Orange Book* contains the patent expiry dates of 15 NMEs and shows that that 13 of the 15 are invented prior to 1995. A further examination of the patent history of the remaining two NMEs shows that they were also invented prior to 1995. (See Table E.2, Annex V)

Treatment for cardiovascular diseases

The USFDA gave marketing approval for nine NMEs for the treatment of cardiovascular diseases. Of these, generic versions of five are available in India and are all eligible for the immunity under Section 11A(7). The *Orange Book* contains the patent expiry data of all nine NMEs which are all pre-1995 molecules (see Table E.3, Annex V).

Treatment for cancer

NMEs for cancer treatment obtained the maximum number of marketing approvals from the USFDA during the transition period, i.e., 33 NMEs. Of these, 22 are available from generic manufacturers in India of which 16 are eligible for the Section 11A(7) immunity. The *Orange Book* provides the patent expiry data of 30 of the NMEs of which 26 were invented prior to 1995. A more detailed examination of the patent history of the three NMEs not listed in the *Orange Book* and the four NMEs that show a patent expiry date beyond 2015 reveal that all except one NME are pre-1995 (see Table E.4, Annex V).

Treatment for HIV/AIDS

There were 15 NMEs approved by the USFDA for the treatment of HIV and AIDS between 1995 and 2004. The *Orange Book* contains the patent expiry date of all 15 which reveals that except one, Atazanavir, all other NMEs are pre-1995. This means that patent applications on the pre-1995 NMEs must attract the strict scrutiny of the Indian Patent Office. As a result of patent oppositions by civil society groups and generic companies, the patent application on one HIV combination (*lamivudine/zidovudine*) was withdrawn by GSK and applications for the syrup form of *Nevirapine*, salt forms of *Tenofovir* and some patent applications related to *Darunavir* have been rejected in India. Generic versions of 12 of the 15 NMEs are currently available in India, of which five generic versions are eligible for immunity under Section 11 A(7). (See Table E.5, Annex V)

VII. Analysis and recommendations

The information from the databases created as part of this study indicates that the application of strict patentability criteria by the Indian Patent Office can be expected to significantly reduce the number of patents granted in India on the mailbox applications. As is evident from the USFDA *Orange Book* listings, NMEs approved between 1995 and 2004 are predominantly pre-1995 medicines and therefore in the public domain as far as India is concerned. The only way that patent applicants can claim patents on these are to file for patents on known substances, which would automatically attract the strict patentability criteria of India's patent law including section 3(d). Even where some of these patents are granted, the case study of the five major diseases areas indicates that several generic versions of these NMEs were already on the Indian market prior to 2005.

The landscape of the pharmaceutical patent applications in the mailbox shows that the vast majority of patent applications filed in India's mailbox are from developed countries. Pharmaceutical MNCs clearly dominate the mailbox applications and as noted above several of these could fall within the scrutiny of section 3(d). The large number of mailbox applications itself raises doubts as to the quality of the claimed inventions. However, an examination of the quality of these applications is a challenging task for any government, considering the sheer number and volume of these applications.

The study offers an alternative approach of a process of elimination by attempting to locate new medicines introduced during the transition period in the US. The analysis of the patent expiry data provided in the USFDA *Orange Book* and further research to trace the patent history of NMEs reveals that of 301 NMEs approved by the USFDA between 1995 and 2004, 291 were invented prior to 1995. Such an approach not only provides guidance for those generic companies or patients or health groups as to which patent oppositions to file, it also brings much more predictability for governments and health services providers to assess the implications of product patents on access to medicines in the immediate future.

However, the effectiveness of these flexibilities is dependent on their application by the Indian Patent Office. According to the Indian Patent Office, between 2007 and March 2010, 3470 pharmaceutical products patents have been granted.[155] The huge number of patents raises serious concerns as to the quality of claims that have been approved for patenting. Moreover, a recent study published by the National Intellectual Property Organization (NIPO) notes that section 3(d) is not being applied to its full extent.[156] The NIPO study identifies at least 86 patents granted on known substances or combinations of substances bypassing section 3(d). One of the important limitations of section 3(d) is that it can be used only on a case-by-case basis. As a result, its effectiveness depends on the individual examiner's capability to apply the provision in actual situations. This could act as encouragement for a patent applicant to try out the possibility of obtaining the patent irrespective of section 3(d). In other words, section 3(d) does not act as a disincentive for patents applications on known substances.

155 Details of product patents granted by Indian patent office in 2007-2010, Indian Patent Office, 2010, available at *http://patentoffice.nic.in/iponew/totalpharma_200708_200809.pdf*.

156 T.C. James, 'Patent Protection and Innovation: Section 3(d) of the Patents Act and Indian Pharmaceutical Industry,' NIPO, 2010 available at *www.nipoonline.org/section-report.doc*.

In light of the findings of this study, developing countries, including LDCs (as well as India), could consider the following recommendations:

- **Absolute exclusion of patents on substances in the public domain prior to 1995**: India's patent law should have ideally excluded patents on substances known prior to 1995. However, the Indian Patents Act, 1970 did not explicitly reject the product patent claims for substances invented prior to 1995 but instead provided a small window to patent applicants to get a patent on a new form of a known substance if they could demonstrate increased therapeutic efficacy. However, this has meant that nearly every mailbox application has to undergo the scrutiny under section 3(d) increasing significantly the burden on patent offices as well as providing greater room for patents on known substances to be granted. This is an important lesson for LDCs to not only use their transition periods to the full extent but also to enact provisions in their domestic laws that exclude substances invented before or during the transition period from patentability. Since there is no obligation on the part of the LDCs to provide a mailbox facility, such a safeguard would help the LDCs limit the impact of product patent monopolies on medicines.

- **Improvement in infrastructure and human resources in the Patent Office**: Further infrastructure limitations of the Indian Patent Office act as a major factor in the effective application of Section 3(d). There has been a fourfold increase in patent applications filed in India since 1995/96 to 2007/08 from 7036 to 35218 and a 17 fold increase in the granting of patents from 907 in 1995/96 to 15261 in 2007/08.[157] Similarly there is an increase in patent applications on chemical and drugs. In 2007/08, the Indian Patent office received 4267 patent applications on drugs and 6375 applications on chemicals while the number of granted patents on chemicals and drugs are 4071 and 1469 respectively.[158] However, the infrastructure of Patent Offices especially in terms of human resources is not enough to meet the challenges of the product patent regime. There are 62 patent examiners with their specialization in chemistry (31), biotech (11), microbiology (11), biochemistry (8) and biopharma (1), who are capable of examining patents on pharmaceuticals and health-related technology. These 62 examiners have granted 7166 patents during 2007/08. The breakup of 7166 patents is: chemicals (4071), drugs (1469), biochemistry (91,149), biotech (314), biomedical (138) and microbiology (25). This shows that each examiner granted 155 patents in 2007/08.[159] This heavy workload is bound to result in overlooking the safeguards related to patentability in the Indian law including section 3(d). Infrastructure limitations are a limiting factor to the effective application of section 3(d). Hence countries with limited infrastructure need to apply more stringent safeguards to prevent the patenting of known substances. In other words patent legislations of developing countries should have an inbuilt mechanism which can act as a disincentive for filing patent applications for trivial inventions. Further, developing and LDCs should provide support and funding for patent

157 See 'Annual Report of the Office of the Controller General of Patents, Designs, Trademarks and Geographical Indications for the year 2004-05,' and 'Annual Report of the Office of the Controller General of Patents, Designs and Trademarks including GIR and PIS/NIIPM(IPTI) – 2007-08'.

158 See 'Appendix E – Number of patent applications filed during last five years from 2003-2004 to 2007-2008 under various fields of inventions,' and 'Appendix F – Number of patents granted during last five years from 2003-2004 to 2007-2008 under various fields of inventions,' Annual Report of the Office of the Controller General of Patents, Designs and Trademarks including GIR and PIS/NIIPM(IPTI) – 2007-08.

159 See Appendix A(1) – Details of the Technical Field of Specialisation of Working Examiners, Annual Report of the Office of the Controller General of Patents, Designs and Trademarks including GIR and PIS/NIIPM(IPTI) – 2007-2008'.

oppositions as these assist the Patent Office in their scrutiny of patent applications and help ensure that frivolous patents are not granted.

- **Mandatory declaration of INNs in patent applications**: The study also indicates the benefits of an NME-based approach in the analysis of patents for developing countries and public health. A patent application does not provide a clear picture of the implications of its grant on access to medicines. In other words, the name of an NME, often the INN provides a face to an otherwise abstract patent application. Patents legislations of developing countries including India should impose an obligation on patent applicant to declare the INN at the time of filing of the application if the INN is already allotted or immediately on allocation. This would lessen the burden of Patent Offices while examining patents. It also helps other actors, including the generic industry, consumer groups, patient groups, the health ministry, to examine the quality of patent applications and invoke the necessary safeguard mechanisms contained in the patent legislation to protect public health.

- **Creation of a regularly updated database of NMEs**: The Indian Patent office should make a database of NMEs introduced between 1995 and 2010 and the history of these inventions. This would enable them to examine these applications more accurately. As shown in this Study, the vast majority of NMEs introduced from 1995 to 2004 were invented prior to 1995 and there is no obligation for India or any other developing country to provide product patent protection. It suggests a change in the approach of the Indian Patent Office to view each pharmaceutical patent application in the context of the NME, if the details of the NMEs are available. The database of NMEs from 1995 to 2010 will definitely help the patent offices in identifying patent applications on known substances. The Indian Patent Office should be proactive in identifying these applications and weeding them out. Developing countries like India should also undertake an analysis of NMEs approved by the USFDA from 1995 to 2010 to determine the public health importance of the patent applications, the cost of production, technological dimensions, the patent status (current and potential) and identify potential candidates for compulsory licenses and other health safeguards in the flexibilities foreseen in the Patents Act, 1970. Such an analysis would present governments with a clear picture on public health requirements in the coming days and prepare in advance to use the appropriate TRIPS flexibilities to address the situation.

- **Establishment of an Institutional Mechanism for the review of granted patents and their impact on access to medicines with an operational mandate to recommend the use of TRIPS flexibilities**: Since India has completed five years under the product patent regime it is time to review how far the existing safeguards including section 3(d) have succeeded in preventing the patenting of known substances. The government should conduct an independent review of granted products patents since 2005 with an objective of further strengthening the existing safeguards to prevent the patenting of known substances. Further there should be an institutional mechanism to monitor and review granted patents and their implications on public health. Such a mechanism would enable the government to invoke appropriate safeguard mechanisms at the appropriate time to meet the challenges of the product patent regime.

AFTERWORD ◊

The future of Access to Affordable Medicines and India's Role Post TRIPS

India's robust generic pharmaceutical industry and its emergence as the world's largest supplier of affordable medicines is in large part due India's public health oriented patent policy. India's compliance with the TRIPS Agreement in 2005 was accompanied by concerns about its ability to maintain its comparative advantage in the manufacture and export of quality generic medicines. The Indian experience in balancing the TRIPS regime with public interest is being closely watched by several other countries attempting to strike similar balances. This study documents and analyzes the impact of the new regime and the responses to it not only from an industry perspective but also a legal one. This study hopes to contribute to the assessment of the Indian response to global rules and whether this response can fulfill the need for access to affordable medicines not only in India but across the developing world.

In December 2009, UNDP organized a technical consultation to discuss India's role in the domain of sustainable supply and access to affordable medicines and some of the preliminary findings of the study. The consultation reviewed the studies in this publication and comments and recommendations of participants were considered by the authors in the finalization of their respective chapters. The deliberations also provided policy recommendations from national and international perspectives for the sustainability of global access to affordable medicines. The frontiers of South--South collaborations in this area, especially using existing networks such as the IBSA framework were also explored. This section summarizes some of the key discussions that took place at the consultation.

I. Key Issues

In the course of the discussions on the three studies, a few topics came up repeatedly in all the sessions. These are discussed here in detail.

Full use of Public Health Safeguards

The findings in all three studies of the potential of the safeguards included in India's patent law were highlighted by several participants. It was noted however, that the increasing number of patents being granted in India was an indication that these safeguards were not being employed fully. This was also similar in the case of other developing countries that have safeguards in their patent laws but are not implementing them fully. Also, it was noted that developing countries should include strict patentability criteria in their laws along with other safeguards. Discussions ensued that the implementation of the TRIPS regime imposed significant institutional and financial burdens on developing countries for which they require assistance.

◊ This afterword prepared by Kajal Bharadwaj with Savita Mullapudi Narasimhan relies heavily on notes and the meeting report prepared by Mr. Anil Kumar, India Global, Delhi for UNDP, 2010. For the sake of brevity, this note does not discuss presentations or the comments received on the respective chapters of this study.

Civil society participants felt that instead of discussions on how to improve the use of current safeguards, the government was constantly drawn into discussions on adopting even higher intellectual property standards. Instead, there should be a clear and focused strategy to fully and strictly apply the existing safeguards in India's patents law.

Data exclusivity

The issue of data exclusivity was brought up by several discussants and participants. It was pointed out that the imposition of data exclusivity would nullify the impact of section 3(d) as companies would gain exclusivity on all products that they provide clinical data for, including new uses, new forms, etc., of existing medicines. The demands of developed countries in this regard and their claims that data exclusivity would incentivize R&D were discussed. Civil society and national experts pointed out that the patent system was the compromise that developing countries accepted on the promise of increased R&D. Not only has this system not delivered drugs required by developing countries, but where medicines do exist they are priced out of the reach of these countries. Additional exclusivity, they noted, would only make the situation worse. An industry representative reiterated that TRIPS does not require data exclusivity.

It was noted that the attempts to introduce data exclusivity were being made through various forums. During discussions on an inter-ministerial committee established by the Indian government on the subject, it was clarified that the report on data exclusivity that everyone cited as an Indian government report was in fact only the recommendation of the Department of Chemicals. The inter-ministerial committee itself was unable to arrive at any conclusion due to objections from various ministries. Pressure on this subject was also taking the form of litigation by MNCs. Participants also discussed that data exclusivity is being pushed by the EU through FTA negotiations. It was noted that data exclusivity would have an extremely detrimental impact on the Indian generic industry as it would create an additional monopoly on medicines, separate from the one created by patents. The effect of the safeguards in the Indian patent law would be nullified by data exclusivity. Also, the issue of the lack of transparency in the discussions on data exclusivity going on within the government was raised. It was pointed out that several experts have warned against the adoption of data exclusivity including UNDP, the WHO, the CIPIH and the Special Rapporteur on the Right to Health.

India's Free Trade Agreement negotiations

Several participants noted that while discussions at the consultation were focused on the use and implementation of the existing safeguards in India's patent law, there was also immense pressure on India through FTA negotiations with developed countries to adopt TRIPS-plus standards. [TRIPS-plus standards refer to standards for intellectual property protection and implementation greater than those specified in the TRIPS Agreement. Ed]

Another participant highlighted provisions that will likely feature in the FTA negotiations between the EU and India including extension of patent terms, the imposition of data exclusivity and border measures. In particular participants were concerned with the latter and some noted that the EU was attempting to impose its higher standards of intellectual property protection on India. Border measures in the EU have led to the seizure of Indian generic medicines in transit from India to Africa and Latin America (discussed below). Civil society representatives noted that the EU's negotiations in this regard have become more aggressive on intellectual property not only with India but also with countries in Africa, Latin America and Asia. It was also noted that all

free trade negotiations have to be closely watched as even the negotiations with the EFTA include demands of data exclusivity from India. Civil society participants noted that there had been no information available and no consultations by the Indian government. Nor have any impact assessments of these FTAs on access to medicines been conducted.

It was also pointed out that even in the absence of FTA negotiations with the US, there is an Agreement on Intellectual Property Rights that is being pursued by both countries. According to civil society participants, this is of great concern given the consistent attacks on India's patent law through the Special 301 reports of the USTR.

Confusing generic medicines as counterfeit

The ongoing attempts at various forums to confuse generic medicines with fake medicines were also a topic of repeated discussion. Participants noted that the term 'counterfeit' was being used to refer both to fake medicines and to those subject to patent and trademark disputes. One participant noted that interests at the various forums had become extremely entrenched. Another noted that there were commercial interests behind all these initiatives. It was raised that the Indian government has commenced discussions with various African governments on this subject.

It was pointed out the debates on 'counterfeit' medicines were taking a serious turn as some groups were going so far as to link this issue with world peace and trying to bring in the UN Security Council. Some participants cautioned that India must seek collaboration on this issue or it will be targeted for protecting business interests. Participants also felt that this was feeding into attempts to heighten the enforcement of intellectual property rights and that there was an attempt to involve several organizations into the enforcement of intellectual property such as Interpol, the Universal Postal Union and the World Customs Organization. Participants recommended that this could be an area of collaboration for IBSA which should consider adopting a declaration on intellectual property and development and promoting a shared understanding on intellectual property and other issues. A long-term strategy, they felt, was required to address this issue as several African countries were starting to draft anti-counterfeit laws.

Participants also felt that the tone of the discussions on 'counterfeit' should be countered by positive collaborations on R&D and the building of technological alliances with a focus on building technological support, human resource capability, sharing of knowledge, etc.

Seizures of Indian generics

Much of the discussion focused on the seizures of generic medicines being sent from India to Africa and Latin America. Participants noted that this created non-tariff barriers on pharmaceutical trade and discussed the options before the Indian government in this context including using WTO norms to challenge the seizures. Some asked if it was possible for the generic industry to use other routes for the export of medicines and the economic feasibility of a new trade route by involving Brazil was also discussed. However, civil society participants noted that this was a defensive and unnecessary position; nor was it a feasible solution with developed countries attempting to have similar laws passed in more countries. In this context, the secret negotiations on the ACTA by the US, EU and other key port countries were raised as another worrying development.

II. Special session: Innovation and health — Possible South–South collaborations

A key session at the consultation was devoted to discussing possible South-South collaboration in the area of innovation and health. Representatives from Brazil and UNDP presented the experiences of Latin America and Africa in addressing the adverse impacts of the TRIPS regime. The discussion was underscored by the emerging crisis in HIV treatment with a scale-down of funding for treatment on the horizon and the decreasing avenues for generic production which only threatened to deepen the crisis.

The experience of African countries with the implementation of TRIPS ranged from that of South Africa that has included several safeguards in its law for parallel importation, compulsory licensing and government use as well as a strong competition law to those countries that have adopted the patent laws of colonial powers without adapting them to local priorities. In the case of regional patent organisations in Africa like the African Regional Intellectual Property Organization (ARIPO) and Organisation Africaine de la Propriété Intellectuelle (OAPI), both are characterized by lower standards of patentability.

In Brazil the approach to intellectual property and health is conditioned by the Brazilian healthcare system which is premised on the concept of 'universal access'. The Ministry of Health is the only buyer of high cost drugs through a system of centralized procurement; as a result the health sector is also involved in the analysis of applications for patents on pharmaceutical products and processes. An Inter-ministerial Group on Intellectual Property is also very active on matters of policy. The clear relationship between patents, prices and access also shapes the Brazilian approach to compulsory licenses. Prices in other countries, the availability of a registered generic version, whether the medicines would be produced locally or have to be imported and the quantity of medicine required are some of the important issues considered in Brazil while issuing compulsory licenses.

Apart from IBSA, Brazil is also a part of other South-South collaborations such as the Technology network on HIV/AIDS which includes Argentina, Brazil, China, Cuba, Nigeria, Russia, Thailand and Ukraine. India attended the first meeting of this network which focuses on the production of ARVs and other medicines, universal access, price reduction and the effective and rational use of generics. Another initiative of the Brazilian government focuses on facilitating and fostering South-South horizontal technical cooperation projects, in order to strengthen and scale up sustainable national responses to HIV/AIDS in developing countries. The Brazilian experience has shown that the challenges of ensuring access to treatment in the future include ensuring universal access, fair pricing, the use of TRIPS flexibilities and the cooperation and exchange of information and technology transfer among developing countries.

Observations on South-South Collaboration

A representative of the Ministry of External Affairs stated that given the capabilities of India, Brazil and South Africa, there is lot of potential for South--South cooperation and that within the IBSA framework, there is a working Group on public health issues. It was felt that the protection of traditional knowledge is a key area for South-South cooperation as are the discussions at different forums on research and development. However, the challenges in this area are also increasing with several entrenched interests in international forums like the WTO, the World Intellectual Property Organization (WIPO), WHO, etc. where the issues are discussed. The changing scenario with the financial crisis was highlighted, as well as the need for an exchange of experts and delegations to strengthen the intellectual property and R&D capabilities in the South. Such

cooperation could help increase the focus and work on neglected diseases. South–South cooperation alone would not be sufficient and governments needed to work towards greater international support, tax incentives, international funding, etc. to focus more on neglected diseases. Pointing out the various forums and mechanisms for consultations between developing countries, it was noted that these were early days for IBSA and in the current international environment progress has been slow but that the Indian government and the political leadership are committed to IBSA.

National experts and participants from the civil society highlighted the scope for expanding the IBSA initiative. It was noted that the lack of information and understanding on previous positions of the Indian government and the lack of reasons, evidence and data for those positions have had a detrimental impact on negotiations at several levels. There needs to be some improvement in the capabilities of the government for institutional memory and that, inter-ministerial and inter-departmental efforts should be made in this area.

Participants felt that there was a window of opportunity for cooperation to address the various challenges posed by the TRIPS regime including the counterfeit issue which was one where developing countries must work together. The IBSA forum must also be used by the governments to refine their negotiating positions on several issues. It was suggested that IBSA also take the initiative for policy dialogue with civil society.

It was noted that the impact of shrinking generic competition for access to medicines cannot be underestimated and that South-South cooperation is an area where capacity can be built in a very cost-effective manner and IBSA could be an important entry point for this collaboration.

A representative from the industry felt that IBSA would benefit from greater participation and inputs from the generic industry as well as a clear focus on pharmaceuticals and technology transfer. It was suggested that IBSA take up scientific and training initiatives such as the Industrial Training Institutes or ITIs.

IBSA Dialogue

At the Academic Forum of the 4th IBSA Dialogue Process held in Brasilia in April 2010, these issues were further discussed. The process culminated with the following recommendations presented to the heads of the three States by UNDP in the areas of Health Innovation, Intellectual Property Rights and Access to Essential Drugs:

- Co-operation between the patent offices in the IBSA countries, particularly to stop the awarding of frivolous patents and to prioritize access to essential medicines;
- Consultation between IBSA countries on bilateral processes including free-trade agreements, which may have adverse impacts on access to essential drugs in the other IBSA countries;
- Sharing information on cost effectiveness analyses undertaken by the three countries; and
- Collaboration in R&D especially on priority and neglected diseases

UNDP is dedicated to supporting IBSA countries in building capacities and providing advisory policy support for all of the recommendations presented.

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ANNEX I (CHAPTER 1)

Methodology for Study of the Industry Response and Classification of the Indian pharmaceutical industry

No systematic information is available on the actual number of pharmaceuticals manufacturers in India. Using a variety of sources NPPA (2007) has estimated that the total number of manufacturing units in India is 10,563, of which 8,174 are formulation manufacturers and 2389 API manufacturers.[1] Proper statistics are not available for most of the units. A standard source of information for the retail formulations market is the *Stockist Secondary Audit*, a market survey based on 2400 stockists covering 40,000 retailers conducted by ORG-IMS. Company-wise information is available from this source for 468 companies including small companies. The more elaborate general source is the Prowess corporate sector database of the CMIE. But unlike the ORG-IMS Audit, Prowess covers mainly large and medium companies which are registered under the Companies Act. Company-wise data are provided on diverse aspects including the background of the company and financial variables including sales, exports, R&D expenditure etc. Prowess (version 2) listed 323 companies in the pharmaceutical manufacturing sector when accessed on 9 April 2009. We added to this list two more units (Jubilant Organosys and Hikal) which are listed in Prowess in the organic chemicals sector but these two companies have significant pharmaceutical manufacturing operations. A basic problem with Prowess is that information is not available nor provided for all the variables for all the companies for all the years. Sales and other financial variables data are available for 179 companies — 166 Indian companies and 13 foreign companies[2] from Prowess for 2007/08. Table A lists these companies together with the available information on ORG-IMS retail formulations retail sales. This sample is more important than what the number suggests. CMIE companies accounted for 77 percent of India total drugs and pharmaceutical exports in 2007/08 of INR 291,395.7 million. Thirteen foreign pharmaceutical companies included in the CMIE sample accounted for 10.5 percent of total CMIE pharmaceutical sales in 2007/08.

Our analysis of the performance of the Indian pharmaceutical industry is largely based on this sample of 166 Indian companies. It must be kept in mind that these are mainly in the large and medium sector.

For the purpose of analyzing the financial performance of the Indian pharmaceutical industry (Tables 8 to 10), we have classified the industry into the following mutually exclusive groups:

- Groups in terms of size of sales:
  - Top 10 companies in terms of net sales in 2007/08 and the rest
  - Top 50 companies in terms of net sales in 2007/08 and the rest
  - Smallest 50 companies in terms of net sales in 2007/08
- Groups in terms of size of exports:
  - "Major exporters" and the rest ("Other exporters"). 34 companies each with exports of INR 1,000 million or more in 2007/08 are considered as "Major exporters"

1 The number of pharmaceutical companies would be less because many companies have multiple manufacturing units.

2 We treat as foreign companies all those identified by CMIE as belonging to a foreign group, such as Glaxo or those which are "Private (Foreign)" companies. As clarified by CMIE to us, the identification is made on the basis of available information on equity holdings and management control. Ranbaxy, Matrix Laboratories and Fresenius Kabi Oncology (formerly Dabur Pharma) which have been recently taken over by foreign companies have been treated by us as Indian companies for the purpose of this analysis. These 13 foreign companies — referred to as MNCs in the text — are: Glaxosmithkline Pharmaceuticals Ltd., Aventis Pharma Ltd., Pfizer Ltd., Abbott India Ltd., Novartis India Ltd. Wyeth Ltd., Merck Ltd., Astrazeneca Pharma India Ltd., Organon (India) Ltd., Solvay Pharma India Ltd., Fulford (India) Ltd., Biddle Sawyer Ltd., Global Remedies Ltd. CMIE lists two other foreign pharmaceutical companies (Bayer Polychem (India) Ltd., Sanofi-Synthelabo (India) Ltd) for which sales etc data are not available for 2007/08.

- » Group in terms of size of R&D expenditure:
  - "Major R&D spenders" and the rest ("Other R&D spenders"). 37 companies each with R&D expenditure of INR 100 million or more in 2007/08 are considered as "Major R&D spenders"
- » Groups in terms of market orientation:
  - "Domestic market oriented" and "Export market oriented" companies. 82 companies each with exports more than 10 percent of net sales in 2007/08 are considered as "Export market oriented" companies. The remaining 84 companies with exports share of less than 10 percent are considered as "Domestic market" oriented.

The financial ratios that we have employed to analyze the financial performance are:

- Net Profit margin
- Return on equity
- Return on assets

Net profit margin is defined:

(PBIT-taxes)/Net sales, where

PBIT = Profits before interest and taxes

Return on equity is defined as:

(PAT-Preference stock dividend)/Equity, where

PAT= Profits after tax and

Equity = Paid up capital + Reserves & surpluses

Return on total assets is defined as:

(PBIT-taxes)/Total assets

Table A: List of CMIE companies, 2007/08

CMIE companies	CMIE rank	CMIE Net sales, INR million, 2007/08	ORG rank	ORG, retail sales, INR million, 2007/08	ORG Market share, 2007/08
Cipla Ltd.	1	41966.4	1	16831	5.24
Ranbaxy Laboratories Ltd.	2	40799.6	2	15995	4.98
Dr. Reddy's Laboratories Ltd.	3	37822.9	10	7490	2.33
Lupin Ltd.	4	25706	8	8513	2.65
Sun Pharmaceutical Inds. Ltd.	5	23032.4	6	10684	3.33
Aurobindo Pharma Ltd.	6	22718.9	NA	NA	NA
Jubilant Organosys Ltd	7	20013	NA	NA	NA
Piramal Healthcare Ltd.	8	18989.9	5	11592	3.61
Cadila Healthcare Ltd.	9	17154	4	11902	3.71
Glaxosmithkline Pharmaceuticals Ltd.	10	16232.8	3	15126	4.71
Glenmark Pharmaceuticals Ltd.	11	13466	26	4369	1.36
Orchid Chemicals & Pharmaceuticals Ltd.	12	12376.4	74	748	0.23
Wockhardt Ltd.	13	11728	17	6361	1.98
Ipca Laboratories Ltd.	14	10895.6	27	4015	1.25
Divi'S Laboratories Ltd.	15	10358.7	NA	NA	NA
Torrent Pharmaceuticals Ltd.	16	9954.5	16	6584	2.05
Alembic Ltd.	17	9907.2	18	6075	1.89
Matrix Laboratories Ltd.	18	9510	NA	NA	NA
Aventis Pharma Ltd.	19	9191.2	13	7213	2.25
Biocon Ltd.	20	8782.4	88	565	0.18
Panacea Biotec Ltd.	21	8376.2	48	1350	0.42
Hetero Drugs Ltd.	22	8305.3	53	1102	0.34
Nectar Lifesciences Ltd.	23	7384.4	NA	NA	NA
Pfizer Ltd.	24	6966.2	9	7885	2.46
U S V Ltd.	25	6780	25	4579	1.43
Ankur Drugs & Pharma Ltd.	26	6737.2	NA	NA	NA
Abbott India Ltd.	27	5945.8	11	7346	2.29
Unichem Laboratories Ltd.	28	5779.6	23	5002	1.56
Novartis India Ltd.	29	5659.9	22	5328	1.66
J B Chemicals & Pharmaceuticals Ltd.	30	5568.4	36	2058	0.64
Elder Pharmaceuticals Ltd.	31	5472.5	29	2912	0.91
Arch Pharmalabs Ltd.	32	5142	NA	NA	NA
Ind-Swift Ltd.	33	5130.8	37	1849	0.58

Table A: List of CMIE companies, 2007/08 (contd.)

CMIE companies	CMIE rank	CMIE Net sales, INR million, 2007/08	ORG rank	ORG, retail sales, INR million, 2007/08	ORG Market share, 2007/08
F D C Ltd.	34	4876.2	20	5570	1.74
Ind-Swift Laboratories Ltd.	35	4446.2	NA	NA	NA
Plethico Pharmaceuticals Ltd.	36	4414.1	NA	NA	NA
Shasun Chemicals & Drugs Ltd.	37	4342.7	NA	NA	NA
Emcure Pharmaceuticals Ltd.	38	4276.5	15	6590	2.05
Strides Arcolab Ltd.	39	3937.4	NA	NA	NA
Dishman Pharmaceuticals & Chemicals Ltd.	40	3590	NA	NA	NA
Indoco Remedies Ltd.	41	3494.1	32	2656	0.83
Wyeth Ltd.	42	3291.5	34	2434	0.76
Merck Ltd.	43	3247.2	33	2640	0.82
Aarti Drugs Ltd.	44	3107.3	NA	NA	NA
Astrazeneca Pharma India Ltd.	45	3026.4	35	2133	0.66
Hikal Ltd	46	3007.9	NA	NA	NA
Twilight Litaka Pharma Ltd.	47	2948	NA	NA	NA
Ajanta Pharma Ltd.	48	2849	70	800	0.25
Fresenius Kabi Oncology Ltd.	49	2393.2	146	159	0.05
Marksans Pharma Ltd.	50	2368.3	NA	NA	NA
Natco Pharma Ltd.	51	2263.1	104	363	0.11
Themis Medicare Ltd.	52	2187.7	105	362	0.11
Neuland Laboratories Ltd.	53	2183	NA	NA	NA
Venus Remedies Ltd.	54	2126.3	NA	NA	NA
Parenteral Drugs (India) Ltd.	55	2103.5	117	288	0.09
S M S Pharmaceuticals Ltd.	56	2095.3	NA	NA	NA
Organon (India) Ltd.	57	2067.8	49	1256	0.39
T T K Healthcare Ltd.	58	1987.1	NA	NA	NA
Indian Immunologicals Ltd.	59	1914.1	NA	NA	NA
Granules India Ltd.	60	1854.4	NA	NA	NA
Arvind Remedies Ltd.	61	1756.6	315	11	0
Sharon Bio-Medicine Ltd.	62	1710	NA	NA	NA
Solvay Pharma India Ltd.	63	1676.1	46	1410	0.44
Vasudha Pharma Chem Ltd.	64	1650.6	NA	NA	NA
Fulford (India) Ltd.	65	1602.4	52	1112	0.35
Albert David Ltd.	66	1558.7	50	1137	0.35

Table A: List of CMIE companies, 2007/08 (contd.)

CMIE companies	CMIE rank	CMIE Net sales, INR million, 2007/08	ORG rank	ORG, retail sales, INR million, 2007/08	ORG Market share, 2007/08
Vivimed Labs Ltd.	67	1543.2	NA	NA	NA
Jagsonpal Pharmaceuticals Ltd.	68	1501	69	828	0.26
Anu'S Laboratories Ltd.	69	1450.2	NA	NA	NA
Zandu Pharmaceutical Works Ltd.	70	1356.3	99	419	0.13
Alpa Laboratories Ltd.	71	1353.8	NA	NA	NA
Morepen Laboratories Ltd.	72	1257.6	144	169	0.05
Hiran Orgochem Ltd.	73	1193.1	NA	NA	NA
R P G Life Sciences Ltd.	74	1182.8	NA	NA	NA
Suven Life Sciences Ltd.	75	1172.3	NA	NA	NA
Kilitch Drugs (India) Ltd.	76	1171.8	NA	NA	NA
K D L Biotech Ltd.	77	1114.2	NA	NA	NA
Anuh Pharma Ltd.	78	1108.5	NA	NA	NA
Shilpa Medicare Ltd.	79	969.8	NA	NA	NA
Sarabhai Zydus Animal Health Ltd.	80	949.3	NA	NA	NA
Kopran Ltd.	81	932.8	325	8	0
Lyka Labs Ltd.	82	932.1	NA	NA	NA
Mangalam Drugs & Organics Ltd.	83	917.8	NA	NA	NA
Sanjivani Paranteral Ltd.	84	917.1	NA	NA	NA
East India Pharmaceutical Works Ltd.	85	883	72	779	0.24
Lincoln Pharmaceuticals Ltd.	86	862.3	106	351	0.11
Bal Pharma Ltd.	87	852.2	NA	NA	NA
Medicamen Biotech Ltd.	88	768.8	NA	NA	NA
Vimta Labs Ltd.	89	765.4	NA	NA	NA
Amrutanjan Health Care Ltd.	90	710.2	160	140	0.04
Syncom Formulations (India) Ltd.	91	688.6	147	158	0.05
Elder Health Care Ltd.	92	686.7	NA	NA	NA
P I Drugs & Pharmaceuticals Ltd.	93	673.5	NA	NA	NA
Ozone Pharmaceuticals Ltd.	94	666.6	93	526	0.16
Ambalal Sarabhai Enterprises Ltd.	95	608	303	12	0
Span Diagnostics Ltd.	96	607	NA	NA	NA
Gufic Biosciences Ltd.	97	544.9	161	133	0.04
Smruthi Organics Ltd.	98	541.7	NA	NA	NA
Krebs Biochemicals & Inds. Ltd.	99	492	NA	NA	NA

Table A: List of CMIE companies, 2007/08 (contd.)

CMIE companies	CMIE rank	CMIE Net sales, INR million, 2007/08	ORG rank	ORG, retail sales, INR million, 2007/08	ORG Market share, 2007/08
Makers Laboratories Ltd.	100	477.7	NA	NA	NA
Group Pharmaceuticals Ltd.	101	407.2	130	234	0.07
Bafna Pharmaceuticals Ltd.	102	395.5	NA	NA	NA
Omega Biotech Ltd.	103	390.1	NA	NA	NA
Jenburkt Pharmaceuticals Ltd.	104	383.5	NA	NA	NA
Alpex International Ltd.	105	382.7	NA	NA	NA
Sun Pharma Advanced Research Co. Ltd.	106	374.1	NA	NA	NA
Suyash Laboratories Ltd.	107	367.4	NA	NA	NA
Coral Laboratories Ltd.	108	329.2	NA	NA	NA
Tonira Pharma Ltd.	109	323.5	NA	NA	NA
Zandu Chemicals Ltd.	110	317.7	NA	NA	NA
Hester Biosciences Ltd.	111	314.2	NA	NA	NA
Biddle Sawyer Ltd.	112	312.2	NA	NA	NA
Fermenta Biotech Ltd.	113	306.7	NA	NA	NA
Samrat Pharmachem Ltd.	114	297.4	NA	NA	NA
Tyche Industries Ltd.	115	292.3	NA	NA	NA
Transchem Ltd.	116	276.3	NA	NA	NA
Endo Labs Ltd.	117	274.9	366	1	0
Welcure Drugs & Pharmaceuticals Ltd.	118	264.1	NA	NA	NA
Sunil Healthcare Ltd.	119	257.1	NA	NA	NA
Creative Health Care Pvt. Ltd.	120	253.9	NA	NA	NA
Aarey Drugs & Pharmaceuticals Ltd.	121	250.3	NA	NA	NA
Sven Genetech Ltd.	122	243.9	NA	NA	NA
Arch Life Sciences Ltd.	123	242.7	NA	NA	NA
Siris Ltd.	124	230.6	NA	NA	NA
Gennex Laboratories Ltd.	125	221.7	NA	NA	NA
Adinath Bio-Labs Ltd.	126	216.9	NA	NA	NA
Resonance Specialties Ltd.	127	206.2	NA	NA	NA
Natural Capsules Ltd.	128	201.8	NA	NA	NA
Denis Chem Lab Ltd.	129	182.5	NA	NA	NA
Medi-Caps Ltd.	130	181	NA	NA	NA
Panchsheel Organics Ltd.	131	180.2	NA	NA	NA
Vikram Thermo (India) Ltd.	132	174	NA	NA	NA

Table A: List of CMIE companies, 2007/08 (contd.)

CMIE companies	CMIE rank	CMIE Net sales, INR million, 2007/08	ORG rank	ORG, retail sales, INR million, 2007/08	ORG Market share, 2007/08
Kerala Ayurveda Ltd.	133	172.7	NA	NA	NA
A B L Biotechnologies Ltd.	134	168.6	NA	NA	NA
Pure Pharma Ltd.	135	154.9	NA	NA	NA
B D H Industries Ltd.	136	149.7	NA	NA	NA
Wintac Ltd.	137	149.4	NA	NA	NA
Gujarat Themis Biosyn Ltd.	138	147.2	NA	NA	NA
Sandu Pharmaceuticals Ltd.	139	134.3	NA	NA	NA
Bharat Immunologicals & Biologicals Corpn. Ltd.	140	131.6	NA	NA	NA
N G L Fine-Chem Ltd.	141	126.2	NA	NA	NA
Gujarat Terce Laboratories Ltd.	142	124.7	191	92	0.03
Roopa Industries Ltd.	143	117.1	NA	NA	NA
Capsugel Healthcare Ltd.	144	108.4	NA	NA	NA
Phaarmasia Ltd.	145	86.9	NA	NA	NA
Zyden Gentec Ltd.	146	83.4	NA	NA	NA
Vysali Pharmaceuticals Ltd.	147	80.9	NA	NA	NA
Kamron Laboratories Ltd.	148	76.7	278	21	0.01
Laurel Organics Ltd.	149	76.3	NA	NA	NA
Global Remedies Ltd.	150	71.9	NA	NA	NA
D I L Ltd.	151	66.7	NA	NA	NA
Beryl Drugs Ltd.	152	61	NA	NA	NA
Pharmax Corporation Ltd.	153	58.2	NA	NA	NA
Elder Projects Ltd.	154	50.9	NA	NA	NA
Colinz Laboratories Ltd.	155	48.2	249	39	0.01
Fredun Pharmaceuticals Ltd.	156	47.1	NA	NA	NA
Godavari Drugs Ltd.	157	39.4	NA	NA	NA
Dr. Sabharwal'S Manufacturing Labs Ltd.	158	38.1	NA	NA	NA
Ishita Drugs & Inds. Ltd.	159	37.1	NA	NA	NA
Harleystreet Pharmaceuticals Ltd.	160	36.8	NA	NA	NA
Zenith Health Care Ltd.	161	30.4	NA	NA	NA
Unjha Formulations Ltd.	162	30.2	NA	NA	NA
Yenkey Drugs & Pharmaceuticals Ltd.	163	29.9	NA	NA	NA
Triochem Products Ltd.	164	28.7	NA	NA	NA

Table A: List of CMIE companies, 2007/08 (contd.)

CMIE companies	CMIE rank	CMIE Net sales, INR million, 2007/08	ORG rank	ORG, retail sales, INR million, 2007/08	ORG Market share, 2007/08
Ticel Biopark Ltd.	165	27.8	NA	NA	NA
Sword & Shield Pharma Ltd.	166	17.4	NA	NA	NA
Epsom Properties Ltd.	167	13.8	NA	NA	NA
Perk Pharmaceuticals Ltd.	168	13	NA	NA	NA
Rubra Medicaments Ltd.	169	10.5	NA	NA	NA
Vista Pharmaceuticals Ltd.	170	10.2	NA	NA	NA
Wockhardt Biopharm Ltd.	171	8.9	NA	NA	NA
Country Condo'S Ltd.	172	7.7	NA	NA	NA
Biofil Chemicals & Pharmaceuticals Ltd.	173	7.6	NA	NA	NA
Inwinex Pharmaceuticals Ltd.	174	4.8	NA	NA	NA
Pharmaids Pharmaceuticals Ltd.	175	4.5	NA	NA	NA
Sigachi Laboratories Ltd.	176	4.3	NA	NA	NA
Combat Drugs Ltd.	177	3.7	NA	NA	NA
Principal Pharmaceuticals & Chemicals Ltd.	178	2.6	NA	NA	NA
Shyama Infosys Ltd.	179	0.1	NA	NA	NA

Sources: CMIE Prowess database (version 2) and ORG-IMS, *Stockist Secondary Audit*.

ANNEX II (CHAPTER 2A)

All of the information below was obtained from Indian Patent offices in Delhi, Mumbai, Chennai and Calcutta for the purposes of the study. Details of the methodology can be referred to in the study

Table B: List of Patents Requested from Patent Offices

	Date Of Publication	Patent No	Application No	Title	Patentee	Office
1.	23/05/08	218768	160/Chenp/2005	A Pharmaceutical Composition For Treating Neoplasm	Combinator X	Chennai
2.	21/11/08	222564	In/Pct/2002/921/Che	An Analgesic Composition	Reckitt Benckiser	Chennai
3.	05/12/08	225032	1675/Chenp/2005	A Composition Comprising Alkanesulfonic Acid And Acetycholinesterase Inhibitor For B-Amlyoid Related Disease	Bellus Health	Chennai
4.	14/12/07	211539	In/Pct/2000/84/Che	A Pharmaceutical Formulation	Pfizer	Chennai
5.	02/02/07	202348	In/Pct/2001/1043/Che	A Spontaneously Dispersible Pharmaceutical Composition For Oral Administration	Novartis	Chennai
6.	28/12/07	211807	952/Chenp/2003	Pharmaceutical Composition Comprising Benazepril And Amlodipine	Novartis	Chennai
7.	14/12/07	209504	In/Pct/2002/1587/Che	Pharmaceutically Acceptable Composition Comprising Molecular Disperse Solution Of Carvedilol	Hoffmann-La Roche	Chennai
8.	05/10/07	204314	230/Chenp/2003	Prodrug Acid Esters Of [2-(4-Benzyl-3-Hydroxy-Piperindin-1-Yl)-Ethansulfonyl] Phenol	Hoffmann-La Roche	Chennai
9.	28/03/08	213086	897/Chenp/2004	A Stable Liquid Formulation Comprising Ribavirin	Schering	Chennai
10.	21/11/08	222545	In/Pct/2001/1636/Che	Substantially Oil-Free Cyclosporin Compositions	Novartis	Chennai
11.	11/01/08	211967	In/Pct/2001/1589/Che	A Multilayer Pharmaceutical Product	Rohm	Chennai
12.	06/06/08	218923	1553/Chenp/2005	Enantiomers Of Thiophene Hydroxamic Acid Derivatives	Hoffmann-La Roche	Chennai
13.	25/07/08	220446	2471/Chenp/2004	Medicaments Comprising Liposomes Of Particular Sizes	Esperion Luv Development	Chennai
14.	02/11/07	207625	140/Chenp/2003	A Pharmaceutical Composition For Dementia	Dainippon Sumitomo	Chennai
15.	28/03/08	213075	364/Chenp/2004	C-14 Oxidation Of Morphine Derivatives	N.V. Organon	Chennai

Table B: List of Patents Requested from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office
16.	04/07/08	219691	1265/Chenp/2004	Pharmaceutical Nanoparticulate Composition Of A Tachykinin Receptor Antagonist	Merck	Chennai
17.	02/02/07	202371	In/Pct/2001/435/Che	A Sustained Release Oral Pharmaceutical Composition Containing Rivastigmine	Novartis	Chennai
18.	28/03/08	216453	In/Pct/2002/17/Che	A Pharmaceutical Composition For Regulating, Inducing Or Enhancing Cell Migration	Novo Nordisk	Chennai
19.	28/03/08	214337	1559/Chenp/2003	A Pharmaceutical Composition And Process For Preparing The Same	Pharmacia	Chennai
20.	15/02/08	212246	1164/Chenp/2004	A Composition Comprising Riboflavin, An Effector Of The Urea Cycle And Amino Acids	Burzynski	Chennai
21.	28/12/07	211745	In/Pct/2002/692/Che	Pharmaceutical Composition For Anti-Tumor Compounds Suitable For Oral Administration	Pharmacia	Chennai
22.	29/06/07	206746	1902/Chenp/2003	Pharmaceutical Composition Comprising A Lipase Inhibitor And A Sucrose Fatty Acid Ester	Hoffmann-La Roche	Chennai
23.	29/06/07	205037	In/Pct/2000/619/Che	A Liquid Nutritional Composition For A Person Having Renal Failure	Novartis	Chennai
24.	05/12/08	224886	1632/Chenp/2003	Orally Deliverable Pharmaceutical Composition Comprising An Active Compound Having An Aminosulfonyl Group (Cox-2 Inhibitor), A Polyethylene Glycol And A Free Radical Scavenging Antioxidant	Pharmacia	Chennai
25.	28/03/08	213044	In/Pct/2001/460/Che	Controlled Release Pharmaceutical Compositions	Rohm	Chennai
26.	21/11/08	222356	723/Chenp/2005	Sustained-Release Tramadol Formulations With 24 Hour Efficacy	Labopharm	Chennai
27.	14/12/07	209514	In/Pct/2002/1826/Che	A Pharmaceutical Composition For Intravenous Administration	Novo Nordisk	Chennai
28.	02/02/07	202076	1300/Chenp/2003	Compositions Containing A Ruthenium (Iii) Complex And A Hetercycle	Faustus Forschungs Cie Translational Cancer Research	Chennai
29.	28/12/07	211741	In/Pct/2001/766/Che	A Pharmaceutical Composition For Topical Administration For Treatment Of Skin Disorders	Novartis	Chennai
30.	23/05/08	218826	711/Chenp/2005	Combination Drug	Eisai R & D	Chennai
31.	01/08/08	220861	00806/Delnp/2004	A Suspension Of Nanoparticulates Of An Antimitotic Drug	Crititech	Delhi

Table B: List of Patents Requested from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office
32.	10/10/08	219478	In/Pct/2001/00402/ Del	Combination Of A-Tocopherol And Of Riluzole Or Of A Pharmaceutically Acceptable Salt Thereof	Aventis	Delhi
33.	14/11/08	224805	2916/Delnp/2004	Pharmaceutical Compositions	Boehringer Ingelheim	Delhi
34.	27/06/08	219612	01345/Delnp/2003	Pharmaceutical And Cosmetic Compositions	Indena	Delhi
35.	31/10/08	224580	00756/Delnp/2003	A Pharmaceutical Composition For Use In The Treatment And Or Prevention Of Fibrotic Disease	Laboratories Serono	Delhi
36.	12/09/08	222767	In/Pct/2002/00743/ Del	A Novel Sustained Release Solid Oral Galenical Composition Of Molsidomine	Therabel	Delhi
37.	03/10/08	218212	1095/Delnp/2004	Crystalline 3-{(3r,4r)-4-Methyl-3-[Methyl-[7h-Pyrrolo[2,3-D]Pyrimidin-4-Yl)- Amino]-Piperidin-L-Yl}-3-Oxo-Propinitrile Monocitrate Salt And Its Method Of Preparation	Pfizer	Delhi
38.	25/07/08	220865	In/Pct/2000/00062/ Del	A Pharmaceutical Composition For The Management Of Attention Dificit Disorder (Add) And Attention Deficit Hyperactivity Disorder (Adhd)	Noven	Delhi
39.	28/03/08	216703	3779/Delnp/2004	A Pharmaceutical Composition	Tibotec	Delhi
40.	15/08/08	218289	2107/Delnp/2004	Dry Granulated Formulations Of Azithromycin	Pfizer	Delhi
41.	30/05/08	218216	627/Delnp/2004	Oily Paclitaxel Composition And Formulation For Chemoembolization And Preparation Method Thereof	Daehwa	Delhi
42.	05/09/08	222458	01757/Delnp/2003	A Medical Composition For Preventing Human Liver Cancer	Kansai	Delhi
43.	30/05/08	217926	1746/Delnp/2003	Anhydrous Crystal Of B-Lactam Compound And Method For Preparation Thereof	Otsuka	Delhi
44.	01/08/08	221465	1785/Delnp/2005	A Pharmaceutical Composition Comprising A Vehicle	Pharmacia & Upjohn	Delhi
45.	25/04/08	217746	1232/Delnp/2003	A Synergistic Composition Useful For Hepatocurative Action Against Cyp 450 Bio-Activation Mediated Hepatotoxicity, Induced By One Or More Drugs	Council Of Scientific & Industrial Research	Delhi
46.	17/10/08	224121	2150/Delnp/2005	Pharmaceutical Composition Comprising For The Treatment Of Functional Bladder Problems	Boehringer Ingelheim	Delhi
47.	25/07/08	220331	01575/Delnp/2003	Aripiprazole Oral Solution	Bristol-Myers Squibb	Delhi
48.	17/10/08	224064	2114/Delnp/2005	A Pharmaceutical Composition	Warner-Lambert	Delhi

Table B: List of Patents Requested from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office
49.	21/03/08	215817	00070/Delnp/2003	Pharmaceutical Compositions For The Treatment Of Mucositis, Stomatitis And Behcet's Syndrome	Sinclair	Delhi
50.	12/09/08	218083	1074/Delnp/2004	"Succinaate Salt Of E-2-Methoxy-N-[3-[4-[3- Methyl-Pyridin-3-Yloxyl]-Phenylamino]-Quinazolin-6-Yl]-Allyl]-Acetamide And Preparation Thereof"	Pfizer	Delhi
51.	13/06/08	218624	00606/Delnp/2003	A Pharmaceutical Composition For Treatment Of Proliferative Disorders	Temple University	Delhi
52.	07/03/08	215104	In/Pct/2001/00576/Del	A Pharmaceutical Composition For Treatment Of Helpatitis B Virus Infection	Centre National De La Recherche Scientifique	Delhi
53.	29/02/08	214821	In/Pct/2001/00452/Del	A Coated Effervescence Composition	Procter & Gamble	Delhi
54.	27/06/08	219639	2385/Delnp/2005	A Pharmaceutical Composition For The Prevention Or Treatment Of A Diesease Associated With Hyperglycemia	Kissei	Delhi
55.	12/09/08	217699	305/Delnp/2005	"A Nutritional Or Pharmaceutical Composition Designed To Stimulate Bone Formation And/Or Inhibit Bone Resorption In Man Or Animals	Institut National De La Recherche Agronomique	Delhi
56.	19/09/08	223014	3370/Delnp/2004	Pharmaceutical Composition For Oral Administration Comprising A Tablet Core, Containing Flibanserin Polymorph A	Boehringer Ingelheim	Delhi
57.	28/11/08	225324	00141/Delnp/2003	"A Pharmaceutical Composition Being A Tablet Comprising N-[(1-Nbutyl-4-Piperidinyl)Methyl]-3,-4-Dihydro-2h- [1,3]Oxazino[3,2-A]Indole-10-Carboxamide	Glaxosmithkline	Delhi
58.	08/08/08	222070	1568/Delnp/2004	Stable Oxaliplatin Solution Formulation	Nerviano Medical Sciences	Delhi
59.	01/08/08	221624	4719/Delnp/2005	A Crystal Of 1-(2-Methoxyethyl)-2-Methyl-4, 9-Dioxo-3-(Pyrazin-2-Ylmethyl)-4, 9- Dihydro-1 H-Naphtho [2,3-D] Imidazol-3- Ium Bromide	Astellas	Delhi
60.	11/07/08	221070	02209/Delnp/2003	A Pharmaceutical Composition For Altering The Affinity Of A Nucleic Acid Ligand	Duke University	Delhi
61.	28/03/08	215154	362/Mumnp/2005	Y Crystalline Form Of Perindopril Tert-Butylamine Compound Of Formula (I)	Les Laboratoires Servier	Mumbai
62.	25/05/07	204079	In/Pct/2002/00605/ Mum	A Pharmaceutical Composition Comprising (S)-(-)-A-Ethyl-2-Oxo-1- Pyrrolidineacetamide	Ucb	Mumbai

Table B: List of Patents Requested from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office
63.	13/07/07	205788	In/Pct/2002/00867/Mum	Pharmaceutical Compositions Comprising A Hmg Coa Reductase Inhibitor	Astrazeneca	Mumbai
64.	26/10/07	210490	667/Mumnp/2005	Pharmaceutical Composition For Preventing And Treating Microbe Mediated Epithelial Disorders	University Of Chicago	Mumbai
65.	13/06/08	203084	In/Pct/2001/01216/Mum	An Oral Pharmaceutical Formulation Comprising An Ibat Inhibitor Compound And A Bile Acid Binder	Astrazeneca	Mumbai
66.	13/04/07	202295	In/Pct/2002/00475/Mum	Pharmaceutical Compositions Providing Enhanced Drug Concentrations	Pfizer	Mumbai
67.	26/10/07	208357	512/Mumnp/2005	Compositions For Transdermal Oxybutynin Therapy	Watson Laboratories	Mumbai
68.	28/03/08	214087	26/Mumnp/2004	An Isomer, Enantiomer, Diastereoisomer Or Tautomer Of A Compound	Boehringer Ingelheim	Mumbai
69.	25/05/07	203998	315/Mumnp/2004	A Liquid Pharmaceutical Composition Comprising A Gamma- Aminobutyric Acid (Gaba) Analog	Warner-Lambert	Mumbai
70.	29/08/08	221718	In/Pct/2002/01101/Mum	Pharmaceutical Composition For Oral Administration	Nicox	Mumbai
71.	10/08/07	208151	In/Pct/2002/00403/Mum	Stable Liquid Formulation	Astrazeneca	Mumbai
72.	13/06/08	219034	1180/Mumnp/2003	S-Omeprazole (Esomeprazole) Inclusion Complex With Cyclodextrins	Cipla	Mumbai
73.	10/08/07	207881	333/Mumnp/2005	Crystals Of P1-(2'-Deoxycytidine 5'-) P4-(Uridine 5'-) - Tetraphosphate Or A Salt Thereof	Yamasa	Mumbai
74.	10/08/07	208150	In/Pct/2000/00074/Mum	Water-Soluble Eye-Drop	Otsuka	Mumbai
75.	02/03/07	200906	540/Mumnp/2003	Method For Inhibiting The Expression Of A Target Gene And Medicament For Treating A Tumor Disease	Ribopharma	Mumbai
76.	09/11/07	210476	250/Mumnp/2004	Pharmaceutical Composition For Controlled Release Of A Beta-Lactam Antibiotic	Lupin	Mumbai
77.	29/08/08	221507	In/Pct/2002/00025/Mum	Pharmaceutical Composition Containing Fenofibrate And Method For The Preparation Thereof	Ethypharm	Mumbai
78.	26/10/07	210902	In/Pct/2002/01494/Mum	Novel Formulations Of A-2, 4-Disulfophenyl-N-Tert-Butylnitrone	Astrazeneca	Mumbai
79.	17/08/07	206475	598/Mumnp/2005	Pharmaceutical Formulations Comprising B-2 Adrenoreceptor Agonists And Xanthines	Cipla	Mumbai

Table B: List of Patents Requested from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office
80.	31/08/07	208786	779/Mumnp/2005	A Composition Comprising Epidemium Extract For Treatment Of Prostatic Hyperplasia And Method Of Epimedium Herb Extraction	Bright Future Pharamaceutical	Mumbai
81.	21/03/08	213576	445/Mumnp/2003	A Composition Comprising 11b-(4-Acetylphenyl)-17b-Hydroxy-17a-(1,1,2,2,2,-Pentafluoroethyl) Estra-4,9-Dien-3-One Or A Pharmaceutically Accepatble Derivative Or Analogue Thereof	Schering	Mumbai
82.	09/11/07	211338	In/Pct/2001/01478/Mum	A Metastable Polymorph (Crystal A) Of 2-(3-Cyano-4-Isobutyloxyphenyl)-4- Methyl-5-Thiazolecarboxylic Acid	Teijin	Mumbai
83.	28/03/08	214218	393/Mumnp/2004	Controlled Release Formulation Of Lamotrigine	Torrent	Mumbai
84.	15/08/08	219970	In/Pct/2002/00899/Mum	Electrospun Pharmaceutical Compositions	Smithkline Beecham	Mumbai
85.	28/03/08	214214	In/Pct/2002/01774/Mum	A Pharmaceutical Composition For The Treatment Of Rheumatoid Arthritis	Bristol-Myers Squibb	Mumbai
86.	26/10/07	210943	220/Mumnp/2004	Antitubercular Pharmaceutical Composition In Fixed Dose Combination Comprising Four Drugs	Lupin	Mumbai
87.	15/06/07	204605	In/Pct/2001/00548/Mum	Sustained Release Pharmaceutical Containing 5-[4-[2-(N-Methyl-N-(2-Pyridyl)Amino)Ethoxy]Benzyl] Thiazolidine-2,4-Dione	Smithkline Beecham	Mumbai
88.	31/08/07	209032	84/Mumnp/2004	Composition For Lowering Blood Cholesterol	Hindustan Lever	Mumbai
89.	13/07/07	206328	In/Pct/2002/00066/Mum	Synergistic Combination Of Roflumilast And Salmeterol	Altana	Mumbai
90.	31/08/07	208866	313/Mumnp/2003	A Bilayer Tablet Consisting Of Pharmaceutical Compositions Containing Epinastine Or Pseudoephedrine	Boehringer Ingelheim	Mumbai
91.	27/06/08	221578	739/Kolnp/2003	Method And Compositions Employing Formulations Of Lecithin Oils And Nsaids For Protecting The Gastrointestinal Tract And Providing Enhanced Therapeutic Activity	The Board Of Regents Of The University Of Texas System	Kolkata
92.	20/06/08	221140	01670/Kolnp/2004	Aerosol Containing A Particulate Active Substance	Nektar	Kolkata
93.	21/03/08	216861	01691/Kolnp/2004	Transdermal Delivery System With Two Superimposed Adhesive Layers Having Different Affinities To The Active Substance Comprised	Thalas	Kolkata

Table B: List of Patents Requested from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office
94.	31/08/07	208786	779/Mumnp/2005	A Composition Comprising Epidemium Extract For Treatment Of Prostatic Hyperplasia And Method Of Epimedium Herb Extraction	Bright Future Pharamaceutical	Mumbai
95.	21/03/08	213576	445/Mumnp/2003	A Composition Comprising 11b-(4-Acetylphenyl)-17b-Hydroxy-17a-(1,1,2,2,2,-Pentafluoroethyl) Estra-4,9-Dien-3-One Or A Pharmaceutically Accepatble Derivative Or Analogue Thereof	Schering	Mumbai
96.	09/11/07	211338	In/Pct/2001/01478/Mum	A Metastable Polymorph (Crystal A) Of 2-(3-Cyano-4-Isobutyloxyphenyl)-4- Methyl-5-Thiazolecarboxylic Acid	Teijin	Mumbai
97.	28/03/08	214218	393/Mumnp/2004	Controlled Release Formulation Of Lamotrigine	Torrent	Mumbai
98.	15/08/08	219970	In/Pct/2002/00899/Mum	Electrospun Pharmaceutical Compositions	Smithkline Beecham	Mumbai
99.	28/03/08	214214	In/Pct/2002/01774/Mum	A Pharmaceutical Composition For The Treatment Of Rheumatoid Arthritis	Bristol-Myers Squibb	Mumbai
100.	26/10/07	210943	220/Mumnp/2004	Antitubercular Pharmaceutical Composition In Fixed Dose Combination Comprising Four Drugs	Lupin	Mumbai
101.	15/06/07	204605	In/Pct/2001/00548/Mum	Sustained Release Pharmaceutical Containing 5-[4-[2-(N-Methyl-N-(2-Pyridyl)Amino)Ethoxy]Benzyl] Thiazolidine-2,4-Dione	Smithkline Beecham	Mumbai
102.	31/08/07	209032	84/Mumnp/2004	Composition For Lowering Blood Cholesterol	Hindustan Lever	Mumbai
103.	13/07/07	206328	In/Pct/2002/00066/Mum	Synergistic Combination Of Roflumilast And Salmeterol	Altana	Mumbai
104.	31/08/07	208866	313/Mumnp/2003	A Bilayer Tablet Consisting Of Pharmaceutical Compositions Containing Epinastine Or Pseudoephedrine	Boehringer Ingelheim	Mumbai
105.	27/06/08	221578	739/Kolnp/2003	Method And Compositions Employing Formulations Of Lecithin Oils And Nsaids For Protecting The Gastrointestinal Tract And Providing Enhanced Therapeutic Activity	The Board Of Regents Of The University Of Texas System	Kolkata
106.	20/06/08	221140	01670/Kolnp/2004	Aerosol Containing A Particulate Active Substance	Nektar	Kolkata
107.	21/03/08	216861	01691/Kolnp/2004	Transdermal Delivery System With Two Superimposed Adhesive Layers Having Different Affinities To The Active Substance Comprised	Thalas	Kolkata

Table B: List of Patents Requested from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office
108.	25/01/08	214002	00304/Kolnp/2004	Microparticulate Oral Galenical Form For The Delayed And Controlled Release Of Pharmaceutical Active Principle	Flamel	Kolkata
109.	09/05/08	219534	In/Pct/2000/233/Kol	An Orally Administerable Galenic Formulation Allowing Improved Absorption By The Transmembrane In The Gastrointestinal Tract	Merck	Kolkata
110.	21/11/08	225650	441/Kolnp/2005	1,3-Diamino-2-Hydroxypropane Prodrug Derivatives	Elan	Kolkata
111.	15/02/08	214622	01813/Kolnp/2004	Implantable Polymeric Device For Sustained Release Of Buprenorphine	Titan	Kolkata
112.	09/05/08	219511	01951/Kolnp/2004	Pharmaceutrical Composition Containing Permeabilizing Petide For Enhanced Mucosal Delivery Of Therapeutic Compounds	Nastech	Kolkata
113.	21/03/08	216870	155/Kolnp/2005	A Composition Comprising Loteprednol And Dfho For Respiratory Diseases, Allergic Diseases Asthma Nad Chronic Obstructive Pulmonary Diseases	Viatris	Kolkata
114.	29/02/08	215514	00097/Kolnp/2004	An Antineoplastic Combinations	Wyeth	Kolkata
115.	12/09/08	223381	02033/Kolnp/2005	A Topical Pharmaceutical Composition	Berlin-Chemie	Kolkata
116.	20/04/07	206182	In/Pct/2001/01376/Kol	Oralpharmaceutical Compositions Containing Taxanes And Methods Of Preparation	Thereforivax Research	Kolkata
117.	27/06/08	221578	739/Kolnp/2003	Method And Compositions Employing Formulations Of Lecithin Oils And Nsaids For Protecting The Gastrointestinal Tract And Providing Enhanced Therapeutic Activity	The Board Of Regents Of The University Of Texas System	Kolkata
118.	28/03/08	217471	00640/Kolnp/2004	Orodispersible Tablets Containing Fexofenadine	Ethypharm	Kolkata
119.	07/03/08	216080	In/Pct/2001/637/Kol	Pharmaceutical Aerosol Formulations For Use In A Pressurized Aerosol Container	Ivax	Kolkata
120.	14/12/07	212684	00370/Kolnp/2004	Pharmceutical Composition For Treating Hypertension And Heart Failure	Research Foundation Of State University Of New York	Kolkata

Table C: List of Patents Successfully Obtained from Patent Offices

	Date Of Publication	Patent No	Application No	Title	Patentee	Office	Type of Claim(s)
1.	23/05/08	218768	160/Chenp/2005	A Pharmaceutical Composition For Treating Neoplasm	Combinator X	Chennai	Composition
2.	21/11/08	222564	In/Pct/2002/921/ Che	An Analgesic Composition	Reckitt Benckiser	Chennai	Composition
3.	05/12/08	225032	1675/Chenp/ 2005	A Composition Comprising Alkanesulfonic Acid And Acetycholinesterase Inhibitor For B-Amlyoid Related Disease	Bellus Health	Chennai	Composition
4.	14/12/07	211539	In/Pct/2000/84/ Che	A Pharmaceutical Formulation	Pfizer	Chennai	Formulation/ Method Of Treatment
5.	02/02/07	202348	In/Pct/2001/ 1043/Che	A Spontaneously Dispersible Pharmaceutical Composition For Oral Administration	Novartis	Chennai	Composition
6.	28/12/07	211807	952/Chenp/2003	Pharmaceutical Composition Comprising Benazepril And Amlodipine	Novartis	Chennai	Composition
7.	14/12/07	209504	In/Pct/2002/ 1587/Che	Pharmaceutically Acceptable Composition Comprising Molecular Disperse Solution Of Carvedilol	Hoffmann-La Roche	Chennai	Composition
8.	05/10/07	204314	230/Chenp/2003	Prodrug Acid Esters Of [2-(4-Benzyl-3-Hydroxy-Piperindin-1-Yl)-Ethansulfonyl] Phenol	Hoffmann-La Roche	Chennai	Ester Prodrug
9.	28/03/08	213086	897/Chenp/2004	A Stable Liquid Formulation Comprising Ribavirin	Schering	Chennai	Formulation
10.	21/11/08	222545	In/Pct/2001/ 1636/Che	Substantially Oil-Free Cyclosporin Compositions	Novartis	Chennai	Composition
11.	11/01/08	211967	In/Pct/2001/ 1589/Che	A Multilayer Pharmaceutical Product	Rohm	Chennai	Composition
12.	06/06/08	218923	1553/Chenp/ 2005	Enantiomers Of Thiophene Hydroxamic Acid Derivatives	Hoffmann-La Roche	Chennai	Enantiomer
13.	25/07/08	220446	2471/Chenp/ 2004	Medicaments Comprising Liposomes Of Particular Sizes	Esperion Luv Development	Chennai	Particle Size
14.	02/11/07		140/Chenp/ 2003	A Pharmaceutical Composition For Dementia	Dainippon Sumitomo	Chennai	Composition

Table C: List of Patents Successfully Obtained from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office	Type of Claim(s)
15.	28/03/08	213075	364/Chenp/2004	C-14 Oxidation Of Morphine Derivatives	N.V. Organon	Chennai	Process/Intermediate
16.	04/07/08	219691	1265/Chenp/2004	Pharmaceutical Nanoparticulate Composition Of A Tachykinin Receptor Antagonist	Merck	Chennai	Composition
17.	02/02/07	202371	In/Pct/2001/435/ Che	A Sustained Release Oral Pharmaceutical Composition Containing Rivastigmine	Novartis	Chennai	Composition
18.	28/03/08	216453	In/Pct/2002/17/ Che	A Pharmaceutical Composition For Regulating, Inducing Or Enhancing Cell Migration	Novo Nordisk	Chennai	Composition/ Swiss Style Claim
19.	28/03/08	214337	1559/Chenp/2003	A Pharmaceutical Composition And Process For Preparing The Same	Pharmacia	Chennai	Composition
20.	15/02/08	212246	1164/Chenp/2004	A Composition Comprising Riboflavin, An Effector Of The Urea Cycle And Amino Acids	Burzynski	Chennai	Composition
21.	28/12/07	211745	In/Pct/2002/692/ Che	Pharmaceutical Composition For Anti-Tumor Compounds Suitable For Oral Administration	Pharmacia	Chennai	Composition
22.	29/06/07	206746	1902/Chenp/2003	Pharmaceutical Composition Comprising A Lipase Inhibitor And A Sucrose Fatty Acid Ester	Hoffmann-La Roche	Chennai	Composition
23.	29/06/07	205037	In/Pct/2000/619/ Che	A Liquid Nutritional Composition For A Person Having Renal Failure	Novartis	Chennai	Composition
24.	05/12/08	224886	1632/Chenp/2003	Orally Deliverable Pharmaceutical Composition Comprising An Active Compound Having An Aminosulfonyl Group (Cox-2 Inhibitor), A Polyethylene Glycol And A Free Radical Scavenging Antioxidant	Pharmacia	Chennai	Composition
25.	28/03/08	213044	In/Pct/2001/460/ Che	Controlled Release Pharmaceutical Compositions	Rohm	Chennai	Composition
26.	21/11/08	222356	723/Chenp/ 2005	Sustained-Release Tramadol Formulations With 24 Hour Efficacy	Labopharm	Chennai	Formulation
27.	14/12/07	209514	In/Pct/2002/1826/ Che	A Pharmaceutical Composition For Intravenous Administration	Novo Nordisk	Chennai	Composition
28.	02/02/07	202076	1300/Chenp/2003	Compositions Containing A Ruthenium (Iii) Complex And A Hetercycle	Faustus Forschungs Cie Translational Cancer Research	Chennai	Swiss-Style Claim; Product-By-Process
29.	28/12/07	211741	In/Pct/2001/766/ Che	A Pharmaceutical Composition For Topical Administration For Treatment Of Skin Disorders	Novartis	Chennai	Composition

Table C: List of Patents Successfully Obtained from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office	Type of Claim(s)
30.	23/05/08	218826	711/Chenp/2005	Combination Drug	Eisai R & D	Chennai	Combination
31.	28/03/08	216703	3779/Delnp/2004	A Pharmaceutical Composition	Tibotec	Delhi	Composition/ Method Of Treatment
32.	28/03/08	215154	362/Mumnp/2005	Y Crystalline Form Of Perindopril Tert-Butylamine Compound Of Formula (I)	Les Laboratoires Servier	Mumbai	Polymorph/Crystal Form
33.	13/07/07	205788	In/Pct/2002/ 00867/Mum	Pharmaceutical Compositions Comprising A Hmg Coa Reductase Inhibitor	Astrazeneca	Mumbai	Composition
34.	26/10/07	210490	667/Mumnp/2005	Pharmaceutical Composition For Preventing And Treating Microbe Mediated Epithelial Disorders	University Of Chicago	Mumbai	Swiss-Style Claim
35.	13/06/08	203084	In/Pct/2001/ 01216/Mum	An Oral Pharmaceutical Formulation Comprising An Ibat Inhibitor Compound And A Bile Acid Binder	Astrazeneca	Mumbai	Formulation
36.	26/10/07	208357	512/Mumnp/2005	Compositions For Transdermal Oxybutynin Therapy	Watson Laboratories	Mumbai	Formulation
37.	28/03/08	214087	26/Mumnp/2004	An Isomer, Enantiomer, Diastereoisomer Or Tautomer Of A Compound	Boehringer Ingelheim	Mumbai	Compound
38.	25/05/07	203998	315/Mumnp/2004	A Liquid Pharmaceutical Composition Comprising A Gamma- Aminobutyric Acid (Gaba) Analog	Warner-Lambert	Mumbai	Composition
39.	29/08/08	221718	In/Pct/2002/ 01101/Mum	Pharmaceutical Composition For Oral Administration	Nicox	Mumbai	Composition
40.	10/08/07	208151	In/Pct/2002/ 00403/Mum	Stable Liquid Formulation	Astrazeneca	Mumbai	Formulation
41.	13/06/08	219034	1180/Mumnp/ 2003	S-Omeprazole (Esomeprazole) Inclusion Complex With Cyclodextrins	Cipla	Mumbai	Inclusion Complex
42.	10/08/07	208150	In/Pct/2000/ 00074/Mum	Water-Soluble Eye-Drop	Otsuka	Mumbai	Formulation
43.	10/08/07	207881	333/Mumnp/2005	Crystals Of P1-(2'-Deoxycytidine 5'-) P4-(Uridine 5'-) - Tetraphosphate Or A Salt Thereof	Yamasa	Mumbai	Crystal Form
44.	02/03/07	200906	540/Mumnp/2003	Method For Inhibiting The Expression Of A Target Gene And Medicament For Treating A Tumor Disease	Ribopharma	Mumbai	Method Of Treatment

Table C: List of Patents Successfully Obtained from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office	Type of Claim(s)
45.	09/11/07	210476	250/Mumnp/2004	Pharmaceutical Composition For Controlled Release Of A Beta-Lactam Antibiotic	Lupin	Mumbai	Composition
46.	29/08/08	221507	In/Pct/2002/ 00025/Mum	Pharmaceutical Composition Containing Fenofibrate And Method For The Preparation Thereof	Ethypharm	Mumbai	Composition
47.	26/10/07	210902	In/Pct/2002/ 01494/Mum	Novel Formulations Of A-2, 4-Disulfophenyl-N-Tert- Butylnitrone	Astrazeneca	Mumbai	Formulation
48.	17/08/07	206475	598/Mumnp/2005	Pharmaceutical Formulations Comprising B-2 Adrenoreceptor Agonists And Xanthines	Cipla	Mumbai	Tablet Formulation
49.	21/03/08	213576	445/Mumnp/2003	A Composition Comprising 11b-(4-Acetylphenyl)-17b-Hydroxy-17a-(1,1,2,2,2,-Pentafluoroethyl) Estra-4,9-Dien-3-One Or A Pharmaceutically Accepatble Derivative Or Analogue Thereof	Schering	Mumbai	Composition
50.	09/11/07	211338	In/Pct/2001/ 01478/Mum	A Metastable Polymorph (Crystal A) Of 2-(3-Cyano-4- Isobutyloxyphenyl)-4- Methyl-5-Thiazolecarboxylic Acid	Teijin	Mumbai	Polymorph/ Crystal Form
51.	28/03/08	214218	393/Mumnp/2004	Controlled Release Formulation Of Lamotrigine	Torrent	Mumbai	Dosage Formulation
52.	15/08/08	219970	In/Pct/2002/ 00899/Mum	Electrospun Pharmaceutical Compositions	Smithkline Beecham	Mumbai	Composition
53.	28/03/08	214214	In/Pct/2002/ 01774/Mum	A Pharmaceutical Composition For The Treatment Of Rheumatoid Arthritis	Bristol-Myers Squibb	Mumbai	Composition/ Method Of Treatment
54.	26/10/07	210943	220/Mumnp/2004	Antitubercular Pharmaceutical Composition In Fixed Dose Combination Comprising Four Drugs	Lupin	Mumbai	Composition
55.	15/06/07	204605	In/Pct/2001/ 00548/Mum	Sustained Release Pharmaceutical Containing 5-[4-[2-(N-Methyl-N-(2-Pyridyl)Amino)Ethoxy] Benzyl]Thiazolidine-2,4-Dione	Smithkline Beecham	Mumbai	Sustained Release Composition
56.	31/08/07	209032	84/Mumnp/2004	Composition For Lowering Blood Cholesterol	Hindustan Lever	Mumbai	Composition
57.	31/08/07	208866	313/Mumnp/2003	A Bilayer Tablet Consisting Of Pharmaceutical Compositions Containing Epinastine Or Pseudoephedrine	Boehringer Ingelheim	Mumbai	Tablet Formulation
58.	27/06/08	221578	739/Kolnp/2003	Method And Compositions Employing Formulations Of Lecithin Oils And Nsaids For Protecting The Gastrointestinal Tract And Providing Enhanced Therapeutic Activity	The Board Of Regents Of The University Of Texas System	Kolkata	Composition/ Swiss Style Claim

Table C: List of Patents Successfully Obtained from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office	Type of Claim(s)
59.	20/06/08	221140	01670/Kolnp/2004	Aerosol Containing A Particulate Active Substance	Nektar	Kolkata	Formulation/ Particle Size
60.	21/03/08	216861	01691/Kolnp/2004	Transdermal Delivery System With Two Superimposed Adhesive Layers Having Different Affinities To The Active Substance Comprised	Thalas	Kolkata	Delivery Device
61.	19/12/08	226499	881/Kolnp/2004	Compressed Oral Pharmaceutical Dosage Form, With An Enteric Coating, Which Contains An Acid-Labile Benzimidazole Compound	Laboratorios Del Dr. Esteve,	Kolkata	Dosage Formulation
62.	06/07/07	208002	In/Pct/2000/00187/Kol	Pharmaceutical Composition Comprising A Combination Of Metformin And Fibrate, And Its Use For The Preparation Of Medicines Intended To Reduce Hyperglycaemia	Merck	Kolkata	Composition/ Method Of Treatment
63.	11/01/08	213673	In/Pct/2000/88/Kol	Tablet For Instant And Prolonged Release Of One Or More Active Substances	Merck	Kolkata	Composition
64.	11/05/07	206705	In/Pct/2001/00876/Kol	Orally Dispersible Tablet With Low Friability And Method For Producing Same	Ethypharm	Kolkata	Composition
65.	26/12/08	226731	1272/Kolnp/2004	Dry Powder Inhalation For Pulmonary Delivery And Manufacturing Method Thereof	Astellas	Kolkata	Process For Preparing Composition
66.	26/09/08	223771	01090/Kolnp/2004	A Composition Containing Substantially Purified Cytokine Inhibitory Factor	Arkion	Kolkata	Composition/ Method Of Treatment
67.	02/05/08	219330	01677/Kolnp/2003	Pharmaceutical Composition For Therapy Of Interstitial Cystitis	Yamanouchi	Kolkata	Process For Preparing Composition
68.	07/12/07	212614	In/Pct/2000/00621/Kol	Tablet Comprising Levothyroxine Sodium, Gelatine And Fillers	Merck	Kolkata	Composition
69.	21/03/08	216832	00221/Kolnp/2004	A Pharmaceutical Composition For Enhancing The Mobilization Of Multilineage Hematopoietic Stem Cels To The Peripheral Blood	Yissum Researh Development	Kolkata	Composition/Method Of Treatment
70.	23/05/08	220287	In/Pct/2001/338/Kol	An Olanzapine Pamoate Salt Land Pharmaceutically Acceptable Folvate Thereof	Eli Lilly	Kolkata	Salt/Composition
71.	28/03/08	217464	00051/Kolnp/2004	Methyl-Thieno-Benzodiazepine Lyophilized Formulation	Eli Lilly	Kolkata	Formulation/ Method Of Treatment
72.	01/02/08	214078	01627/Kolnp/2005	Liquid Intranasal Pharmaceutical Formulation	Schwarz Pharma	Kolkata	Formulation

Table C: List of Patents Successfully Obtained from Patent Offices (contd.)

	Date Of Publication	Patent No	Application No	Title	Patentee	Office	Type of Claim(s)
73.	14/03/08	216304	01077/Kolnp/ 2004	Sustained Release Pharmaceutical Composition	Societe De Conseils De Recherches Et D'applications	Kolkata	Composition
74.	25/01/08	214002	00304/Kolnp/ 2004	Microparticulate Oral Galenical Form For The Delayed And Controlled Release Of Pharmaceutical Active Principle	Flamel	Kolkata	Composition
75.	09/05/08	219534	In/Pct/2000/233/ Kol	An Orally Administerable Galenic Formulation Allowing Improved Absorption By The Transmembrane In The Gastrointestinal Tract	Merck	Kolkata	Formulation
76.	15/02/08	214622	01813/Kolnp/ 2004	Implantable Polymeric Device For Sustained Release Of Buprenorphine	Titan	Kolkata	Delivery Device/ Method Of Treatment
77.	21/03/08	216870	155/Kolnp/2005	A Composition Comprising Loteprednol And Dfho For Respiratory Diseases, Allergic Diseases Asthma Nad Chronic Obstructive Pulmonary Diseases	Viatris	Kolkata	Composition/ Method Of Treatment
78.	29/02/08	215514	00097/Kolnp/ 2004	An Antineoplastic Combinations	Wyeth	Kolkata	Composition/ Method Of Treatment
79.	12/09/08	223381	02033/Kolnp/ 2005	A Topical Pharmaceutical Composition	Berlin-Chemie	Kolkata	Composition
80.	20/04/07	206182	In/Pct/2001/ 01376/Kol	Oralpharmaceutical Compositions Containing Taxanes And Methods Of Preparation	Thereforivax Research	Kolkata	Composition
81.	27/06/08	221578	739/Kolnp/2003	Method And Compositions Employing Formulations Of Lecithin Oils And Nsaids For Protecting The Gastrointestinal Tract And Providing Enhanced Therapeutic Activity	The Board Of Regents Of The University Of Texas System	Kolkata	Composition
82.	28/03/08	217471	00640/Kolnp/ 2004	Orodispersible Tablets Containing Fexofenadine	Ethypharm	Kolkata	Composition
83.	07/03/08	216080	In/Pct/2001/637/ Kol	Pharmaceutical Aerosol Formulations For Use In A Pressurized Aerosol Container	Ivax	Kolkata	Formulation
84.	14/12/07	212684	00370/ Kolnp/2004	Pharmceutical Composition For Treating Hypertension And Heart Failure	Research Foundation Of State University Of New York	Kolkata	Composition/Method Of Treatment

ANNEX IV (CHAPTER 2B)

Table D: Examples of Patent Applications on pre-1995 medicines

Application No.	Date of Filing	Title of Invention	Name of Applicant
00755/Kolnp/2004	03/06/2004	Method For Preparing The Crystalline Form 1 Of Meloxi Cam"	Esteve Quimica S.A.
1019/Mumnp/2003	05/11/2003	Novel Galenic Formulations Of Meloxicam For Oral Administration	Boehringer Ingelheim Pharma Gmbh & Co. Kg.
1026/Mum/2006	28/06/2006	Once A Day Pharmaceutical Composition Comprising Diclofenac Potassium In An Extended Release Form And Meloxicam In An Immediate Release Form	Wockhardt Limited
1575/Delnp/2004	07/06/2004	"Peroral Active Agent Suspension"	Boehringer Ingelheim Pharma Gmbh & Co Kg.,
1632/Delnp/2005	21/04/2005	"Water Soluble Granules"	Boehringer Ingelheim Vetmedica Gmbh
2263/Mum/2007	16/11/2007	Taste Masked Meloxicam Oral Film	Vinita V. Kale
2612/Delnp/2008	28/03/2008	"Pharmaceutical Preparation Containing Meloxicam"	Boehringer Ingelheim Vetmedica Gmbh
317/Mum/2004	15/03/2004	A Process For Preparation Of A Pharmaceutical Composition Containing Cyclooxegenase Inhibitor Substance For Oral Administration	Unichem Laboratories Limited
4195/Delnp/2006	20/07/2006	"Use Of Meloxicam For The Treatment Of Respiratory Diseases In Pigs"	Boehringer Ingelheim Vetmedica Gmbh
5108/Delnp/2007	02/07/2007	"Process For Preparation Of High-Purity Meloxicam And Meloxicam Potassium Salt"	Egis Gyogyszergyar Nyrt
5737/Delnp/2006	03/10/2006	Use Of Meloxicam Formulations In Veterinary Medicine	Boehringer Vetmedica Gmbh.
834/Mum/2000	13/09/2000	A Process For Preparation Of Pharmaceutical Composition Containing A Non-Steroidal Anti-Inflammatory Drug(Nsaid)	Macleods Pharmaceuticals Ltd
853/Mum/2006	01/06/2006	Once A Day Pharmaceutical Composition Comprising Diclofenac Sodium In An Extended Release Form And Meloxicam In An Immediate Release Form	Wockhardt Ltd
863/Mum/2006	05/06/2006	Process For The Preparation Of Crystalline Form-I Of Meloxicam	Cadila Healthcare Limited
883/Mum/2004	16/08/2004	A Pharmaceutical Composition Containing Cyclooxygenase Inhibitor Substance For Oral Administration	Unichem Laboratories Limited
In/Pct/2000/00286/Mum	10/08/2000	A Process For Preparing An Orally Administered Solid Pharmaceutical Preparation At Meloxicam	Boehringer Ingelheim Pharma Kg.
In/Pct/2002/01776/Mum	11/12/2002	Aqueous Cyclodextrine-Free Solution Of Meloxicam	Boechringer Ingelheim Vetmedica Gmbh

ANNEX V (CHAPTER 2B)

Tabular presentation of the five case studies.

Source of information and details of methodology used to obtain the information is referred to in the study.

Table E.1: NMEs for the Treatment of Diabetes

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Patent Expiry Date	Generic Availability
1	Metfomin Hydrochloride	03-03-1995		07-01-2011	Yes
2	Glimepiride	30-11-1995	01-1999	6-10-2005	Yes
3	Acarbose	06-09-1995			Yes
4	Insulin Lispro	14-06-1996		7-5-2013	
5	Miglitol	18-12-1996	08-2004	27-1-2009	Yes
6	Troglitazone	29-01-1997		9-11-2008	
7	Repaglinide	22-12-1997	03-2000	5-9-2006	Yes
8	Pioglitazone Hydrochloride	15-07-1999	10-2000	17-01-2011	Yes
9	Rosiglitazone Maleate	25-09-1999	07-2000	14-04-2007	Yes
10	Insulin Glargine	20-04-2000		12-9-2014	Yes
11	Nateglinide	22-12-2000	05-2002	8-9-2009	Yes
12	Insulin Aspart Recombinant	07-06-2000		08-04-2014	
13	Insulin Glulisine	16-04-2004		16-04-2009	
				Total	**9**

Table E.2: NMEs for the Treatment of Hypertension

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Patent Expiry Date	Generic Availability
1	Nisoldipine	02-02-1995		07-10-2005	Yes
2	Losartan Potassium	14-04-1995	06-1998	11-8-2009	Yes
3	Moexipril Hydrochloride	19-04-1995		24-2-2007	
4	Carvedilol	14-09-1995	10-1998	5-3-2007	Yes
5	Epoprostenol Sodium	20-09-1995		12-5-2006	
6	Trandolapril	26-04-1996	10-2003	12-6-2007	Yes
7	Valsartan	23-12-1996	12-2001	21-5-2012	Yes
8	Hydrochlorothiazide; Irbesartan	30-09-1997		30-9-2011	Yes
9	Fenoldopam Mesylate	23-09-1997		NA	
10	Eprosartan Mesylate	22-12-1997		9-2-2010	
11	Candesartan Cilexetil	04-06-1998	08-2000	4-6-2012	Yes
12	Telmisartan	10-11-1998	11-2002	7-1-2014	Yes
13	Bosentan	20-11-2001		20-11-2015	Yes
14	Olmesartan Medoxomil	25-04-2002	07-2005	25-04-2016	Yes
15	Eplerenone	27-09-2002	06-2005	9-4-2006	Yes
16	Treprostnil Sodium	21-05-2002		06-10-2009	Yes
17	Iloprost	29-12-2004		NA	Yes
				Total	**13**

Table E.3: NCEs for the Treatment of Cardiovascular Diseases

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Patent Expiry Date	Generic Availability
1	Dexrazoxane	26-05-1995	02-2002	21-12-2007	Yes
2	Ibutilide Fumarate	28-12-1995		28-12-2009	
3	Cerivastatin Sodium	26-06-1997	05-2000	26-6-2011	Yes
4	Arbutamine Hydrochloride	12-09-1997		28-4-2009	
5	Clopidogrel Bisulfate	17-11-1997	02-2001	17-11-2011	Yes
6	Eptifibatide	18-05-1998	08-1999	11-11-2014	Yes
7	Tirofiban Hydrochloride	14-05-1998	08-2003	27-9-2010	Yes
8	Dofetilide	01-10-1999		25-9-2012	
9	Nesirde	10-08-2001		19-05-2009	
				Total	**5**

Table E.4: NMEs for the Treatment of Cancer

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Patent Expiry Date	Generic Availability
1	Bicalutamide	04-10-1995	03-2002	1-10-2008	Yes
2	Amifostine	08-12-1995	03-1996	31- 07-2012	Yes
3	Porfimer Sodium	2712-1995		12-06-2007	
4	Anastrozole	27-12-1995	02-2003	27-12-2009	Yes
5	Docetaxel	14-05-1996	06-1996	14-6-2010	Yes
6	Gemcitabine Hydrochloride	15-05-1996	01-1996	15-6-2010	Yes
7	Topotecan Hydrochloride	28-05-1996	06-1999	28-6-2010	Yes
8	Nilutamide	19-09-1996		NA	
9	Toremifene Citrate	29-05-1997		29-9-2009	
10	Letrozole	25-07-1997	03-1998	3-6-2011	Yes
11	Dolasetron Mesylate	11-09-1997		12-7-2011	
12	Sterile Talc Powder	24-12-1997		NA	
13	Capecitabine	30-04-1998	10-2000	13-01-2011	Yes
14	Temozolomide	11-08-1999	01-2000	11-08-2013	Yes
15	Epirubicin Hydrochloride	15-09-1999		NA	Yes
16	Exemestane	21-10-1999	10-2001	7-07-2006	Yes
17	Entacapone	19-10-1999	12-2004	27-11-2007	Yes
18	Dofetilide	01-10-1999		25-09-2012	
19	Bexarotene	29-12-1999		22-04-2012	
20	Alitretinoin	02-02-1999		03-08-06	
21	Triptorelin Pamoate	15-06-2000		20-07-2010	
22	Arsenic Trioxide	25-09-2000		10-11-2018	Yes
23	Zoledronic Acid	20-08-2001	11-2001	24-07-2007	Yes
24	Imatinib Mesylate	10-05-2001	12-2001	04-01-2015	Yes
25	Oxaliplatin	09-08-2002	10-1998	07-04-2013	Yes
26	Bortezomib	13-05-2003	05-2005	28-10-2014	Yes
27	Aprepitant	26-03-2003	08-2006	29-06-2012	Yes
28	Geftinib	05-05-2003	02-2004	19-01-2013	Yes
29	Palonosetron Hydrochloride	25-07-2003		13-04-2010	Yes
30	Abarelix	25-11-2003		07-06-2015	
31	Erlotinib Hydrochloride	18-11-2004	07-2005	30-03-2015	Yes
32	Pemetrexed Disodium	04-02-2004		29-03-2011	Yes
33	Clofarabine	28-12-2004		23-05-2009	
				Total	**22**

Table E.5: NMEs for the Treatment of HIV/AIDS

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Patent Expiry Date	Generic Availability
1	Lamivudine	17-11-1995	03-1998	17-11-2009	Yes
2	Saquinavir Mesylate	6-12-1995	08-1997	19-11-2010	Yes
3	Nevirapine	21-06-1996	03-2000	22-11-2011	Yes
4	Ritonavir	01-03-1996	09-2007	30-07-2013	Yes
5	Indinavir	13-03-1996	02-2007	9-05-2012	Yes
6	Nelfinavir Mesylate	14-03-1997	07-2001	10-7-2013	Yes
7	Delvirdine	4-04-1997		8-10-2013	
8	Efavirenz	17-09-1998	06-2001	7-08-2012	Yes
9	Abacavir	17-12-1998		18-12-2011	Yes
10	Amprenavir	15-04-1999		17-12-2013	
11	Lopinavir+Ritonavir	15-09-2000		10-07-2013	Yes
12	Tenofovir	26-10-2001	05-2005	25-07-2017	Yes
13	Enfuviride	13-03-2003		07-06-2013	
14	Atazanavir Sulfate	20-06-2003	12-2006	09-08-2017	Yes
15	Emtrictabine	2-07-2003	06-2005	11-05-2010	Yes
				Total	**12**

ANNEX VI (CHAPTER 2B)

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
1995					
1	Nisoldipine	02-02-95		Hypertension	07-10-2005
2	Tramadol Hydrochlorid,	03-03-95	01-93	Analgesic	22-03-2013
3	Metfomin Hydrochloride	03-03-95		Anti-Diabetic	07-01-2011
4	Losartan Potassium	14-04-95	06-98	Hypertension	11-8-2009
5	Nalmefene Hydrochloride	17-04-95		Opioid Antagonist	Not Avail.
6	Moexipril Hydrochloride	19-04-95		Hypertension	24-2-2007
7	Mycophenolate Mofetil	03-05-95	02-99	Immunosuppressive	Not Avail.
8	Iopromide	10-05-95	07-90	Contrast Media	Not Avail.
9	Lansoprazole	10-05-95	12-94	Gastric Acid, Secretion Inhibitor	29-7-2005
10	Dexrazoxane	26-05-95	02-02	Cardio-Protective	21-12-2007
11	Sevoflurane	07-06-95	07-96	Anesthetic, General	27-1-2017
12	Dirithromycin	19-06-95		Antibiotic, Macrolide	Not Avail.
13	Acarbose	06-09-95		Alpha-Glucosidase Inhibitor	27-2-2007
14	Azelaic Acid	13-09-95	07-03	Inflammatory Acne Vulgaris	17-1-2006
15	Carvedilol	14-09-95	10-98	Hypertension	5-3-2007
16	Epoprostenol Sodium	20-09-95		Pulmonary Hypertension	12-5-2006
17	Alendronate Sodium	29-09-95	09-97	Bone-Resorption Inhibitor	6-8-2007
18	Bicalutamide	04-10-95	03-02	Antiandrogen	1-10-2008
19	Lamivudine	17-11-95	03-98	Antiviral	17-11-2009
20	Glimepiride	30-11-95	01-99	Blood Glucose Regulator	6-10-2005
21	Saquinavir Mesylate	06-12-95	08-97	Antiviral	19-11-2010
22	Cetirizine Hydrochloride	08-12-95	06-93	H1-Receptor Antagonist	25-06-2007
23	Amifostine	08-12-95	03-96	Cytoprotective	31- 07-2012
24	Riluzole	12-12-95	10-97	Neuroprotective	18-06-2013

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
25	Ceftibuten Dihydrate	20-12-95	11-96	Cephalosporin	Not Avail.
26	Ioxilan	21-12-95		Diagnostic Radiopaque	21-12-2009
27	Porfimer Sodium	2712-95		Esophageal Cancer	12-06-2007
28	Anastrozole	27-12-95	02-03	Non-Steroidal Aromatase Inhibitor	27-12-2009
29	Ibutilide Fumarate	28-Dec-95		Antiarrhythmic	28-12-2009
1996					
1	Cefepime Hydrochloride	18-1-96	10-02	Cephalosporin	Not Avail.
2	Technetium Tc-99m	09-02-96		Radioactive Diagnostic	9-2-2010
3	Ritonavir	01-03-96	09-07	Antiviral	30-7-2013
4	Indinavir Sulfate	13-03-96	02-01	Antiviral	9-5-2012
5	Iodixanol	22-03-96		Contrast Media	20-9-2011
6	Trandolapril	26-04-96	10-03	Treatment Of Hypertension	12-6-2007
7	Sodium Phenylbutyrate	30-04-96		Management Of Chronic Urea Cycle Disorders	Not Avail.
8	Docetaxel	14-05-96	06-96	Breast Cancer	14-6-2010
9	Gemcitabine Hydrochloride	15-05-96	01-96	Advanced Or Metastatic Adenocarcinoma Of The Pancreas	15-6-2010
10	Corticorelin Ovine Triflutate	23-05-96		Cushing's Syndrome	Not Avail.
11	Topotecan Hydrochloride	28-05-96	06-99	Ovarian Cancer	28-6-2010
12	Adapalene	31-05-96		Antiacne	31-6-2010
13	Latanoprost	05-06-96	05-98	Glaucoma And Ocular Hypertension.	28-6-2006
14	Albendazole	11-06-96		Neurocysticercosis And Hydatid Disease	Not Avail.
15	Mirtazapine	14-06-96	02-01	Antidepressant	12-1-2010
16	Insulin Lispro	14-06-96		Diabetes Mellitus	7-5-2013
17	Irinotecan Hydrochloride	14-06-96	05-97	Colon Or Rectum Cancer	20-8-2007
18	Nevirapine	21-06-96	03-00	Antiviral	22-11-2011
19	Meropenem	21-06-96	01-02	Antibiotic, Carbapenem	Not Avail.
20	Cidofovir	26-05-96		Antiviral	26-6-2010
21	Remifentanil Hydrochloride	12-07-96		Analgesic	15-2-2009

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
22	Fexofenadine Hydrochloride	25-07-96	09-98	Anti-Histamine	26-11-2013
23	Fosphenytoin Sodium	05-08-96	10-02	Anti-Convulsant	5-8-2007
24	Bentoquatam	26-08-96		Protectant	Not Avail.
25	Ferumoxides	30-08-96		An Adjunct Io MRI	13-9-2005
26	Olanzapine	30-09-96	01-00	Psychotic Disorders	23-4-2011
27	Zafirlukast	26-09-96	12-01	Asthma	26-9-2010
28	Pentosan Polysulfate Sodium	26-09-96		Interstitial Cystitis	19-6-2010
29	Penciclovir	24-09-96		Treatment Of Herpes	24-9-2010
30	Ropivacaine Hydrochloride Monohydrate	24-09-96		Anesthesia For Surgery	24-9-2010
31	Nilutamide	19-09-96		Prostate Cancer	Not Avail.
31	Urea, C-13	17-09-96		H Pylori	24-8-2009
32	Brimonidine Tartrate	06-09-96	05-99	Glaucoma Or Ocular Hypertension	13-6-2012
33	Midodrine Hydrochloride	06-09-96		Orthostatic Hypotension	Not Avail.
34	Betaine, Anhydrous	25-10-96		Homocystinuria	Not Avail.
35	Butenafine Hydrochloride	18-10-96	02-01	Tinea Pedis	18-10-2010
36	Tizanidine Hydrochloride	27-11-96	02-02	Spasticity	28-11-2021
37	Donepezil Hydrochloride	25-11-96	03-01	Alzheimer's	25-11-2010
38	Ivermectin	22-11-96		Treatment Of Strongyloidiasis And Onchocerciasis	Not Avail.
39	Azelastine Hydrochloride	01-11-96	07-97	Treatment Of The Symptoms Of Seasonal Allergic Rhinitis	1-11-2010
40	Topiramate	24-12-96	08-99	Adjunctive Treatment For Partial Onset Seizures In Adults	26-9-2008
41	Danaparoid Sodium	24-12-96		Thrombosis	3-10-2010
42	Valsartan	23-12-96	12-01	Treatment Of Hypertension	21-5-2012
43	Cabergoline	23-12-96	09-22	Treatment Of Hyperprolactinemic Disorders, Either Idiopathic Or Due To Pituitary Adenomas	29-12-2005

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
44	Glatiramer Acetate	20-12-96		Reduction Of Relapses In Patients With Relapsing-Remitting Multiple Sclerosis	24-5-2014
46	Fosfomycin Tromethamine	19-12-96		Uncomplicated Urinary Tract Infections(Acute Cystitis) In Women Due To Susceptible Strains Of Escherichia Coli And Enteroccus Faecalis	Not Avail.
47	Sparfloxacin	19-12-96	11-96	Community-Acquired Pneumonia, Acute Bacterial Exacerbations Of Chronic Bronchitis, And Acute Maxillary Sinusitis	4-2-2010
48	Olopatadine Hydrochloride	18-12-96		For The Temporary Prevention Of Itching Of The Eye Due To Allergic Conjunctivitis	3-10-2006
49	Miglitol	18-12-96	08-04	An Adjunct To Dsiet Or Diet Plus Sulfonylurea Therapy To Improve Glycemic Control In Patients With Non-Insulin-Dependent Diabetes Mellitus (Type Ii)	27-1-2009
50	Atorvastatin Calcium	17-12-96	09-99	Cardiovascular	24-9-2009
51	Amlexanox	17-12-96		Treatment Of Signs And Symptoms Of Aphthous Ulcers In Immunocompetent Individuals	8-11-2011
52	Zileuton	09-12-96		Prophylaxis And Chronic Treatment Of Asthma In Adults And Children 12 Years Of Age And Older	10-12-2010
53	Ferumoxsil	06-12-96		Oral Use With Magnetic Resonance Imaging To Enhance The Delineation Of The Bowel To Distinguish It From Organs And Tissues That Are Adjacent To The Upper Regions Of The Gastrointestinal Tract	13-9-2005
1997					
1	Troglitazone	29-01-97		For Use In Type II Diabetes Patients Whose Hyperglycemia Is Inadequately Controlled Despite Insulin Therapy	9-11-2008
2	Imiquimod	27-02-97	12-04	Treatment Of External Genital And Perianal Warts/ Condyloma Acuminata In Adults	25-8-2009
3	Samarium Sm 153 Edtmp	28-03-97		For Relief Of Pain In Patients With Confirmed Osteoblastic Metastatic Bone Lesions That Enhance On Radionuclide Bone Scan	6-2-2007
4	Nelfinavir Mesylate	14-03-97	07-01	Treatment Of HIV Infection When Therapy Is Warranted	7-10-2013
5	Anagrelide Hydrochloride	14-03-97		Treatment Of Patients With Essential Thrombocythemia To Reduce The Elevated Platelet Count And The Risk Of Thrombosis And Ameliorate Associated Systems	Not Avail.
6	Tiludronate Disodium	07-03-97		Treatment Of Paget's Disease Of Bone	6-4-2009

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
7	Tamsulosin Hydrochloride	15-04-97	04-02	For The Treatment Of The Signs And Symptoms Of Benign Prostatic Hyperplasia (BPH)	27-2-2006
8	Delavirdine Mesylate	04-04-97		Treatment Of HIV-1 Infection In Combination With Appropriate Antiretroviral Agents When Therapy Is Warranted	8-10-2013
9	Toremifene Citrate	29-05-97		Treatment Of Metastatic Breast Cancer In Postmenopausal Women With Estrogen Receptor Positive Or Receptor Unknown Tumors	29-9-2009
10	Urea C-14	09-05-97		For Use In The Detection Of Gastric Urease As An Aid In The Diagnosis Of Helicobacter Pylori Infection In The Human Stomach	15-5-2006
11	Cerivastatin Sodium	26-06-97	05-00	Cardiovascular	26-6-2011
12	Tazarotene	13-06-97	09-03	For The Topical Treatment Of Patients With Stable Plaque Psoriasis Of Up To 20% Body Surface Area Involvement And Topical Treatment Of Patients With Facial Acne Vulgaris Of Mild To Moderate Severity	13-6-2011
13	Letrozole	25-07-97	03-98	For Treatment Of Advanced Breast Cancer In Postmenopausal Women	3-6-2011
14	Pramipexole Dihydrochloride	01-07-97	07-05	Treatment Of The Signs And Symptoms Of Idiopathic Parkinsons Disease	23-11-2007
15	Irbesartan	30-09-97		Treatment Of Hypertension	30-9-2011
16	Tiagabine Hydrochloride	30-09-97	05-04	As Adjunctive Therapy In Adults And Children 12 Years And Older In The Treatment Of Partial Seizures	30-9-2011
17	Quetiapine Fumarate	26-09-97	05-02	Treatment Of The Manifestations Of Psychotic Disorders	26-9-2011
18	Fenoldopam Mesylate	23-09-97		Hypertension	Not Avail.
19	Ropinirole Hydrochloride	19-09-97	12-01	Treatment Of The Signs And Symptoms Of Idiopathic Parkinson's Disease	7-12-2007
20	Arbutamine Hydrochloride	12-09-97		Aid In Diagnosing The Presence Or Absence Of Coronary Artery Disease In Patients Who Cannot Exercise Adequately When Used In Conjunction With Radionuclide Myocardial Perfusion Imaging Or Echocardiography	28-4-2009
21	Dolasetron Mesylate	11-09-97		For The Prevention Of Chemotherapy-Induced Nausea And Vomiting, And Prevention Of Postoperative Nausea And Vomiting	12-7-2011

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
22	Mangafodipir Trisodium	26-11-97		As An Adjunct To Mri To Enhance The T1-Weighted Images Used In The Detection, Localization, Characterization, And Evaluation Of Lesions Of The Liver	12-2-2008
23	Zolmitriptan	25-11-97		Treatment Of Migraine Headaches	14-11-2012
24	Sibutramine Hydrochloride	22-11-97		Management Of Obesity, Including Weight Loss And Maintenance Of Weight Loss, And Should Be Used In Conjunction With A Reduced Calorie Diet	29-5-2007
25	Clopidogrel Bisulfate	17-11-97	02-01	For The Reduction Of Atherosclerotic Events (Myocardial Infarction, Stroke, And Vascular Death) In Patients With Atherosclerosis Documented By Recent Stroke, Recent Myocardial Infarction, Or Established Peripheral Arterial Disease	17-11-2011
26	Grepafloxacin Hydrochloride	06-11-97		Provides For The Indications Of Acute Bacterial Exacerbations Of Chronic Bronchitis, Community-Acquired Pneumonia, Uncomplicated Gonorrhea (Urethral In Males And Endocervial And Rectal In Females), And Nongonococcal Urethritis And Cervicitis	28-10-2013
27	Emedastine Difumarate	29-12-97		For The Temporary Relief Of The Signs And Symptoms Of Allergic Conjunctivitis	14-8-2005
28	Sterile Talc Powder	24-12-97		For The Prevention Of The Recurrence Of Malignant Pleural Effusions In Symptomatic Patients	Not Avail.
29	Repaglinide	22-12-97	03-00	Diatebetics	5-9-2006
30	Eprosartan Mesylate	22-12-97		For Use In The Management Of Essential Hypertension	9-2-2010
31	Alatrofloxacin Mesylate	18-12-97		Antibiotic, Broad-Spectrum Antibacterial Agent Indicated For The Treatment Of Infections Caused By Susceptible Strains Of Microorganisms	17-11-2009
32	Trovafloxacin Mesylate	18-12-97		Broad-Spectrum Antibacterial Agent Indicated For The Treatment Of Infections Caused By Susceptible Strains Of Microorganisms	18-12-2011
33	Raloxifene Hydrochloride	09-12-97	05-01	For The Prevention Of Osteoporosis In Postmenopausal Women	28-6-2012
34	Fomepizole	04-12-97		Antidote To Ethylene Glycol (Antifreeze) Poisoning In Patients Who Have Ingested, Or Are Suspected Of Having Ingested Ethylene Glycol	Not Avail.
35	Cefdinir	04-12-97			04-12-2011
	1998				
1	Tolcapone	29-01-98		As An Adjunct To Levodopa And Carbidopa For The Treatment Of The Signs And Symptoms Of Idiopathic Parkinson's Disease	29-7-2012

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
2	Naratriptan Hydrochloride	10-02-98		For The Acute Treatment Of Migraine Headache	7-7-2010
3	Montelukast Sodium	10-02-98		Asthama	3-22012
4	Sildenafil Citrate	27-03-98	01-01	Treatment Of Erectile Dysfunction	27-3-2012
5	Tolterodine Tartrate	25-03-98	09-01	Treatment Of Patients With An Overactive Bladder With Symptoms Of Urinary Frequency, Urgency, Or Urge Incontinence	25-3-2012
6	Risedronate Sodium	25-03-98		Osteoporosis	0-12-2013
7	Loteprednol Etabonate	09-03-98	03-02	For The Treatment Of Steroid Responsive Inflammatory Conditions Of The Palpebral And Bulbar Conjunctiva, Cornea And Anterior Segment Of The Eye	9-3-2012
8	Lepirudin	06-03-98		For Anticoagulation In Patients With Heparin-Induced Thrombocytopenia (Hit) And Thromboembolic Disease In Order To Prevent Further Thromboembolic Complications	19-1-2010
9	Capecitabine	30-04-98	10-00	Breast Cancer	13-1-2011
10	Paricalcitol	17-04-98		For The Prevention And Treatment Of Secondary Hyperparathroidism Encountered With Chronic Renal Failure	27-4-2012
11	Brinzolamide	01-04-98		Treatment Of Elevated Intraocular Pressure In Patients With Ocular Hypertension Or Open-Angle Glaucoma	31-8-2010
12	Eptifibatide	18-05-98	08-99	Treatment Of Patients With Acute Coronary Syndrome (Ua/Nqmi), Including Patients Who Undergoing Percutaneous Coronary Intervention (Pci).	11-11-2014
13	Tirofiban Hydrochloride	14-05-98	08-03	Use In Combination With Heparin, For The Treatment Of Acute Coronary Syndrome, Including Patients Who Are To Be Managed Medically And Those Undergoing PTCA Or Atherectomy	27-9-2010
14	Rizatriptan Benzoate	29-06-98	02-03	Acute Treatment Of Migraine Headache	29-6-2012
15	Rifapentine	22-06-98		Treatment Of Pulmonary Tuberculosis	Not Avail.
16	Candesartan Cilexetil	04-06-98	08-00	Treatment Of Hypertension	4-6-2012
17	Citalopram Hydrobromide	17-07-98	10-01	Treatment Of Depression	Not Avail.

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
18	Thalidomide	16-07-98	08-02	Acute Treatment Of The Cutaneous Manifestations Of Moderate To Severe Erythema Nodosum Leprosum (Enl) And As Maintenance Therapy For Prevention And Suppression Of The Cutaneous Manifestations Of Enl Recurrences	28-8-2018
19	Calfactant	01-07-98		Prevention And Treatment Of Respiratory Distress Syndrome (Rds) In Neonates	Not Avail.
20	Fomivirsen Sodium	26-08-98		Local Treatment Of Cytomegalovirus (Cmv) Retinitis In Patients With (Aids) Who Are Intolerant Of Or Have A Contraindication To Other Treatment(S) For Cmv Retinitis Or Who Were Insufficiently Responsive To Previous Treatment(S) For Cmv Retinitis	23-11-2010
21	Valrubicin	25-09-98		For Intravesical Therapy Of Bcg-Refractory Carcinoma In Situ(Cis) Of The Urinary Bladder In Patients For Whom Immediate Cystectomy Would Be Associated With Unacceptable Morbidity Or Mortality	Not Avail.
22	Efavirenz	17-09-98	06-01	Treatment Of Hiv-1 Infection	7-8-2012
23	Technetium Tc-99m Apcitide	14-09-98		For Scintigraphic Imaging Of Acute Venous Thrombosis In The Lower Extremities Of Patients Who Have Signs And Symptoms Of Acute Venous Thrombosis	22-8-2012
24	Leflunomide	10-09-98	10-01	For The Treatment Of Active Rheumatoid Arthritis (Ra) To Reduce Signs And Symptoms And To Retard Structural Damage As Evidenced By X-Ray Erosions And Joint Space Narrowing	Not Avail.
25	Sevelamer Hydrochloride	30-10-98	05-05	For The Reduction Of Serum Phosphorus In Patients With End Stage Renal Disease Who Are On Hemodialysis	11-8-2013
26	Telmisartan	10-11-98	11-02	For The Treatment Of Hypertension	7-1-2014
27	Thyrotropin Alfa	30-11-98		Thyroid Cancer	24-11-15
28	Celecoxib	31-12-98	02-00	For The Signs And Symptoms Of Osteoarthritis And Rheumatoid Arthritis	30-11-2013
29	Modafinil	24-12-98	12-03	For The Treatment Of Narcolepsy	22-5-2007
30	Abacavir Sulfate	17-12-98		HIV/AIDS	18-12-2011
	1999				
1	Cilostazol	15-01-99	01-03	For The Reductions Of Symptoms Of Intermittent Claudication.	Not Avail.
2	Ferric Sodium Gluconate	18-02-99		For The Treatment Of Iron Deficiency Anemia In Patients Undergoing Chronic Hemodialysis Who Are Receiving Supplemental Erythropoetin Therapy	Not Avail.

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
3	Orlistat	23-04-99	10-04	For The Use Of Xenical Capsules For Obesity Management Including Weight Loss And Weight Maintenance When Used In Conjunction With A Reduced Calorie Diet And Indicated To Reduce The Risk Of Weight Regain After Prior Weight Loss.	18-6-2009
4	Ganirelix Acetate	29-07-99		Provides For The Inhibition Of Premature Lh Surges In Women Undergoing Controlled Ovarian Hyperstimulation	5-2-2007
5	Zanamivir	26-07-99	02-06	For Treatment Of Uncomplicated Acute Illness Due To Influenza Virus In Adults And Adolescents Twelve Years And Older Who Have Been Symptomatic For No More Than Two Days	26-7-2013
6	Rapacuronium Bromide	18-08-99		For Outpatients And Inpatients As An Adjunct To General Anesthesia To Facilitate Tracheal Intubation, And To Provide Skeletal Muscle Relaxation During Surgical Procedures	14-4-2013
7	Zaleplon	13-08-99	01-02	For The Short-Term Treatment Of Insomnia	6-6-2008
8	Temozolomide	11-08-99	01-00	For The Treatment Of Adult Patients With Refractory Anaplastic Astrocytoma, Ie., Patients At First Relapse Who Have Experienced Disease Progression On A Drug Regimen Containing A Nitrosourea And Procarbazine.	11-8-2013
9	Technetium Tc-99m Depreotide	03-08-99		For Patients Presenting With Pulmonary Lesions On Computed Tomography And/Or Chest X-Ray Who Have Known Malignancy Or Who Are Highly Suspect For Malignancy	5-7-2005
10	Pemirolast Potassium	24-09-99		For The Prevention Of Itching Of The Eye Due To Allergic Conjunctivitis	23-12-2008
11	Dalfopristin; Quinupristin	21-09-99		For The Treatment Of Complicated Skin And Skin Structure Infections	Not Avail.
12	Sirolimus	15-09-99	07-02	For The Prophylaxis Of Organ Rejection In Patients Receiving Renal Transplants	6-6-2009
13	Epirubicin Hydrochloride	15-09-99		For Use As A Component Of Adjuvant Therapy In Patients With Evidence Of Axillary Node Tumor Involvement Following Resection Of Primary Breast Cancer	Not Avail.
14	Oseltamivir Phosphate	27-10-99	10-05	For The Treatment Of Uncomplicated Acute Illness Due To Influenza Infections In Adults Who Have Been Symptomatic For No More Than Two Days.	2-2-2016

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
15	Rabeprazole Sodium	19-08-99	12-01	Aciphex Is Indicated For 1) Healing Of Erosive Or Ulcerative Gastroesophageal Reflux Disease (Gerd); 2) Maintenance Of Healing Of Erosive Or Ulcerative Gerd; 3) Healing Of Duodenal Ulcer; 4) Treatment Of Pathological Hypersecretory Conditions, Including Zollinger-Ellison Syndrome.	4-4-2009
16	Exemestane	21-10-99	10-01	For The Treatment Of Advanced Breast Cancer In Postmenopausal Women Whose Disease Has Progressed Following Tamoxifen Therapy	7-7-2006
17	Entacapone	19-10-99	12-04	For The Use Of Comtan As An Adjunct To Levodopa/Carbidopa To Treat Patients With Idiopathic Parkinson's Disease Who Experience The Signs And Symptoms Of End-Of-Dose "Wearing-Off" (So-Called "Fluctuating" Patients)	27-11-2007
18	Dofetilide	01-10-99		For The Maintenance Of Normal Sinus Rhythym (Delay In Time To Recurrence Of Atrial Fibrillation/ Atrial Flutter [Af/Afi]) In Patients With Atrial Fibrillation/Atrial Flutter Of Greater Than One Week Duration Who Have Been Converted To Normal Sinus Rhythym.	25-9-2012
19	Levetriacetam	30-11-99	02-05	Provides For The Use Of Keppra As Adjunctive Therapy In The Treatment Of Partial Onset Seizures In Adults With Epilepsy	14-7-2008
20	Poractant Alpha	18-11-99	12-02	For The Treatment (Rescue) Of Respiratory Distress Syndrome (RDS) In Premature Infants	Not Avail.
21	Bexarotene	29-12-99		For The Treatment Of Cutaneous Manifestations Of Cutaneous T-Cell Lymphoma In Patients Who Are Refractory To At Least One Prior Systemic Therapy.	22-4-2012
22	Nitric Oxide	23-12-99		For The Treatment Of Term And Near-Term (>34 Weeks) Neonates With Hypoxic Respiratory Failure Associated With Clinical Or Echocardiographic Evidence Of Pulmonary Hypertension, Where It Improves Oxygenation And Reduces The Need For Extracorporeal Membrane Oxygenation	23-12-2013
23	Gatifloxacin	17-12-99	10-01	Pneumonia; Acute Bacterial Exacerbation Of Chronic Bronchitis; Acute Sinusitis; Uncomplicated Urinary Tract Infections; Complicated Urinary Tract Infections; And Pyelonephritis; Uncomplicated Urethal, Pharyngeal, And Rectal Gonorrhea In Males; As Well As Endocervical, Pharyngeal, And Rectal Gonorrhea In Females	15-12-2009
24	Moxifloxacin Hydrochloride	10-12-99	06-01	For The Acute Bacterial Sinusitis, Acute Bacterial Exacerbation Of Chronic Bronchitis, Community-Acquired Pneumonia.	30-6-2009

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
25		08-12-99		For The Use Of Optimark With Magnetic Resonance Imaging (Mri) In Patients With An Abnormal Blood Brain Barrier Or Abnormal Vascularity Of The Brain, Spine And Associated Tissues; And With Mri	14-6-2009
26	Aminolevulinic Acid Hcl	03-12-99		For The Use With A Blue Light Irradiation Using The Blu-U Illuminator For The Photodynamic Therapy Of Actinic Keratoses Of The Face And Scalp	28-7-2009
27	Alitretinoin	02-02-99		For The Treatment Of Cutaneous Lesions In Patients With Aids-Related Kaposi's Sarcoma.	03-08-2006
28	Ketotifen Fumarate	02-07-99		For The Prevention Of Itching Of The Eye Due To Allergic Conjunctivitis	13-01-2019
29	Amprenavir	15-04-99		For The Treatment Of HIV-1 Infection.	17-12-2013
30	Rofecoxib	20-05-99	06-00	For The Relief Of The Signs And Symptoms Of Osteoarthritis, For The Management Of Acute Pain And For The Treatment Of Primary Dysmenorrhea.	24-06-2013
31	Pioglitazone Hydrochloride	15-07-99	10-00	For The Improvement Of Glycemic Control In Patients With Type 2 Diabetes As Monotherapy, Or In Combination With A Sulfonylurea, Metformin Or Insulin When Diet And The Single Agent Does Not Result In Adequate Glycemic Control.	17-01-2011
31	Doxercalciferol	09-06-99		For The Reduction Of Elevated Ipth Levels In The Management Of Secondary Hyperparathyroidism In Patients Undergoing Chronic Renal Dialysis.	02-08-2008
32	Rosiglitazone Maleate	25-09-99	07-00	For The Treatment Of Type 2 Diabetes Mellitus As Monotherapy Or In Combination With Metformin.	14-04-2007
33	Mequinol; Tretinoin	10-12-99		For The Treatment Of Solar Lentigines.	16-03-2010
34		17-12-99		For The Sedation Of Initially Intubated And Mechanically Ventilated Adult Patients In An Icu Setting.	15-07-2008
2000					
1	Oxcarbazepine	14-01-00	10-01	For Use As Monotherapy Or Adjunctive Therapy In The Treatment Of Partial Seizures In Children Ages 4-16 With Epilepsy	Not Avail.
2	Cevimeline Hydrochloride	11-01-00		For The Treatment Of Symptoms Of Dry Mouth In Patients With Sjorgren's Syndrome	30-8-2009
3		17-02-00		Skin Exposure Reduction Paste Against Chemical Warfare Agents (Serpacwa) Only In Conjunction With Mission Oriented Protective Posture (Mopp) Gear To Reduce Or Delay The Absorption Of Chemical Warfare Agents Through The Skin When Serpacwa Is Applied Prior To Exposure	Not Avail.

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
4	Alosetron Hydrochloride	9-02-00		For The Treatment Of Irritable Bowel Syndrome (Ibs) In Women Whose Predominant Bowel Symptom Is Diarrhea	19-12-2013
5	Pantoprazole Sodium	2-02-00	12-98	For Short-Term Treatment (Up To 8 Weeks) In The Healing And Symptomatic Relief Of Erosive Esophagitis	19-7-2010
6	Zonisamide	27-03-00	12-05	Provides For The Use Of Zonegran Capsules As Adjunctive Therapy In The Treatment Of Partial Seizures In Adults With Epilepsy.	Not Avail.
7	Linezolid	18-04-00	10-01	For The Treatment Of Adult Patients With Vancomycin-Resistant Enterococcus Faecium Infections, Nosocomial Pneumonia, Complicated And Uncomplicated Skin And Skin Structure Infections, And Community-Acquired Pneumonia.	18-11-2014
8	Rivastigmine Tartrate	21-04-00	07-98	For The Treatment Of Mild To Moderate Dementia Of The Ahzheimer's Type	14-8-2007
9	Insulin Glargine	20-04-00		Type 1 Diabetes Mellitus Or Adult Patients With Type 2 Diabetes Mellitus For The Control Of Hyperglycemia	12/9/2014
10	Meloxicam	13-04-00	02-99	For Relief Of The Signs And Symptoms Of Osteoarthritis	25-3-2019
11	Verteporfin	12-04-00		Age-Related Macular Degeneration	20-1-2007
12	Triptorelin Pamoate	15-06-00		For The Palliative Treatment Of Advanced Prostate Cancer	20-7-2010
13	Docosanol	25-07-00		For The Treatment Cold Sore/Fever Blister	28-4-2014
14	Tinzaparin Sodium	14-07-00		Deep Vein Thrombosis With Or Without Pulmonary Embolism	Not Avail.
15	Cetrorelix	11-08-00		For The Prevention Of Premature Lh Surges In Women Undergoing Controlled Ovarian Stimulation	17-7-2007
16	Unoproston Isopropyl	3-8-2000	11-03	Indicated For The Lowering Of Intraocular Pressure In Patients With Open-Angel Glaucoma Or Ocular Hypertension Who Are Intolerant Of Other Intraocular Pressure Lowering Medications Or Insufficiently Responsive (Failed To Achieve Target Iop Determined After Multiple Measurements Over Time) To Another Intraocular Pressure Lowering Medication.	19-03-08
17	Mifepristone	28-09-00	02-02	Mifeprex Is Indicated For Medical Termination Of Intrauterine Pregnancy Through 49 Days' Pregnancy.	Not Avail.
18	Arsenic Trioxide	25-09-00		Acute Promyelocytic Leukemia (APL)	10-11-2018

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
19	Nateglinide	22-12-00	05-02	Provides For The Use Of Starlix As Monotherapy, As An Adjunct To Diet And Exercise To Improve Gylcemic Control In Patients With Type 2 Diabetes. In Addition, It Provides For The Use Of Starlix Concomitantly With Metformin To Improve Glycemic Control.	8-9-2009
20	Bivalirudin	15-12-00	08-05	Anticoagulant Percutaneous Transluminal Coronary Angioplasty (PTCA)	23-3-2010
21	Gemtuzumab Ozogamicin	17-05-00		Cancer (Leukemia)	17-12-2013
22	Articaine Hydrochloride, Epinephrine	03-04-00		Indicated For Infiltration Or Nerve Block Anesthesia For Dentistry	Na
23	Colesevelam Hydrochloride	26-05-00		For The Reduction Of Elevated LDL-Cholesterol, Alone Or In Combination With An Hmg-Coa Reductase Inhibitor, In Patients With Primary Hypercholesterolemia (Frederickson Type IIa).	29-04-2014
24	Argatroban	30-06-00		Indicated As An Anticoagulant For Prophylaxis Or Treatment Of Thrombosis Patients With Heparin-Induced Thrombocytopenia.	30-06-2014
25	Insulin Aspart Recombinant	07-06-00		For The Treatment Diabetes Mellitus, For The Control Of Hyperglycemia.	08-04-2014
26	Balsalazide Disodium	18-07-00	11-02	For The Treatment Of Mildly To Moderate Active Ulcerative Colitis.	18-07-2005
27	Lopinavir, Ritonavir	15-09-00		For The Treatment Of Hiv-1 Infections In Adults And Pediatric Patients Age Six Months And Older.	10-07-2013
2001					
1	Formoterol Fumarate	16-02-01		For The Long- Term, Administration In The Maintenance Treatment Of Asthma And In The Prevention Of Bronchospasm In Adults And Children 5 Years Of Age And Older With Reversible Obstructive Airways Disease, Including Patients With Symptoms Of Nocturnal Asthma. Foradil Is Also Indicated For The Acute Prevention Of Exercise-Induced Bronchospasm (Eib) In Adults And Children 12 Years Of Age And Older, When Administered On An Occasional, As-Needed Basis	8/3/2019
2	Bimatopros	16-03-01		Indicated For The Reduction Of Elevated Intraocular Pressure In Patients With Open-Angle Glaucoma Or Ocular Hypertension Who Are Intolerant Of Other Intraocular Pressure Lowering Medications	21-09-2012

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
3	Desloratadine	21-12-01	1-Oct	For The Relief Of The Nasal And Non-Nasal Symptoms Of Seasonal Allergic Rhinitis In Patients 12 Years Of Age And Older.	21-04-2006
4	Etonogestrel; Ethinyl Estradiol Vaginal Ring	03-10-01	5-Feb	For The Prevention Of Pregnancy In Women Who Elect To Use This Product As A Method Of Contraception.	23-4-2008
5	Fondaparinux Sodium	7/12/2001	3-Oct	For The Following: The Prophylaxis Of Deep Vein Thrombosis, Which May Lead To Pulmonary Embolism: 1) In Patients Undergoing Hip Fracture Surgery; 2) In Patients Undergoing Hip Replacement Surgery; 3) In Patients Undergoing Knee Replacement Surgery.	Not Avail.
6	Travoprost	16-03-01	5-Dec	For The Reduction Of Intraocular Pressure In Patients With Open-Angle Glaucoma Or Ocular Hypertension Who Are Intolerant Of Other Intraocular Pressure Lowering Medications Or Insufficiently Responsive To Another Intraocular Pressure Lowering Medication.	3/8/2013
7	Galantamine Hydrobromide	28-02-01		For The Treatment Of Mild To Moderate Dementia Of The Alzheimer's Type.	Not Avail.
8	Almotriptan Maleate	7/5/2001		For The Acute Treatment Of Migraine.	7/5/2015
9	Perflutren Lipid Microsphere	31-07-01		For The Treatment In Patients With Suboptimal Echocardiograms To Opacify The Left Ventricular Chamber And To Improve The Delineation Of The Left Ventricular Endocardial Border.	22-12-2009
10	Frovatriptan Succinate	8/11/2001		For The Acute Treatment Of Migraine.	7/11/2012
11	Dutasteride	20-11-01	4-Feb	For The Treatment Of Symptomatic Benign Prostatic Hyperplasia (Bph) In Men With An Enlarged Prostate Gland.	17-9-2013
12	Zoledronic Acid	20-08-01	1-Nov	For The Treatment Of Hypercalcemia Of Malignancy.	24-07-2007
13	Cefditoren Pivoxil	29-08-01	6-Mar	For The Treatment Of Acute Bacterial Exacerbation Of Chronic Bronchitis, Pharyngitis/Tonsillitis, And Uncomplicated Skin And Skin Structure Infections.	13-06-2006
14	Imatinib Mesylate	10/5/2001	1-Dec	For The Treatment Of Patients With Chronic Myeloid Leukemia (Cml) In Blast Crisis, Accelerated Phase, Or In Chronic Phase After Failure Of Interferon-Alpha Therapy.	4/1/2015
15	Nesiritide	10/8/2001		For The Intravenous Treatment Of Patients With Acutely Decompensated Congestive Heart Failure Who Have Dyspnea At Rest Or With Minimal Activity.	19-05-2009

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
16	Drospirenone, Ethinyl Estradiol	11/5/2001	5-May	For Oral Contraception	29-10-2013
17	Bosentan	20-11-01		For The Treatment Of Pulmonary Arterial Hypertension	20-11-2015
18	Norelgestromin; Ethinyl Estradiol	20-11-01		For The Prevention Of Pregnancy.	Na
19	Ertapenem Sodium	21-11-01		For The Following: (1) Complicated Intra-Abdominal Infections (2) Complicated Skin And Skin Structure Infections (3) Community Acquired Pneumonia (4) Complicated Urinary Tract Infections Including Pyelonephritis (5) Acute Pelvic Infections Including Postpartum Endomyometritis, Septic Abortion And Post Surgical Gynecologic Infections.	2/2/2013
20	Pimecrolimus	13-12-01	4-Jul	For Short-Term And Intermittent Long-Term Therapy In The Treatment Of Mild To Moderate Atopic Dermatitis In Non-Immunocompromised Patients 2 Years Of Age And Older, In Whom The Use Of Alternative, Conventional Therapies Is Deemed Inadvisable Because Of Potential Risks, Or In The Treatment Of Patients Who Are Not Adequately Responsive To Or Intolerant Of Alternative, Conventional Therapies.	26-10-2015
21	Caspofungin Acetate	26-01-01	5-Dec	For The Treatment Of Invasive Aspergillosis In Patients Who Are Refractory To Or Intolerant Of Other Therapies.	16-03-2013
22	Valdecoxib	16-11-01	2-Aug	For The Relief Of Signs And Symptoms Of Osteoarthritis And Adult Rheumatoid Arthritis And For The Treatment Of Primary Dysmenorrhea.	13-02-2015
23	Ziprasidone Hydrochloride	5/2/2001	2-Mar	For The Treatment Of Schizophrenia	2/3/2007
24	Tenofovir Disproxil Fumarate	26-10-01	5-Aug	To Be Used In Combination With Other Antiretroviral Agents For The Treatment Of Hiv-1 Infection In Adults.	25-07-2007
	2002				
1	Adefovir Dipivoxil	20-09-02	3-04	For The Treatment Of Chronic Hepatitis B In Adults With Evidence Of Active Viral Replication And Either Evidence Of Persistent Elevations In Serum Alanine Aminotransferase (ALT)/Aspartate Aminotransferase (AST) Or Histologically Active Disease.	21-04-2006
2	Aripiprazole	15-11-02	06-03	For The Treatment Of Schizophrenia.	20-10-2004
3	Eplerenone	27-09-02	06-05	For The Treatment Of Hypertension, Alone Or In Combination With Other Agents.	9-4-2006

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
4	Ezetimibe	25-10-02	5-2005	For (1) Primary Hypercholesterolemia - As Adjunctive Therapy To Diet For Reduction Of Elevated Total-C, Ldl-C And Apo B In Patients With Primary (Heterozygous Familial And Non-Familial) Hypercholestrolemia Either Alone Or With An Hmg-Co A Reductase Inhibitor. (2) Homozygous Familial Hypercholesterolemai - In Combination With Either Atorvastatin Or Simvastatin, As An Adjunct To Other Lipid-Lowering Treatments (E.G., Ldl Apheresis) Or, If Such Treatments Are Unavailable, In Combination With Either Atorvastatin Or Simvastatin Alone. (3) Homozygous Familial Sitosterolemia - As Adjunctive Therapy To Diet For The Reduction Of Elevated Sitosterol And Campesterol Levels.	21-09-2013
5	Nitazoxanide	22-11-02	03-04	For The Treatment Of Diarrhea Caused By Cryptosporidium Parvum And Giardia Lamblia.	7-22012
6	Olmesartan Medoxomil	25-04-02	07-05	For The Treatment Of Hypertension.	25-04-2016
7	Tegaserod Maleate	24-07-02	11-2002	For The Short-Term Treatment Of Women With Irritable Bowel Syndrome (Ibs) Whose Primary Bowel Symptom Is Constipation.	26-04-2013
8	Voriconazole	24-05-02	9-2004	For The Treatment Of Invasive Aspergillosis And Serious Fungal Infections Caused By Scedosporium Apiospermum And Fusarium Spp., Including Fusarium Solani, In Patients Intolerant Of, Or Refractory To, Other Therapy.	11-8-2009
9	Atomoxetine Hydrochloride	26-11-02	11-04	For The Treatment Of Attention-Deficit Hyperactivity Disorder (Adhd) For Children And Adolescents Ages 6-18 And Adults.	Not Avail.
10	Nitisinone	18-01-02		For The Use For Adjunctive Therapy To Dietary Restriction Of Tyrosine And Phenylalanine In The Treatment Of Hereditary Tyrosinemia Type 1.	09-04-2008
11	Fulvestrant	25-04-02	08-06	For The Treatment Of Hormone Receptor Positive Metastatic Breast Cancer In Postmenopausal Women With Disease Progression Following Antiestrogen Therapy.	01-10-2005
12	Treprostinil Sodium	21-05-02		For The Treatment Of Pulmonary Arterial Hypertension (Pah).	06-10-2009
13	Perflexane Phospholipids Microspheres	31-05-02		For The Use In Patients With Suboptimal Echocardiograms To Opacify The Left Ventricular Chamber And To Improve The Delineation Of The Left Ventricular Endocardial Border.	Not Avail.
14	Sodium Oxybate	17-07-02		For The Treatment Of Cataplexy Associated With Narcolepsy.	22-12-2019

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
15	Oxaliplatin	09-08-02	10-98	Indicated In Combination With Infusional 5-Fu/ Lv For The Treatment Of Patients With Metastatic Carcinoma Of The Colon Or Rectum Whose Disease Has Recurred Or Progressed During Or Within 6 Months Of Completion Of First Line Therapy With The Combination Of Bolus 5-Fu/Lv And Irinotecan.	07-04-2013
16	Icodextrin	12-12-02	06-02	For A Single Daily Exchange For The Long (8-16-Hour) Dwell During Continuous Ambulatory Peritoneal Dialysis (Capd) Or Automated Peritoneal Dialysis (Apd) For The Management Of Chronic Renal Failure.	02-08-2005
17	Eletriptan Hydrobromide	26-12-02		Indicated For The Acute Treatment Of Migrane.	13-08-2013
	2003				
1	Bortezomib	13-05-03	05-05	For The Treatment Of Multiple Myeloma Patients Who Have Received At Least Two Prior Therapies And Have Demonstrated Disease Progression On The Last Therapy.	
2	Rosuvastatin Calcium	12-8-03	9-03	Indicated As (1) An Adjunct To Diet To Reduce Elevated Total-C In Patients With Primary Hypercholesterolemia (Heterozygous Familial And Nonfamilial) And Mixed Dyslipidemia (Frederickson Type Iia And Iib). (2) As An Adjunct To Diet For The Treatment Of Patients With Elevated Serum Tg Levels (Frederickson Type Iv). (3) To Reduce Ldl-C, Total-C, And Apob In Patients With Homozygous Familial Hypercholesterolemia As An Adjunct To Other Lipid-Lowering Treatments (E.G., Ldl Apheresis) Or If Such Treatments Are Unavailable).	
3	Memantine Hydrochloride	16-10-03	07-04	Indicated As (1) An Adjunct To Diet To Reduce Elevated Total-C In Patients With Primary Hypercholesterolemia (Heterozygous Familial And Nonfamilial) And Mixed Dyslipidemia (Frederickson Type Iia And Iib). (2) As An Adjunct To Diet For The Treatment Of Patients With Elevated Serum Tg Levels (Frederickson Type Iv). (3) To Reduce Ldl-C, Total-C, And Apob In Patients With Homozygous Familial Hypercholesterolemia As An Adjunct To Other Lipid-Lowering Treatments (E.G., Ldl Apheresis) Or If Such Treatments Are Unavailable)	
4	Tadalafil	21-11-03	9-03	For The Treatment Of Erectile Dysfunction.	
5	Prussian Blue	02-10-03		For The Treatment Of Patients With Known Or Suspected Internal Contamination With Radioactive Cesium And/Or Radioactive Or Non-Radioactive Thallium To Increase Their Rates Of Elimination.	

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
6	Enfuvirtide	13-03-03		For The Use In Combination With Other Antiretroviral Agents, For The Treatment Of Hiv-1 Infection In Treatment Experienced Patients With Evidence Of Hiv-1 Replication Despite Ongoing Antiretroviral Therapy.	
7	Pegvisomant	25-03-03		For The Treatment Of Acromegaly In Patients Who Have An Inadequate Response To Surgery And/Or Radiation Therapy And/Or Other Medical Therapies, Or For Whom These Therapies Are Not Appropriate.	
8	Aprepitant	26-03-03	08-06	To Be Used In Combination With Other Antiemetic Agents, For The Prevention Of Acute And Delayed Nausea And Vomiting Associated With Initial And Repeat Courses Of Highly Emetogenic Cancer Chemotherapy, Including High-Dose Cisplatin.	
9	Gemifloxacin Mesylate	04-04-03	08-06	Factive Is Indicated For The Treatment Of Community-Acquired Pneumonia And Acute Bacterial Exacerbation Of Chronic Bronchitis.	
10	Emtricitabine	02-07-03	06-05	For The Treatment Of Hiv Infection In Adults.	
11	Geftinib	05-05-03	02-04	For The Treatment Of Patients With Locally Advanced Or Metastatic Non-Small Cell Lung Cancer After Failure Of Both Platinum-Based And Docetaxel Chemotherapies.	
12	Ibandronate Sodium	13-05-03		For The Treatment And Prevention Of Postmenopausal Osteoporosis.	
13	Atazanavir	20-06-03	12-06	Indicated In Combination With Other Antiretroviral Agents For The Treatment Of Hiv-1 Infection In Adults.	
14	Palonosetron Hydrochloride	25-07-03		Indicated For 1) The Prevention Of Acute Nausea And Vomiting Associated With Initial And Repeat Courses Of Moderately And Highly Emetogenic Cancer Chemotherapy, And 2) The Prevention Of Delayed Nausea And Vomiting Associated With Initial And Repeat Courses Of Moderately Emetogenic Cancer Chemotherapy.	
15	Miglustat	31-07-03		For The Treatment Of Mild To Moderate Type I Gaucher Disease In Adults For Whom Enzyme Replacement Therapy Is Not A Therapeutic Option (E.G., Due To Constraints Such As Allergy, Hypersensitivity, Or Poor Venous Access).	
16	Vardenafil Hydrochloride	19-08-03		For The Treatment Of Erectile Dysfunction In Men.	

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
17	Sertaconazole Nitrate	10-12-03	01-08	Indicated For The Topical Treatment Of Interdigital Tenea Pedis In Immunocompetent Patients 12 Years Of Age And Older, Caused By Trichophyton Rubrum, Trichophyton Mentagrophytes, And Epidermophyton Floccosum.	
18	Epinastine Hydrochloride	16-10-03	09-06	For The Prevention Of Itching Associated With Allergic Conjunctivitis.	
19	Abarelix	25-11-03		Indicated For The Palliative Treatment Of Men With Advanced Symptomatic Prostate Cancer, In Whom Lhrh Agonist Therapy Is Not Appropriate And Who Refuse Surgical Castration, And Have One Or More Of The Following: (1) Risk Of Neurological Compromise Due To Metastases, (2) Ureteral Or Bladder Outlet Obstruction Due To Local Encroachment Or Metastatic Disease, Or (3) Severe Bone Pain From Skeletal Metastases Persisting On Narcotic Analgesia.	
20	Alfuzosin Hydrochloride	12-06-03	05-04	Indicated For The Treatment Of The Signs And Symptoms Of Benign Prostatic Hyperplasia (Bph).	
21	Daptomycin	12-09-03	01-08	For The Treatment Of Complicated Skin And Skin Structure Infections Caused By Susceptible Strains Of The Following Gram-Positive Microorganisms: Staphylococcus Aureus (Including Methicillin-Resistant Strains), Streptococcus Pyogenes, Streptococcus Agalactiae, Streptococcus Dysgalactiae Subsp. Equisililis And Enterococcus Faecalis (Vancomycin-Susceptible Strains Only).	
2004					
1	Acamprosate Calcium	29-07-04	10-02	For The Maintenance Of Abstinence From Alcohol In Patients With Alcohol Dependence Who Are Abstinent At Treatment Initiation.	Not Avail.
2	Duloxetine Hydrochloride	3-8-04	11-04	For The Treatment Of Major Depressive Disorder (Mdd).	11-6-2008
3	Erlotinib Hydrochloride	18-11-04	07-05	For The Treatment Of Locally Advanced Or Metastatic Non Small-Cell Lung Cancer (Nsclc) After Failure Of At Least One Prior Chemotherapy Regimen.	30-03-2015
4	Gadobenate Dimeglumine	23-11-04	03-03	Indicated For Intravenous Use In Magnetic Resonance Imaging (Mri) Of The Cns In Adults To Visualize Lesions With Abnormal Blood Brain Barrier Or Abnormal Vascularity Of The Brain, Spine, And Associated Tissues.	Not Avail.

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
5	Tiotropium Bromide	30-01-04	04-03	Indicated For The Long-Term, Once-Daily, Maintenance Treatment Of Bronchospasm Associated With Chronic Obstructive Pulmonary Disease (Copd), Including Chronic Bronchitis And Emphysema.	11-3-2014
6	Pregabalin	30-12-04	11-05	Indicated For The Management Of Neuropathic Pain Associated With Diabetic Peripheral Neuropathy.	8-10-2013
7	Lanthanum Carbonate Hydrate	26-10-04		Indicated As An Adjuvant To Increase The Absorption And Dispersion Of Other Injected Drugs; For Hypodermoclysis; And As An Adjunct In Subcutaneous Urography For Improving Resorption Of Radiopaque Agents.	Not Avail.
8	Omega-3-Acid Ethyl Esters	10-11-04		Indicated As An Adjunct To Diet To Reduce Triglyceride (Tg) Levels In Adult Patients With TG Levels > 500 Mg/Dl.	03-10-2006
9	Ovine Hyaluronidase	17-05-04		Subcutaneous Urography For Improving Resorption Of Radiopaque Agents	Not Avail.
10	Pegaptanib Sodium	17-12-04	02-06	Indicated For The Treatment Of Neovascular (Wet) Age-Related Macular Degeneration.	17-10-2012
11	Telithromycin	01-04-04		Indicated For The Treatment Of Infections Caused By Susceptible Strains Of The Designated Microorganisms In The Conditions Listed Below, For Patients 18 Years Old And Above. (1) Acute Bacterial Exacerbation Of Chronic Bronchitis Due To Streptococcus Pneumoniae, Haemophilus Influenzae, Or Moraxella Catarrhalis. (2) Acute Bacterial Sinusitis Due To Streptococcus Pneumoniae, Haemophilus Influenzae, Moraxella Catarrhalis Or Staphylococcus Aureus. (3) Community-Acquired Pneumonia (Of Mild To Moderate Severity) Due To Streptococcus Pneumoniae (Including Multi-Drug Resistant Streptococcus Pneumoniae [Mdrsp] Strains), Haemophilus Influenzae, Moraxella Catarrhalis, Chlamydophila Pneumoniae, Or Mycoplasma Pneumoniae.	21-04-2015
12	Pemetrexed Disodium	04-02-04		Indicated In The Treatment Of Patients With Malignant Pleural Mesothelioma Whose Disease Is Either Unresectable Or Who Are Otherwise Not Candidates For Curative Surgery.	29-03-2011
13	Insulin Glulisine	16-04-04		For The Treatment Of Adult Patients With Diabetes Mellitus For The Control Of Hyperglycemia.	16-04-2009

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
14	Apomorphine Hydrochloride	20-04-04		Indicated For The Acute, Intermittent Treatment Of Hypomobility, "Off" Episodes ("End-Of-Dose Wearing Off" And Unpredictable "On/Off" Episodes) Associated With Advanced Parkinson's Disease.	Not Avail.
15	Tinidazole	17-05-04		Indicated For The Treatment Of Trichomoniasis	Not Avail.
16	Azacitidine	19-05-04		For The Treatment Of Patients With The Following Myelodysplastic Syndrome Subtypes: Refractory Anemia Or Refractory Anemia With Ringed Sideroblasts (If Accompanied By Neutropenia Or Thrombocytopenia And Requiring Transfusions), Refractory Anemia With Excess Blasts, Refractory Anemia With Excess Blasts In Transformation, And Chronic Myelomonocytic Leukemia.	Not Avail.
17	Rifaximin	25-05-04	08-06	For The Treatment Of Patients (> 12 Years Of Age) With Travelers' Diarrhea Caused By Noninvasive Strains Of Escherichia Coli. Xifaxan Should Not Be Used In Patients With Diarrhea Complicated By Fever Or Blood In The Stool Or Diarrhea Due To Pathogens Other Than Escherichia Coli.	Not Avail.
18	Trospium Chloride	28-05-04	05-09	For The Treatment Of Overactive Bladder Associated With Symptoms Of Urge Urinary Incontinence, Urgency, And Urinary Frequency.	Not Avail.
19	Cinacalcet Hydrochloride	08-03-04		For The Treatment Of Secondary Hyperparathyroidism In Patients With Chronic Kidney Disease On Dialysis, And The Treatment Of Hypercalcemia In Patients With Parathyroid Carcinoma.	23-10-2015
20	Human Secretin	09-04-04		Indicated For (1) Stimulation Of Pancreatic Secretions, Including Bicarbonate, To Aid In The Diagnosis Of Pancreatic Exocrine Dysfunction, (2) Stimulation Of Gastrin Secretion To Aid In The Diagnosis Of Gastrinoma, And (3) Stimulation Of Pancreatic Secretions To Facilitate The Identification Of The Ampulla Of Vater And Accessory Papilla During Endoscopic Retrograde Cholangiopancreatography (Ercp).	Not Avail.
21	L-Glutamine	10-06-04		For The Treatment Of Short Bowel Syndrome In Patients Receiving Specialized Nutritional Support When Used In Conjunction With A Recombinant Human Growth That Is Approved For This Indication.	Not Avail.

Table F: Details of 302 NMEs approved by the USFDA between 1995 and 2004 (contd.)

	Name of The Molecule	Year of USFDA Approval (US)	Year of DCGI Approval (India)	Therapeutic Use	Patent Expiry Date
22	Hyaluronidase	26-10-04		Indicated As An Adjuvant To Increase The Absorption And Dispersion Of Other Injected Drugs; For Hypodermoclysis; And As As Adjunct In Subcutaneous Urography For Improving Resorption Of Radiopaque Agents.	26-10-2009
23	Pentetate Zinc Trisodium	11-08-04		For The Treatment Of Internal Contamination With Plutonium, Americium Or Curium To Increase The Rates Of Elimination.	
24	Pentetate Calcium Trisodium	11-08-04		For The Treatment Of Internal Contamination With Plutonium, Americium Or Curium To Increase The Rates Of Elimination.	Not Avail.
25	Solifenacin Succinate	19-11-04	07-06	For The Treatment Of Overactive Bladder With Symptoms Of Urge Urinary Incontinence, Urgency, And Urinary Frequency.	27-12-2015
26	Eszopicline	15-12-04		For The Treatment Of Insomnia.	16-01-2012
27	Trypan Blue	16-12-04		Indicated As An Aid In Ophthalmic Surgery By Staining The Anterior Capsule Of The Lens.	Not Avail.
28	Darifenacin Hydrobromide	22-12-04		For The Treatment Of Overactive Bladder.	13-03-2010
29	Clofarabine	28-12-04		For The Treatment Of Pediatric Patients 1 To 21 Years Old With Relapsed Or Refractory Acute Lymphoblastic Leukemia After At Least Two Prior Regimens.	23-05-2009
30	Ziconotide	28-12-04		Indicated For The Management Of Severe Chronic Pain In Patients For Whom Intrathecal (It) Therapy Is Warranted And Who Are Intolerant Of Or Refractory To Other Treatment, Such As Systemic Analgesics, Adjunctive Therapies, Or It Morphine.	30-12-2011
31	Iloprost	29-12-04		For The Treatment Of Pulmonary Arterial Hypertension.	Not Avail.

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