

An Industry in Transition: The Indian Pharmaceutical Industry

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(Received 28 January 2002)

A brief description of Indian pharmaceutical industry, including public health and health infrastructure, is given. The global healthcare research efforts in general and pharmaceutical R&D in particular are outlined. All aspects of Indian pharmaceutical industry, including the impact of Indian Patents Act, 1970, on it, are discussed in detail. Concerns of all sectors on post 1 January 2005, when India adopts a product patent regime are presented. How stronger patent rights will affect Indian pharmaceutical industry is explained and the possible emerging scenario in coming years is given. Preparing for new realities a few suggestions are given. Need for an appropriate strategy to meet the new challenges is felt. Realizing the fact that TRIPS Agreement strengthens patent rights in most developing countries, stress on innovative R&D in pharmaceutical industry is given.

For the Indian pharmaceutical industry, the period 1965-1995, were watershed years with a plethora of developments within and outside India, impacting heavily on the evolution of this industry to its present structure and profile. Both the Polyannas and the Cassandras of the early sixties were proved to be partly right and partly wrong. For example, on the positive side, investments in this sector which was only Rs 225 crores in 1973 grew to Rs 2500 crores in 1999, production of bulk drugs from Rs 18 crores in 1965-66 to Rs 3777 crores in 1999-00, formulations from Rs 150 crores in 1965-66 to Rs 16,000 crores in 1999-00, exports from Rs 3.05 crores in 1965-66 to Rs 6631 cro-

res in 1999-00 and R&D expenditure from Rs 3 crores in 1965-66 to Rs 320 crores in 1999-00. Coincidentally the Country also witnessed perceptible improvements in its health status, for which the availability of drugs can claim some degree of credit, along with improvements in public health and sanitation and health infrastructure including Doctors, paramedical personnel, hospital beds and medical colleges. Among the health indicators, life expectancy increased by over 50%, from 41.2 (1961-62) to 62.9 (1998-99), Infant mortality decreased from 146 per thousand live births (1960-61) to 69 (1998-99), death rate from 22.8 per thousand (1960-61) to 8.9 (1998-99) and birth

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rate from 41.7 (1960-61) to 26.4 (1998-99). While all these figures look very impressive in absolute terms, it has to be realised that much of it is due to the very low starting base and the general improvement in the economy and infrastructure in the Country.

On the flip side, may be mentioned that imports of drugs grew from Rs 8.2 crores (1965-66), to Rs 3441 crores (1999-00), the number of pharmaceutical units proliferated from 2,257 (1969-70) to 20,059 (1999-00), the average profitability of the industry decreased from 15.47% of sales in 1969-70 to 6.1 % in 1994-95 and further to an all-time low of 1% in 1991-92, with subsequent years showing improvements reaching 8% in 1998-99. Even though the drug industry consistently grew all these years, the annual per capita consumption of drugs even today, is only around \$ 3, compared to \$ 412 for Japan, \$ 222 for Germany and \$ 191 for USA. In fact, Indian spending on drugs is above only that of Bangla Desh, Bhutan and the States in Sub-Saharan Africa. Such a low figure is partly due to the low prices of drugs in India compared to even those prevailing in most of the developing countries. Even though the total number of doctors has grown from 65000 (1965-66) to 500,000 (1999-00), there is still only one doctor for every 2000 of the population and that too concentrated in the urban areas with the rural areas ill-served with modern health facilities.

Global Funding of Healthcare Research

Global Funding of Healthcare Research

Global R&D expenditure on health

was \$ 73.5 billion in 1998, of which \$ 34.5 (49.7 %) was expended by the developed countries' public funding, \$ 30.5 billion by the pharmaceutical industry majors, \$ 6 billion by private not-for-profit agencies and only 3% by the developing countries. For the health sector in India, the Government of India spent Rs 237.5 crores in 1996-97, another Rs 129.2 for medical sciences, while the private Industry spent Rs 366.9 crores and Rs 235.3 crores respectively. Such funding has been supplemented by privately endowed agencies and international organisations, such as Rockefeller Foundation, The Wellcome Trust, Bill and Melinda Gates Foundation, the WHO, UNICEF, World Bank, etc.

Pharmaceutical R&D

Global spending on pharmaceutical R&D in the private sector in 1998 was estimated at \$ 34 billion, of which over 70% was spent by the US companies. The top ten MNCs each spent between \$ 1 billion and 2.2 billion in 1998, together totaling over \$ 16.3 billion. These companies are Astra-Zeneca, Glaxo-Wellcome, Roche, Merck, Novartis, Bristol Myers-Squibb, Johnson & Johnson, Smith Kline Beecham, American Home Products and Rhone-Poulenc-Rorer. During the last three years, there have been further restructuring of these companies through mergers and this order has therefore undergone major changes.

Estimates differ on the costs for developing and marketing a new drug from \$ 500 million to 880 million and a total development period of 12-15 years. With the advent of new technologies such as

development of molecular targets, primarily for drug screening, based on pharmacogenomics, proteomics and high throughput screening, there is an increased belief that the costs of drug discovery and development are going to be lower and the process faster. It is, however, a debatable issue. While the new technologies will yield more specific and better drugs, tailor-made for specific diseases, it is very unlikely that the costs of new drug development are going to be less. Moreover, as the main strength of the genomic era is the potential for custom-made drugs to take care of diseases primarily with genetic aetiology, the new approach is unlikely to result in broad-based therapies for global markets. Consequently, drugs developed through the pharmaco-genomics and proteomics approaches are likely to be less relevant and even more unaffordable to patients in the developing and least developed countries of the World.

The Indian Pharmaceutical Industry- The Past and the Present

The Small and Medium Enterprises

The Indian pharmaceutical industry has grown rather haphazardly since independence, even though, like in all countries, this sector is the most controlled and regulated, among all business segments. Such controls are all-pervasive, including for drug approvals, manufacturing licences with specified capacities, administered prices and tariffs on imports, not only on bulk drugs and formulations, but also on drug intermediates. Under the guise of encouraging entrepreneurship

among the small and medium investors, creating employment and promoting decentralized industrial activity in the country, the small scale sector, defined on the basis of plant and machinery costs, has been exempted from many of the above controls. Certain products were exclusively reserved for production by this sector. Consequently, the number of pharmaceutical units in the country, which were just a handful of MNCs in the 50s proliferated to an alarming number, currently estimated at over 20,000. The so-called organized sector of the industry, even today number only around 250, which control over 70% of the total value of sales. The top ten companies realize over 30 % of drug sales in the country. The small and medium sector units are today in a state of disarray, and in different shades of health, many dying, if not already dead, and many more sick and beyond recovery. The problems of this sector are manifold and in the emerging scenario, their role, however limited, needs to be redefined.

The Public Sector

During the late 50s, while independent India was trying to define the role of the State in building a modern sovereign nation, it was realized that the government had an obligation to cater to the basic healthcare needs of the people, and with that in mind, two major ventures were set up in the Public Sector, The Indian Drugs and Pharmaceuticals Limited (IDPL) and Hindustan Antibiotics Limited (HAL), with their subsidiary units spread out in different parts of the country, in Rishikesh, Muzzafarpur, Hyderabad, Ma-

dras, Pune and satellites in many other cities. These capital-intensive units were set up to produce antibiotics, e.g. penicillin, tetracycline, streptomycin, etc, and a variety of bulk drugs, most of them based on Russian technology. While setting up these plants, there was little regard to the costs of production, since the products they manufactured were exclusively reserved for the public sector with no competition and imports were restricted through the licensing and tariff mechanisms. At the Central and State levels, manufacturing units were set up to produce some of the primary vaccines during this period.

Today, due to inefficient management, obsolete technologies, low productivity and poor marketing muscle, all these units are in complete disarray, with cumulative losses running into hundreds of crores, wiping out their net worth several times over. The relevance of these or any other Public sector enterprise is today questionable; yet the Government finds it difficult to take hard decisions to liquidate them for fear of a populist backlash. In any case, the lesson has hopefully been learnt that development, production and marketing of drugs are best handled by the private sector, even though there are those who still believe that the healthcare industry needs to transcend mere commercial considerations and take into account obligations to the society to meet its medical needs in an equitable and affordable manner. The moral of this story is that with appropriate strategies and policies, it should be possible to define a structure, which will ensure benefits to the needy public and at the same time

make reasonable profits, for the survival and growth of the Industry.

Price Control Measures

The first waves of movement towards controlling the prices of drugs were discernable after the Chinese War in 1962 and in subsequent years several versions of drug prices control orders (DPCOs) were legislated and implemented. The models varied from categorisation of drugs along the lines of essentiality of drugs, volume of sales, number of manufacturers and a whole lot of other parameters. The Industry has been uniformly against any control on prices arguing that the best way to lower prices would be by encouraging competition in the market place. While most of the dispensations under the DPCOs failed to satisfy any of the stake-holders, including the government, industry or the consumers, they had one major impact of reducing the profitability of the industry. The trend was alarming with profit before tax (PBT) reaching an abysmally low figure of 1% of sales in 1994-95. Seeing the writing on the wall, the government relaxed the span of control from 136 drugs to 76 today. The average profitability of the industry has since shown an ascending trend from 4.4% in 1993-94 to 8% in 1998-99. These figures are the averages for the industry and the performance of the individual companies varied according to its product portfolio.

Indian Patents Act, 1970

After almost a decade of deliberations and debates, an amended Indian Patents Act (IPA) was legislated in 1970, which

became operational in April 1972. The impact of this new Act was dramatic on the Indian companies, since under the new Act product patents were not allowed, the period of validity was reduced from 14 years from the date of filing to 5 years from the date of sealing of the patent or 7 years from the date of filing, whichever was shorter. Apart from the compulsory licences provision, pharmaceutical patents were liable for grant of licences of right, if the patented invention was not worked within three years from the date of the grant. The absence of product patents, enabled Indian companies to manufacture and market even patented drugs in India as well as export them to countries where they were not protected by patents. The number of manufacturers of bulk drugs and formulations proliferated resulting in severe competition and price wars. For example, there are today an estimated 40,000 packs manufactured by over 20,000 pharmaceutical companies in the large, medium and small scale sectors. There are around 200 brands of ciprofloxacin, 110 brands of norfloxacin, 69 of amlodipine, 62 of ranitidine, all of them marketed in India during the pendency of their valid patents abroad. India, thus became self-sufficient in the supply of practically all synthetic drugs and several antibiotics, developed considerable expertise in chemical process technology and the exports of generic drugs increased. The consumers benefited and exports surpassed imports, making the pharmaceutical sector, one of the few industrial segments which was a net exporter of sophisticated technology products. Indian pharmaceutical industry

came to be reckoned in the global markets as a major player in bulk drug production.

On the negative side of the impact of IPA, 1970 was the proliferation of companies and brands, sacrifice of quality by some unscrupulous producers, low margins on sales and hence low profitability and non-availability of adequate funds for R&D and new investments. Filing of pharmaceutical patents, by foreign and Indian companies reached an all-time low in the wake of IPA, 1970.

M RTP Act

The Monopolies and Restrictive Trade Practices Act (MRTP) has often been termed as one of the most draconian laws in India, from the industry's perspective. The problem was not so much the basic underlying principles, since anti-competitive laws are common in most countries, but in the definition of what constituted monopolies, whether it was based on assets, capital employed, turnover or market share. In terms of size, the largest Indian companies are pigmies compared even to the smallest of the MNCs. In addition, the industry also suffered since the restricted licences granted by the government forced investments in economically non-viable units, with little competitive strengths in the global arena.

Regulatory Affairs

From a technical standpoint, the pharmaceutical industry is regulated by the Drugs Controller General's Directorate in Delhi and Drug Controller's administrative set-ups in the States. The prevailing statutory provisions are based on the

Drugs and Cosmetics Act, which has been amended several times to accommodate the emerging trends in applications for an Investigational New Drug (IND), New Drugs (NDs), manufacturing licences, current good manufacturing practices (cGMP) requirements, etc. While the Indian regulatory standards are consistent with those of the most stringent regulatory agencies in the world, the problems faced are related to the non-availability of basic infrastructure and implementation. With over 20,000 units and 40,000 product packs in the market, which needs to be monitored and controlled, the manpower and testing facilities available are totally inadequate. Punitive actions for control of the menace of spurious and sub-standard drugs are extremely difficult to enforce in an effective and timely manner. Yet another major problem is related to the division of authority between the Centre and States regulatory bodies. For example, the clearance for manufacture and marketing of fixed dose combinations of approved drugs, new dosage forms and packs are within the purview of the States, which sometimes enforce standards and policies counter to those of the Central Agency.

The Agency has provisions for fast-track clearances of life-saving drugs for which alternatives are not available. Neither, for these or for others are pharmacovigilance and post-marketing surveillance systems to closely monitor adverse reactions in field conditions, readily available.

With the advent of Indian companies entering the field of new drug discovery, drugs which have never been tried abroad need to be evaluated for the first time in

India, under the IND status. The Agency is neither equipped or skilled, to evaluate them and approve them as INDs or new drugs. If major improvements are not brought about, the Indian approval systems may not meet the standards of International Committee on Harmonisation (ICH) and other major regulatory agencies, such as the FDA, USA.

The Central Agency has no regulatory standards for over the counter drug (OTC) products, nutraceuticals and dietary supplements. The products under the Indian Systems of Medicine are within the purview of the State Drugs Controllers. Since all these areas are getting increasingly prominent globally, the present ambiguity in defining the standards for their marketability, lead to avoidable malpractices at various levels.

Pecking Order in the Indian Pharma Industry

The post-1970 scenario saw a new pecking order in the pharmaceutical industry. Since the MNCs could not exploit the 'Free-For-All' status, adopted by the Indian companies, in the wake of IPA, 1970, the Indian companies overtook them and became leaders in the domestic market. Thus, while in the sixties, 7 out of the 10 companies in India were MNCs, today the order is reversed with 6 out of the 10 being Indian companies. In 1997, the order was Glaxo-Wellcome, CIPLA, Ranbaxy, Hoechst-Roussel, Knoll, Torrent, Lupin, Alembic, Wockhardt-Merind and Pfizer. Due to recent acquisition of brands and the introduction of new products and strategic alliances, including co-marketing of certain products, this order

has undergone changes. However, an indication that the market is widely spread is apparent from the fact that no company has a market share in excess of 7%. An appreciation of the value of brands and brand equity is a new trend as evidenced by the sales of brands such as crocin, mox, aten, etc., at prices ranging from 1.5 to 3 times the annual turnover in the domestic market. The strategy of brand acquisition by leading companies, is largely based on the need to fill up the gaps in the therapeutic segment to maintain market shares.

Leading Therapeutic Segments

As a country which has been categorized as a developing nation with per capita annual income hovering around US\$ 150/-, which even if purchasing power parity (PPP) is considered does not exceed \$ 400/-, India possesses certain features distinct from the other countries slated to be in the same developmental status. The medical needs of India are related to a mixture of the diseases of the developed industrial world as well as those of the developing countries. Thus, India is a repository of the tropical infection diseases of bacterial, viral and fungal origin, as well as, those with a life-style aetiology. For example, coronary heart diseases (CHDs), metabolic diseases such as diabetes and stress-related CNS disorders are growing at a pace higher than in most developed countries. However, an analysis of the sales of pharmaceuticals would show that the developing countries markets are not necessarily based on medical needs. For example, in terms of sales, 24% of the market is for anti-

infectives, 15% for vitamins and nutrients, 11.5% for alimentary tract diseases, 9% for analgesics, 7.4% for cough and cold, 6.4% for cardio-vascular diseases, 5.7% for dermatologicals, 4.1% for CNS and 3.2% for anti-TB drugs. As against this, drugs for cardiovascular diseases, gastrointestinal disorders, CNS ailments and Infections are the top 4 in the global scenario.

R&D in the Indian Industry

Prompted by the opportunities offered by the IPA 1970, the leading industrial groups ventured into R&D activities for mastering the process technology required for manufacture of generic equivalents of patented and off-patent bulk drugs. The emphasis has been on synthetic chemistry and scale-up to production levels of multi-step processes. Expertise was also gained in the conversion of bulk drugs to the required oral and parenteral dosage forms as well as conventional sustained release formulations. Over the last three decades, India became self-sufficient in the production of over 30% of the bulk drugs and 96% of formulations, needed for domestic use as well as for exports. Easy access to marketing rights for even patented products was a disincentive to carry out basic research for new drugs discovery. In addition, the capacity of Indian companies to invest in drug discovery was limited and in the absence of a product patent system, they were also vulnerable to unauthorized appropriation by third-parties. However, the compulsions of the changing scenario brought about by our obligations to WTO will leave no option but to find funds for and invest in R&D.

Advent of TRIPS and WTO – A Bane or Boon?

The first indication that the honeymoon days for the Indian pharma industry were numbered became apparent with India signing the General Agreement on Tariffs and Trade (GATT) at Marrakesh in April 1994 which led to the setting up of the World Trade Organization in January 1995. The relevant section for the protection of IPR in GATT is covered under TRIPS, according to which, India has been given time till January 2005 to implement a globally harmonized patent system. The basic requirements and obligations that India has to meet relate to providing for grant of product patents, patent validity period to be extended to 20 years, imports to be considered equivalent to working of the patent, compulsory licences to be granted only in extreme cases of emergency and the onus of proving non-infringement to rest with the defendant. India has defaulted on her commitment to have a legislation amending IPA, 1970 to make it consistent with the above by 2000, as agreed upon. India has, however, amended the Act to allow filing of product patent application from 1.1.1995 and the grant of exclusive marketing rights to the patentee, subject to satisfying the four required conditions.

Post - 2005 Scenario

A topic of great debate is the future of the Indian pharmaceutical industry after 2005, when India will start feeling the impact of a strong product patent regime. Concerns are expressed by all sectors of the Industry, the large, medium and small scale sectors, healthcare policy planners

and the consumers. These concerns are based on the following scenario which will evolve in another three years.

- The grant of product patents will provide exclusivity to the patentee or his licensee to make and sell the products on terms decided by the patent holder or his assignee.
- Indian companies cannot produce or sell patented products without licence from the patent-holder. However, this condition will apply only to products for which patents have been filed on or after 1.1.1995.
- The prices of patented drugs will be higher than for generic versions, since R&D-based companies can recover their costs only from sales of patented drugs.
- Compulsory licences will be granted to domestic industry only in cases of extreme urgency and in public interest during national calamities, such as epidemics. The new and recent Doha Declaration, has reiterated that developing and least developed countries can impose 'compulsory licence' clauses, making patent protection subordinate to local public interest.
- There is no obligation to manufacture patented products. The patentee or his assignee has the right to import the product. This issue may be disputed and India may still insist on local manufacture as Brazil has done in its Patent Act (1996).

How Can India Cope with the Post - 2005 Scenario?

The Indian sector of the industry has been of the opinion that developing countries such as India which were given 10 years for implementation of the system under TRIPS should get a further extension till 2008, and it was hoped that such a proposal would be part of the Agenda for discussions at the just concluded WTO Ministerial Conference in Doha. However, no discussion took place on this issue and, as such, the deadline of 1.1.2005 stays. What are the strategies which should be adopted by the Indian Pharmaceutical companies in the emerging post-2005 scenario to ensure their survival, and growth, both in domestic and global markets? In order to evolve appropriate strategies, it is important to define the basic growth objectives and role of the Indian pharmaceutical industry at the macro level, which are; meeting the medical needs of the country at an equitable and affordable cost to the population, encouraging investments in this sector, developing an R&D culture warranting strong IPR regime, and in general, enabling economic growth of the nation. At the level of individual companies, each company should tailor their approaches to meet the challenges of the post-2005 era. The general scenario in the Industry in the coming years will be:

- The top ten Indian companies, each of which is expected to reach an annual turnover between Rs 700 to Rs 1500 crores by 2005, should invest around 7-10% of their turnover in R&D, much of it on new drug discovery, with its inherent high-costs, high risks and long pay-back periods.
- Indian companies can be major suppliers of generic drugs for the global markets, considering Indian strengths in the manufacture of bulk drugs and conventional formulations.
- India can develop her traditional systems of medicine, fully validated by modern methods, and promote them and their products in global markets. The Department of Indian Systems of Medicine and many private sector companies and national agencies are active in this area.
- India can develop state-of-the-art technologies and products in the area of Biotechnology. The widening gap in the progress in this technology area between the developed countries and India need to be narrowed. The government via the Department of Biotechnology and various other scientific bodies such as CSIR, ICMR and ICAR have chalked out many plans for facilitating this activity.
- Indian companies will actively collaborate with MNCs in R&D, custom and contract production, clinical research and co-marketing through well-orchestrated contractual agreements.
- Indian and foreign companies will set up contract research organisa-

- tions on a commercial scale for R&D and clinical research.
- The patent system will be well-entrenched and respected by all corporations. Global patenting activities will ensure that Indian companies can licence out products and processes on commercial terms to international companies.
 - With the new Doha Declaration on TRIPS and Public Health in place, Indian Companies have an opportunity to take a leadership position in R&D, production and supply of both generic as well as patented drugs for diseases particularly endemic to developing countries, such as malaria, TB, AIDS or any epidemic. Since the other developing countries have little technological strengths, the provision of compulsory licences alone will not enable them to produce their needed drugs. The new agreement which has already endorsed the principle of public good transcending private interest of patentees should also allow Indian Companies access global markets for these drugs.
 - India should bring in pro-active legislations, if necessary, through appropriate *sue generis* systems to make her core strengths to be exploited in areas such as:
 - (i) Discovery and development of new indications for drugs, or in other words, allowing for “Swiss” type of claims.
 - (ii) Petty patents and utility models with less stringent patentability standards, shorter duration and less cost should be allowed under her laws.
 - (iii) Trade secrets and undisclosed information which are key to technological superiority between companies should be protected.
 - (iv) Ways and means should be forced to protect the enormous knowledge, information databases and practices of Indian systems of medicine as well as the unique skills of her artists and artisans.
 - (v) India should enact and implement strict protection systems through patents and/or copyrights, specialized software developed for the Pharmaceutical industry by the IT companies.
 - (vi) India’s biodiversity, geographical indications and plant varieties protection legislations should be catered to exploiting the country’s huge natural assets through R&D, rather than using them as negative tools to prevent others from exploiting the resources.

What Then is the Prognosis?

The ability of the Indian pharmaceutical industry to cope with the emerging scenario will depend heavily on its ability and resilience to adjust to a new global way of thinking and acting. Several classical examples of the US and many developed countries using legislative modalities to encourage industrial activity rather than controlling them are known

and India should adopt those, taking into account her core-strengths and needs. While, at the macro level, the government support and facilitation are needed in a developing economy, corporations, whether in the national or multi-national sector should develop their own core-strengths. With a strong patent system in place, India, to the eyes of the MNCs will be another opportunity site for investments, apart from access to the large market. However, in that process, India will be always compared with China and some of the erstwhile Far-East Tigers

when locational advantages and are considered for investments.

Indian companies in the organized sector need to be R&D and competitive technology savvy, whether they work on it alone or in collaboration with leading international companies. The approach should be to compete where you can, more importantly, collaborate where you must, on mutually beneficial terms. The Industry should be prepared to meet the challenges, which, with appropriate strategies could be turned around to opportunities.