Implications of New Patent Regime on Indian Pharmaceutical Industry: Challenges and Opportunities

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The growth of Indian pharmaceutical industry has been characterized by extensive governmental control and absence of strong patent protection. This paper gives an overview of pharmaceutical industry in India and the likely impact of product patent regime on it. The analysis is based on secondary data published elsewhere. It also reviews the existing patent and drug control laws in India and how they have affected the growth and structure of pharmaceutical industry in the country. Also discussed are strategies to meet the new challenges and the opportunities that Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement presents to pharmaceutical industry in India.

Keywords: Pharmaceutical industry, Indian Patent Act, new patent regime, product patent, TRIPS Agreement

After almost thirty-five years of the process patent system, which encouraged R&D efforts in reformulation and process engineering/re-engineering for generics, India has seen the dawn of Trade-Related Aspects of Intellectual Property Rights (TRIPS) enabled product patent regime on 1 January 2005. Irrespective of the argument for and against strong patent regime, the time has come when Indian pharmaceutical industry (IPI) has been forced to rethink their approach and find alternatives to their current reverse engineering business models. In the product patent era, R&D initiatives, cost control and marketing efficiencies will assume more importance along with partnerships and alliances in the areas of research, marketing, licensing and production. Present TRIPS framework aims at universalising the IPR laws in all areas of technology among the member countries of the WTO. Indian patent law of 1970 has been suitably amended to make Indian IPR laws in the field of pharmaceuticals, chemicals and food at par with TRIPS.

The primary mechanism that justifies investment in research and development (R&D) in knowledge-based industries is the protection that patents and other intellectual property rights (IPR) provide to generate intellectual property (IP). Thus, sustained competitive advantage will depend on the ability of these organizations to create, manage and market ‘value-added’ intellectual assets to derive the advantage of being ‘first in the market’. The absence of strong patent protection for pharmaceuticals in the country has discouraged the industry from conducting original drug discovery research. Developing countries like, India, China, Brazil, etc., have traditionally provided weak patent and other IPR protection. The staple argument given for weak IPR protection was that enforcing this would impact the employment for millions of locals, cause severe price rise and could have adverse socio-economic and welfare implications especially with stronger pharmaceutical patents. This has been a deterrent for multinationals to market their branded products in such places, as price leverage is practically non-existent due to local low cost re-engineered products.

Indian Pharmaceutical Industry—An Insight

The Indian pharmaceutical industry is a successful, high-technology-based industry that has witnessed consistent growth over the past three decades inspite of it operating under severe price competition and government price control. The retail Indian pharmaceutical market is valued at Rs 20, 054 crore for the 12 months ending June 2004. During the same period, it grew by 8.1% in terms of value and 8.5% in terms of volume. The compounded annual growth rate (CAGR) of IPI for the period 1999 to 2003 is approximately 11%. In the global context, IPI stands fourth in terms of sales volume and thirteenth in terms of value.
The Indian pharma sector is highly fragmented with more than 24,000 registered units. It has expanded drastically in the last two decades. Formulations account for 81.5% of the market and bulk drugs account for the remaining 18.5%. The leading 250 pharmaceutical companies control 70% of the market, with market leaders holding nearly 7% of the market share. Requirement for 85% of bulk drugs and almost all formulations is met within India itself. There are around 465 main bulk drugs used in India and out of these, around 425 bulk drugs are totally manufactured in India and there is no import of these. Of the remaining 40 bulk drugs, 30 are totally imported, whereas around 10 are partially imported. Out of the 425 bulk drugs manufactured in India, around 60 are also partially exported\(^4\)\(^5\).

Since independence, efforts of IPI have mostly been directed towards the development of alternative cost effective manufacturing processes for molecules already invented and patented in other countries. Very little or no effort was invested in R&D towards development of new molecules/products. Over the last few decades, this contracted patent regime in India, recognizing only process patent, has had a negative impact on the development of professional expertise in new chemical entity development as potential therapeutic agent. This in turn also gave lesser exposure to conducting advanced clinical trials and drafting patents and patent related litigation in the areas of new chemical entities, genetic engineering, combinatorial chemistry, natural products, agro-chemicals and agricultural products.

The confidence and expertise in reverse engineering became counter productive to an extent that it set in the belief that developing new drugs for domestic and global market apparently was beyond our reach. This also created a dominant opinion against product patent regime taking root in the drug policy formulation apparatus at government level and in the boardrooms of major pharmaceutical companies in India. However, success of Dr Reddy’s lab, Ranbaxy, Torrent, Lupin, Wockhardt and Glenmark in vying for global space for the locally developed technologies and new molecules, has started to change the mindset. Simultaneously, new partnerships between academic and commercial organizations within and outside the country have started emerging. The expenditure on R&D by Indian companies has been abysmally low with a few exceptions. In the year 2000, as against world average of 12-15% of sales for expenditure on R&D, Indian companies hardly spent on an average about 1-2%. The spending is around 3.4 % in case of top Indian pharmaceutical companies\(^6\).

In the years 2003-2004, around 3900 new products have been launched by Indian companies, worth Rs 1578.5 crore which constitute nearly 8% of the market\(^3\). While older brands have resorted to price increase for growth, the new products are experiencing price decline. As a result of this, Indian companies are no longer dependent on price increases as drivers for garnering growth, but the Multi National Companies (MNC’s) are. Some of the other strengths of the IPI include:

(a) Export orientation
(b) Self-reliance in production (70% of bulk drugs and almost the entire requirement of formulations within the country); World class manufacturing facility in India and in European and American countries.
(c) Low cost of production and products
(d) Low R&D costs and abundance of innovative science and technology manpower
(e) Cost effective source for procuring generic drugs, especially the drugs going off patent
(f) World hub for clinical trials in view of the diversity in population. Significant increase in R&D investment by almost every company of reasonable size in the last 5 years. Inspite of the price competition, governmental control, process patent regime discouraging original research and low R&D investment, it is globally accepted that IPI is highly profitable and competitive with large presence in export market.

**Effect of Earlier Patent and Drug Control Laws on IPI**

In the post-independence era, up to the year 1970, India employed western-style patent legislation, and recognized product patents in addition to process patents on drugs. As a result, foreign companies prospered well in the country with over 90% of the IPI’s market share and 80% of ownership dominated by them\(^7\)\(^8\). This made the country increasingly dependent on imports for bulk drugs and formulations and thus, drug prices were amongst the highest in the world. In 1970, the Indian government took two important steps to break the multinational domination and foster a self-reliant indigenous industry. It introduced Drug Price Control Order (DPCO) to
protect consumers against high prices and Indian Patent Act, 1970 to recognize process patent (patenting the process used to make a particular drug formulation), but not product patent (patenting the product itself). These reforms made new drugs available cheaply and promoted import substitution by encouraging local firms to make copies of the drugs by developing their own processes, followed by bulk drug production. Some of the salient features of these acts are:

**Indian Patent Act**

The 1970 Patent Act, which represented a change in favour of local producers and a paradigm shift to process patent regime, consisted of the following key clauses:

- No pharmaceutical product patents were admissible, only process patents were acknowledged;
- The term for a process patent was fourteen years;
- Patents must be worked within three years of filing;
- Three years from sealing of the patent, it shall be deemed to be endorsed with the words ‘Licences of Right’ on the ground that the reasonable requirements of the public with respect to the patented invention have not been satisfied or that the patented invention is not available to the public at a reasonable price;
- The Indian government may use or authorize others to use the patented invention. At any time after the expiration of three years from the date of the sealing of a patent, any person interested may make an application to the Controller alleging that the reasonable requirements of the public with respect to the patented invention have not been satisfied or that the patented invention is not available to the public at a reasonable price;

**Drug Price Control Order (DPCO)**

In 1970, the government introduced the DPCO to guarantee its citizen access to ‘essential drugs’, at a reasonable cost with adequate rate of return to companies without compromising quality. In response to the DPCO, many firms discontinued the production of the controlled item and concentrated on production of nonessential drugs and other combinations to escape the control. As a result, essential drugs were more difficult to access than before the introduction of DPCO. Another derivative effect of the DPCO was that it exempted smaller firms from price controls, thereby encouraging them to participate in the pharmaceutical industry. This caused small companies to be represented more prominently than might otherwise be expected. To address the aforementioned problems while still adhering to its objectives, the government issued a revised DPCO in 1995. The DPCO of 1995 declassified 70 out of 146 drugs, dropped some clauses that favoured small companies, and exempted newly (locally) produced products from price controls.

**National Pharmaceutical Pricing Authority (NPPA)**

The NPPA was established in 1997, to improve the speed and transparency of the process of fixing the prices of bulk drugs and formulations. It is expected to reduce the time lag between price revisions, thereby providing stable margins for formulations, and revise the list of bulk drugs under price control within reasonable time.

**TRIPS and Amendments to Indian Patent Act**

On 15 April 1994, India signed the general agreement on tariffs and trade, joining the World Trade Organization and becoming a party to the agreement on TRIPS. India was therefore required to bring its patent laws into alignment with the standards of TRIPS. Being a developing country with no product patent protection, India availed the 10 years (5 + 5) transition period for full TRIPS compliance. Accordingly, First Amendment to Patent Act of 1970, as notification on 1 January 1995 and later through the 1999 Amendment effective from 1 January 1995, was passed. The steps taken included recognition of product patent with 20 years patent life span,
exclusive marketing rights (EMR) for new products, a mailbox provision for filing product patent applications during the transitional period from 1995–December 2004, shifting of the burden of proof to the alleged infringer and extension of protection to include imported materials and products.

EMR provided the applicant with pipeline protection for a period of five years for drugs and medicines after grant of product patent in convention countries, provided certain other conditions are fulfilled. Only the inventions that do not fall within the purview of Section 3 and 4 of Indian Patent Act, 1970 (which define categories of inventions exempted from patent protection) and that satisfy the criteria of patentability quality are considered for EMR. This enabled applicants to file for EMR as per amended Sec 5(2) and Section 24 A to F. While a few EMRs were applied for, most of them did not qualify. The first EMR to a MNC in India was granted to Novartis for Imatinib mesylate (Trade name- Glivec) and the first Indian company to obtain an EMR was United Phosphorus, Mumbai, for the combination of Carbedazim & Macozeb (Trade name- SAAF). Almost all the EMR applications have been pending since then.

Through the Third Amendment of December 2004, Indian Government has abolished the EMR provision and has included new definition for drugs and provision for patenting of new use and embedded use. It has also revamped the fees structure, penalty provision, qualification of patent agent, and filing and publication procedure. But it has been silent on evergreening strategies and online filing procedures. It also allows for pre-grant opposition in addition to post-grant opposition (within one year of grant of patent). It stresses that provisional specifications should be updated with complete specification within 12 months with no provision for further grace period.

While making the necessary Amendments to the Indian Patent Act (passed by the parliament on 22 Mar 2005), the Indian Government has strived to ensure that not only is India’s commitment to the WTO community for providing strong intellectual property protection is taken care of but also the protection of the domestic industry, the consumers and the economy at large is ensured. The extent to which it is possible to legislate a Indian Patent Act balancing these two, at times representing divergent interests, in an equitable manner has been a contentious issue between political parties in and out of the parliament.

The effect of various patent laws and governmental restrictions on the growth pattern of IPI is summarized here. For comparison purpose, the indicators considered in Table 1 include: cost of the drugs, availability, imports, exports and R&D activities. As evident during post independence and pre 1970, the cost of the drug in India was very high with low availability and high import dependency. Export initiative was very less and R&D activities were practically non-existent. During this period, 80% of the ownership and 90% of the market share was with MNC’s. After the enactment of Indian Patent Act, 1970, which recognized only process patent, the cost of the drug started decreasing and the availability was on the rise. Dependency on imports decreased and Indian pharmaceutical industry became export oriented. India became self sufficient with respect to its needs of essential drugs. Exports started contributing immensely to the revenue of large number of big and medium scale pharmaceutical companies. During this phase, R&D efforts were mostly directed towards formulation development and process optimization.

In the period between 1995-2005 and there after, status quo has been seen with respect to cost of the drug and it is expected to continue that way till 2007. But after 2007 and particularly after 2010, as MNC’s and research based Indian companies start launching their patented molecules, the cost of the drug is going to increase. The availability of drugs in antibiotic segment and other agents used for tropical infections may not be affected but the availability of life-style

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<tr>
<td>Cost of drug</td>
<td>High</td>
<td>Low</td>
<td>Status quo (could increase in future)</td>
</tr>
<tr>
<td>Availability</td>
<td>Low</td>
<td>High</td>
<td>Therapeutic segment dependent</td>
</tr>
<tr>
<td>Imports</td>
<td>High</td>
<td>Low</td>
<td>Constant (may rise in future)</td>
</tr>
<tr>
<td>Exports</td>
<td>Low</td>
<td>High</td>
<td>High (relatively constant)</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>Absent</td>
<td>Negligible to low</td>
<td>Moderate increase (overall still low)</td>
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drugs like the one used to grow hairs, relieve impotence, fight cholesterol, ulcers, depression, anxiety, allergies, arthritis, diabetes and high blood pressure will be affected as most of the MNC’s are engaged in new drug development in this area only. Imports are expected to remain constant or at the same level as they are now but novel drugs in phase III or IV clinical trials, that enjoy patent protection and have been developed by MNC’s to be used for the treatment of cancer or AIDS, may increase. What will be the volume of such imports are not clear since it will depend on the Government health policy and its ability to implement compulsory licensing clause under TRIPS provision. Exports opportunities are bound to increase in the coming years due to contract/ custom manufacturing, in-licensing and abbreviated new drug application (ANDA) route for generics. Post 1995, Indian pharma industry has seen lots of voluntary initiatives in increased R&D spending and activities, which are bound to further increase in the coming years.

Why Strong Product Patent Regime for Pharmaceuticals?

Price of the patented product and their accessibility in India has been the focus of concern ever since the question of adopting product patent has come to front. The fundamental reason why pharmaceutical progress is dependent on IPR protection is the staggering cost of new chemical entity (NCE) development as a potential drug molecule (Table 2) and high attrition rate in the development cycle. Recent studies indicate that 1 out of 5000 molecules synthesized during applied research, eventually reaches the market. Other estimates indicate that of the 100 drugs that enter the clinical testing Phase I, about 70 complete Phase I, 33 complete Phase II, and 25-30 clear Phase III. Only two-thirds of the drugs that enter phase III is ultimately marketed. Without strong patent protection, pharmaceutical companies cannot attract the investment needed to conduct this expensive, high-risk research. The overall cost is further inflated if the opportunity cost of such high investment for such a long time with no guaranteed return is taken into account.

Without strong patent protection, fewer drugs will be developed and the flow of medicines to the public would be greatly slowed to the detriment of patients, public health and economic development throughout the world. Profits are diminishing due to imitation in drugs and pharmaceuticals. In 1998, the ‘Big Pharma’ (top 20 largest pharmaceutical companies across the globe based on market capitalization) company’s price per earning ratio was twice (2.18 times) that of the global stock market and since then the gap has been gradually on the decline. By 2003, this gap was narrowed down to 1.28 times. During this period, sales performances of new molecules also fluctuated with a real decline in 1999-2000 and thereafter the sales performance showing a climb (Figure 1a). Since the duration of exclusivity is gradually decreasing due to introduction of newer congeners of the molecule (Figure 1b), the companies indulge in litigation and compromising marketing strategies to prolong their exclusive rights.

Inspite of the substantial increase in R&D budgets in the last several years, the number of new compounds introduced in the market fell sharply in the late 1990s (Figure 2a) and has been around the historic average ever since. Also, there is a growing realization that the companies cannot no longer rely on blockbusters alone (Figure 2b). Almost 90% of the new molecules introduced earn less than 180 million dollars (USD) in annual sales and out of that close to 35% molecules are never profitable. Around 5% of the introduced molecules earn 180 to 460 million USD. Only a dismal 1-2% of the molecules are capable of earning more than 1 billion USD and attain the blockbuster status.

As a result, most of the company’s are shelving projects where the return on investment is expected to be low (again contributing to high attrition rate as discussed earlier). This trend has lead to exercising options of contract research and manufacturing services in India, China or other developing countries, and also out-licensing of potential molecules developed by smaller companies for advanced studies. This strategy can aid pharmaceutical majors to have broader pipeline product development portfolio without resorting to mergers and acquisitions. Overall cost of product development and marketing is further going to increase considering the fact the

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<tr>
<th>Year</th>
<th>Development Time (Years)</th>
<th>Development Cost* (US$ million)</th>
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<tbody>
<tr>
<td>1970</td>
<td>15</td>
<td>54</td>
</tr>
<tr>
<td>1990</td>
<td>12</td>
<td>231</td>
</tr>
<tr>
<td>2000</td>
<td>10</td>
<td>608</td>
</tr>
<tr>
<td>If started today</td>
<td>8-10</td>
<td>&gt; 800</td>
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*Plus the opportunity cost of risk prone investment.

Table 2—Comparison of development time and cost of new chemical entity
Food and Drug Administration (FDA) of various countries are going to demand more evidences with respect to clinical efficacy and short term and long term safety of the molecules. For example, US Senate has already instituted an independent Drug Safety Oversight Board within the FDA to ensure that safety and toxicity data are not overlooked before a new molecule is approved for use. Also, FDA of each member country, which are signatory to TRIPS, can demand pharmacogenetic evidence regarding efficacy and toxicity of new molecule before they are approved for launch in their respective country. This would entail doing additional clinical trails in the member country where approval is sought thereby increasing the development cost. Further, regulatory hurdles for the approval of manufacturing and marketing of drugs and formulations are also bound to increase in the years to come.

Some of the other arguments favouring strong product patent regime for pharmaceuticals include high cost of patent filing and protection and maintenance of patents in WTO member countries. Also, the patentee does not get any protection against inventing-around. Smaller companies in developing countries can exploit Bolar exemption to engage in R&D of a molecule for developing non-infringing ‘generic’ products during the lifetime of patents, which can threaten the market exclusivity of MNC’s as patent term expires. Patenting of therapeutic targets and tools as in case of biotechnology based
interventions like, rDNA technology, transgenic animals and gene therapy etc. can further lead to the gambit of ‘Patent pool’ where in collaborative research and alliances will be required thereby cutting into already diminishing profit margins. Another argument for strong patent regime has been that availability of newer life-saving drugs and devices can be ensured only through the implementation of the TRIPS Agreement. Study indicates significant increase in US exports to countries where intellectual property protection has been enforced. This leads to the growing realization that MNC’s are keen to increase their stakes only in those countries where they can market their products under exclusive or monopolistic rights, i.e. technology-holders can exclude competition from domestic producers in importing countries or other foreign firms. Also, an agreement within the GATT/WTO facilitates recourse to cross-retaliation for non-fulfillment of specific obligations. In simple words, countries failing to comply with TRIPS could be subjects to trade retaliation if the WTO dispute settlement mechanism identifies the existence of a case of non-compliance within TRIPS Agreement.

Why Product Patent for Drugs and Pharmaceuticals is Resented?

The basic argument against the framework of product patent by developing countries revolve around the facts that poor infrastructure, fragile economy, unemployment and poverty are holding back the development of economy in developing countries. Therefore, pharmaceuticals are health inputs and are not to be treated at par with consumables. Also, World Health Organization’s (WHO) essential drug policy clearly aims at providing a health for all and accessibility of primary health care and medicine to all the human beings of the world, irrespective of colour, creed and economic status. It is continuously impressing upon governments of developed and developing countries alike to bring down prices of the drugs such that, for want of money, no one gets deprived of medicines and suffers morbidity and mortality due to diseases. Considering the fact that the population of India at 1.05 billion is second only to China and of that just 35% of the population has access to essential drugs. Fifty percent of young children are systematically malnourished; India has the highest number of TB patients, HIV positive cases, Hepatitis B, malaria deaths and high rate of infant and maternal mortality. Some of the other arguments against strong product patent regime are:

Introduction of Product Patent in Developed Countries

Except for USA and UK (where product patent was introduced post world war II) and Italy, most of the developed countries have introduced product patent only when their own pharmaceutical industries have become strong to face international challenges. Even today, Switzerland, Japan and many other developed countries retain a number of products on the exempted list. Hence, developing countries should not be denied the opportunity to exercise this option at an appropriate time when they feel their economy (especially agriculture, drug and chemical industry), technical know-how and social condition of their people have reached a stage where it can absorb the effects of product patent regime.

Me-too Drugs

There is a growing consensus that the newer drugs have shown very little therapeutic advantage over their predecessors. The FDA estimates that over the past ten years (up to 2002), 69% of new drug approvals are considered not significantly better than existing therapies. Based upon these data, the share of investments in new products that have significant improvements over existing treatments is estimated to be 20% of the total investment in new products. Also, brand loyalties have made it possible to retain market value for existing molecules even after the expiry of the patent period.

Adoption of ‘Evergreening Strategies’

It is widely acclaimed that the new molecules, introduced in US market post 1980’s, have shorter duration of exclusivity (Figure 1) and lower revenues (Figure 2). To overcome the limitations of decreasing exclusivity, multinational companies adopt several tactics to maintain and extend the length of their patent benefits. Companies may introduce newer formulations, including fixed dose combinations, as part of product life cycle management initiatives. Such products are heavily marketed before the generic version is released into the market. Frivolous patent infringement suits are repeatedly filed which result in activation of an automatic 24-30 months freezing or delay in processing of generic product claim, especially in Canada and USA. For example, Bristol Meyers filed baseless patent infringement suits for several years to prevent competition to their anti-
cancer drugs, Taxol and Platinol and also to the anti-anxiety drug, BuSpar. By this procedure, they could protect more than $2 billion sales annually. Another most common strategy employed is that of ‘second-medical-use patent’ before expiry of first patent for the molecule. For example, original patent holder can apply for exclusive marketing rights for use of a drug in pediatric or geriatric patients. And as the exclusivity period is extended, they can make the earlier patients opt for another similar drug through aggressive marketing strategy. Collusion or understanding with generic manufacturers, to keep products off the market, is also a possibility that cannot be ruled out.

Bolar Provision

This is also referred to as R&D during the life of the patent. Bolar exemption allows R&D work to be carried out on patented products for the purpose of obtaining regulatory approval without any infringement liability. Many countries like, USA, Canada, Israel, Australia, Hungary and Croatia have special provisions for this.

Review of these practices followed by MNC’s and developed countries does prompt to hold an opinion that strong product patent framework may possibly unleash monopolistic tendencies amongst MNC’s, particularly in developing economies.

Implication of Adopting TRIPS Agreement on IPI

The pharmaceutical industry worldwide is the most profitable business sector with an average profit of 16.2% and is ahead of financial companies (11.6%) and beverages (10.0%). The profitability of the pharmaceutical industry is further demonstrated in Figure 3, where a comparison of median profits as percentage of revenue between fortune 500 drug companies and fortune 500 companies from all industries is presented. Inspite of the fact that Indian drug industry has been protected from foreign competition for more than three decades, it is one of the most profitable and competitive industry in the world.

Any discussion on impact of WTO/ TRIPS Agreement essentially involves two issues:

(i) What will be the impact of IPR legislations under TRIPS on public health?

(ii) What will be its impact on IPI and Indian economy?

The first issue concerns with the fear that patenting drugs would raise cost, put them out of the reach of the poor (in this case most of the developing and third world countries), and therefore damage public health. But the size of IPI and the growth rates prompt counter argument that product patenting will encourage introduction of new drugs, either by directly encouraging discovery in India or through newly invented imports that are protected, or through foreign investment in production and possibly in research.

IPI is highly fragmented with numerous small players (more than 90%). These small to medium sized companies, which have been making copies or generic formulations, fear that they will not have sufficient capital or technology to invent new drugs that can be patented. The access to local firms to protected technology will become more difficult because of the enforcement of the patent-holder’s bargaining position through investments in R&D. As a result, they feel that the market will be polarized in favour of foreign multinationals or Indian pharma majors. The larger firms, barring a few, on the other hand, are in full support of patents, which they hope will attract foreign investment, and thereby stimulate joint ventures and research. The idea is reinforced by the fact that several top Indian pharmaceutical

Table 3—Patent applications by Indian pharmaceutical or biotechnology companies with Indian patent office (as on Dec 31, 2004)

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<tr>
<th>Patent office</th>
<th>Application filed</th>
<th>Request filed for examination</th>
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<tbody>
<tr>
<td>Kolkata</td>
<td>1757</td>
<td>703</td>
</tr>
<tr>
<td>Delhi</td>
<td>1952</td>
<td>484</td>
</tr>
<tr>
<td>Mumbai</td>
<td>1545</td>
<td>267</td>
</tr>
<tr>
<td>Chennai</td>
<td>3672</td>
<td>1034</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>8926</strong></td>
<td><strong>2488</strong></td>
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companies have initiated serious R&D activities and have already filed or have been awarded patents (Table 3). Of the more than 8500 applications made in the period between Jan 1995 and Dec 2004, close to 7000 are believed to be in the area of pharmaceuticals and the remaining in the area of agro-chemicals. This transformed section of the Indian pharma industry is itself looking for patent protection, particularly, the biotech sector, in which India has bright prospects. But the proponents of anti-product patent regime do argue that the introduction of product patents may imply significant social costs due to the higher prices charged for medicaments. There is also the possibility that the most dynamic segments of the pharmaceutical market, where the prospects of growth are highest, will be excluded from domestic firms.

Major Opportunities for IPI within Present TRIPS Framework

Under the present TRIPS framework, irrespective of the fact that it is a MNC or an Indian company, the edge exists for only those companies which are innovative in their product profiles and who are continuously innovating and introducing new products. Various opportunities that IPI can exploit to get maximum mileage out of the present TRIPS framework is as given below:

1. The focus needs to be changed from export oriented activity to a global marketing. This involves establishing strategic marketing alliances in developed markets that will provide access to distribution networks and enable Indian pharmaceutical companies to operate as profit sharing partners. This also involves adopting vertical integration in a planned manner into the distribution and using chain, starting from developing markets and moving up to developed markets.

2. More emphasis should be given on rapid development of processes, which are innovative and non-infringing for products (especially for blockbuster products with difficult chemistry) going off patent internationally. It is worth mentioning that of the 250 essential drugs (as listed by WHO), only 10-15% are under patents. Around 28 major patented drugs constitute 80% of India’s drug production and of these, 22 will be off patent by 2005. And post 2005, it is expected that only 6-8 new drugs will be coming into the market every year.

3. Generic opportunities are going to increase by leaps and bound in the coming years and molecules worth US $44 billion will go off patent by 2009. The generics are capable of providing the same therapeutic drug level in the body as the reference drug. And to overcome the rising health care bills, the Government and Insurance companies in America and other west European countries are looking for safer low cost alternatives. A rough estimate indicates that Indian companies have already garnered 5% of the US $17 billion US generic market. Indian companies can reap rich dividends if they launch their products in segments like injectable, technology-intensive drugs and drugs in new dosage forms, where competition is low and a drastic price fall is less likely.

4. Cost effective R&D for the development of low cost bulk drugs, formulation and discovery research as well as clinical studies for the worldwide markets need to be carried out. Discovery research on a therapeutic segment for one molecule involves Rs 150-200 crore in India compared to US $650-800 million in developed countries, to be spent over a period of 8-10 years.

5. Exploiting TRIPS enabled compulsory licensing and parallel imports. Compulsory licensing refers to the right of the Central Government to force the holder of the patent, in the “public interest”, to compulsorily license out the product on agreed commercial terms. Parallel imports refer to the concept of shop around the world for cheaper imports.

6. Government can use affordability as the low threshold for drug pricing, based on annual per capita spending of its citizen, on health care. Annual per capita expenditure in India is merely US $3 when compared to US $191 and 227 in USA and Germany respectively. Even Pakistan has an annual per capita expenditure of US $7.10.17. In such case, Government reserves the right to render a patent void if the patent holder fails to make or import the product or even fails to sell it at prices affordable to average citizens.

7. Patenting of tropical bio-diversity should be emphasized so as to prevent patenting of Neem, Turmeric, Basmati and other components of indigenous system of medicine.
by outsiders. This will help ensure IPR protection to herbal and botanicals to MNC exploitation and also revenue earnings for Indian companies dealing in them.

Many Indian pharmaceutical companies have already geared up for facing the reality of product patent. Several new developments have already taken place in their R&D and strategic efforts. The strength of the industry is in developing cost-effective technologies in the shortest possible time for drug intermediates and bulk actives without compromising on quality. Accordingly, generic drug manufacturing is going to be the main growth driver for the future. The world market is expected to exceed $55 billion by 2005 end. India is set to capture a large portion of this market by leveraging its inherent strengths in technology, R&D facilities and trained human capital. Some of the measures that have been adopted by Indian companies include:

(a) Increased efficiency of R&D investment (details are presented under the section ‘Newer R&D Initiatives’) in the last 5 years in terms of number of patents filed or granted (Table 3)\(^20\).

For example, in the year 2004, the largest users of the Patent Cooperation Treaty (PCT) under WIPO from India have been Ranbaxy with 124 (as against 66 applications in 2003) applications. In 2004, other Indian organizations, which filed for patent protection, were Cipla, Jubilant Organosys, Vaman Technologies (R & D) and Matrix labs with 32, 16, 12 and 12 applications respectively. Hetero Drugs and Wockhardt Ltd had filed 10 applications each.

(b) Top Indian companies have devised unique R&D models to significantly decrease the cost and risks involved in the discovery of new drug or new chemical entity. As against the global average of $1.5-1.7 billion for developing a block buster molecule Indian companies will be able to do it at just $ 300-400 million\(^21\).

(c) Major companies have been establishing offshore production facilities. The Indian pharma industry has the highest number of plants approved by the US Food and Drug Administration (FDA) outside US.

(d) Collaborations/alliances in discovery research and product development tie-ups between Ranbaxy-Eli Lilly, Ranbaxy-Bayer, Dr Reddy’s-Novonordisk, Dr Reddy’s-Novartis, Torrent-Novartis and Cadila-Schering AG are only representative examples to make a case in this regard.

(e) ANDA leverage has been another area where Indian companies have shown remarkable progress. During the financial year 2004-05, as many as 11 Indian pharma companies have filed about 150 ANDA with the US FDA. It also has the largest number of drug master files filed which gives it access to the high growth generic bulk drugs market.

(f) Indian companies are acquiring generic share of global players or niche R&D of start-up companies in US and Europe\(^22\). This would give Indian companies a strong foothold to already established manufacturing, marketing and distribution network in US and Europe in addition to the proprietary technologies of the target company. Some of the high profile acquisitions by Indian pharma majors abroad are listed in table 4.

(g) India could well become the hub of clinical research for pharmaceutical companies across the globe in coming years. India offers a 40% cost advantage for doing bioequivalence study when compared to US\(^23\). But if the recent decision by WHO to remove anti-retro viral (anti-AIDS) drugs manufactured by Indian companies (Ranbaxy, Cipla and Hetero drugs) due to unsatisfactory bioequivalence data, is

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<table>
<thead>
<tr>
<th>Acquirer company</th>
<th>Target company</th>
<th>Deal ($ million)</th>
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<tbody>
<tr>
<td>Ranbaxy</td>
<td>Aventis (France)</td>
<td>70.00</td>
</tr>
<tr>
<td>Wockhardt</td>
<td>CP Pharmaceuticals (UK)</td>
<td>17.72</td>
</tr>
<tr>
<td>Wockhardt</td>
<td>Espharma GmbH(Germany)</td>
<td>11.00</td>
</tr>
<tr>
<td>Cadila Health Care</td>
<td>Alpharma SAS (France)</td>
<td>6.18</td>
</tr>
<tr>
<td>Jubilant Organosys</td>
<td>PSI Supply (Belgium)</td>
<td>16.52</td>
</tr>
<tr>
<td>Dabur India</td>
<td>Redrock (UK)</td>
<td>5.02</td>
</tr>
<tr>
<td>United Phosphorous</td>
<td>Aciflurin compound of BASF (Germany)</td>
<td>NA</td>
</tr>
</tbody>
</table>
any indication then Indian clinical research organizations should upgrade their good laboratory and good clinical practices including documentation and data storage. It is often accepted that Indian clinical research organizations that do bioequivalence studies for less, actually compromise on data storage and documentation\textsuperscript{23}. As a result, retrospective analysis of data and reconstruction of the study results are not possible.

(h) Contract manufacturing is another area where Indian companies are bound to excel. Setting up a plant is 40\% cheaper in India compared to developed countries and the cost of bulk drug production is 60-70\% less. The MNC’s prefer to outsource the bulk drugs as well as formulations, as it is the lowest value added activity in the pharmaceutical business, contributing not more than 6-8\% of selling price. The global players focus their own resources on research and outsource manufacturing of formulations. Outsourcing cuts down on their capital investments. According to International Medical Statistics (IMS), half of the big pharmaceutical companies worldwide have moved towards outsourcing through long-term strategic alliances. Only 28\% of pharmaceutical companies across the globe went in for in-house capacity expansion of bulk activities over the last two years. Some of the global pharmaceutical companies that outsource extensively are American Home Products, Pharmacia & Upjohn, Bristol Meyers Squibb and Glaxo-Wellcome. Indian companies like, Ranbaxy, Lupin labs and Nicholas Piramal are the first Indian companies to have obtained manufacturing contracts from MNC’s. The trend is expected to accelerate in the future.

**Newer R&D Initiatives**

Leading companies are investing on R&D to generate their own IPR and come up with new products. Companies realize that it will take a number of years to develop their own pharmaceutical products. They are eager to join hands with MNC’s for co-developing and/ or co-marketing of patented products of MNC’s. Developing their own IPR is a very important component of their long-term strategy today. Member companies of Indian Pharmaceutical Association, which also include all the research based Indian pharma majors, have increased their R&D spending by 4 times in the last four years. In the year 2000, all these companies put together spend Rs 200 crore on R&D, which steadily rose to Rs 800 crore by the year 2004 and is expected to rise steadily in the years to come\textsuperscript{6}. While, Dr Reddy’s Lab and Ranbaxy have been the prominent spenders for several years with an investment of 10\% and 8\% of their revenue in R&D for the year 2004\textsuperscript{6}. Torrent Pharmaceuticals has, in the year 2004, already earmarked Rs 100 crore for establishing new research facility along side their present R&D facility in Bhat, Gandhinagar. This actually is a three-time increase from their R&D investment of Rs 30 crore in 2003\textsuperscript{6}. Nicholas Primal has commissioned a new R&D centre with Rs 100 crore investments in Mumbai and Wockhardt has commissioned a biotechnology Park at Aurangabad with an investment of Rs 200 crore, catering to the development of biopharmaceuticals. Zydus Cadila has started Zydus research centre with an investment of over Rs 50 crore. Cadila pharma plans to invest close to Rs 150 crores in research facility in the coming years. Glenmark, Aurobindo and Orchid have increased their R&D spending to Rs 22.4 crore, Rs 46 crore and Rs 39.6 crore respectively in the year 2004. Lupin has increased its R&D spending from just 3\% of the sales in 2003 to 8 \% of the sales in 2004 and plans to triple its research allocation in the years to come\textsuperscript{6}. Companies like, Glenmark, Torrent, Dr Reddy’s and Ranbaxy have already out-licensed some molecules to MNC’s for advanced clinical trials in return for milestone payments.

**Conclusion**

The consequence of TRIPS Agreement on IPI does not seem to be too alarming in the short run. For instance, TRIPS does not provide for the retrospective patenting in India of drugs that are already in the market or covered by existing patent applications elsewhere. Taking into account the transitional period, there will be only a minimal effect until 2005 but after that, the price pressure will gradually build as MNC’s progressively introduce newer molecules when older drug patents expire. Such consideration leads to the conclusion, that in value terms, patents will cover not more than 15\% of the Indian market, some time after 2005. The remaining 85\% of the market will continue to be exposed to the impact of generic competition. And for the apprehension about the exorbitant cost of patented drugs have been further quenched by the
Government policy to restrict the patented drug prices to lowest international cost.1

Now, the specific challenge before IPI is to start investing in basic R&D from the current abysmal level of less than 2% of total revenue to the world level of 8-10%. The research and development capacity of Indian pharmaceutical manufacturers has been on the rise. The results indicate that the larger companies have initiated activities to increase investment in research and development (R&D) and applications for process and product patents. On the other hand, efforts in small or medium scale units have been directed at improving the quality of production to meet the international standards and competition in the generic sector as well as to improve the export prospects. Indian companies can also exploit the lower cost of drug discovery R&D in India to their advantage and invite foreign companies for collaborative research. Added to that, the incentive India offers to MNC’s in terms of cost-effective, skilled R&D manpower and facilities for clinical research, might lead to several global companies shifting their R&D activities to India or outsourcing manufacturing and research activities to India. In the post-TRIPS scenario, the pharmaceutical MNC’s are geared for mergers and acquisitions to create large corporate structures to tackle skill requirements and to use already existing market network and established brand equity. This will lead to economic development and rapid increase in the technological capabilities of Indian firms. Patent has assumed great importance in recent times since its basic function-to promote innovation-is an essential component of economic growth and social evolution. Patent is not just an incentive to invest in the innovation process per se, but is also increasingly important for trade and industry worldwide. For developing countries like India, patent is an essential component of the framework to attract foreign investment and faster technology transfer. So the coming days are for innovator companies and the era is for innovation.

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