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Globalization of the Indian Pharmaceutical Industry: Implications for Innovation

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Abstract: In this article we create an industry-wide metrics of innovation based on the characterization of learning potential of foreign direct investment (FDI), technology acquisition and in-house R&D, analysis of patenting activity, assessment of R&D directions and evaluation of innovation outcomes. Our purpose is to reflect on strategies adopted for learning, competence building and innovation and for creating complementarities and linkages within India's pharmaceutical industry during the post- Trade Related Intellectual Property Rights (TRIPs) period. With India facing the challenge of constituting pathways and strategies for accelerated learning, we also explore through whose actions, types of strategies and routes of growth have the limits of Indian pharmaceutical industry innovation been reached within one decade. Finally, how and with what kind of policy design can the Indian state and society intervene to push the frontier of innovation further within this industry. Indian state and business have chosen globalization pathways with specific implications for innovation. We assess systemic connections of these implications, suggesting that for a significant change in domestic and foreign pharmaceutical firms' orientation to disease, as reflected in outcomes of their R&D investment activity, there also has to be a major focus on pathways toward innovation for domestic markets.

Keywords: globalization, innovation, learning, pathways, pharmaceuticals

JEL classifications: O32, O33, O34, O38

1. Introduction

This article appraises prospects of developing new pharmaceutical products for the emerging challenge of double disease burden in India, by examining implications of continuing with a public policy designed to accelerate growth pathways chosen for globalizing domestic pharmaceutical industry during the post-Trade Related Intellectual Property Rights (TRIPS) Agreement period. A critical evaluation is made of the contribution of policy design to

the developments taking place with regard to first, the sale of domestic firms to foreign buyers and second, the failure to realize the potential for product innovation to be carried out for the benefit of providing better pharmaceutical products to the people of India and other developing countries. Evaluated also, are some implications for limits to the realizing of product innovation from the standpoint of both the development of 'systems of innovation' and the improvement of public health goals during the post-TRIPs Agreement period in India.

Analysis of the contribution of domestic and foreign pharmaceutical firms to the key processes of learning, competence building and innovation making, focuses on the directions in which channels of interaction have been forged and complementarities and linkages strengthened among the different domains of health system activities. Evidence is provided on the nature of contribution of foreign direct investment (FDI), technology transfer and overseas R&D of foreign firms to the challenge of undertaking the processes at hand. The role being played by the Government's drug innovation promotion initiatives in realigning its national system of drug innovation is critically assessed from the standpoint of their contribution to the state of new product development. Our innovation metrics focus on the stage of development of the outcomes of R&D investment activity by domestic and foreign pharmaceutical firms operating from India, along with their orientation to disease.

2. Theoretical Considerations

Debate on post-TRIPs initiatives' net effect on improving domestic pharmaceutical firms' performance and strengthening their future, is only beginning to move toward evaluating the sustainability of the policy package supporting the industry and institutions in R&D and innovation activity for new products. Given the criterion of success assessment, which is quite different in terms of expected results for learning and innovation, and the achievement of goals of sustainable development from the choice of growth pathways, we can discern two distinct perspectives from the literature.

The first perspective on Indian policy evaluation acknowledges a significant process of creative destruction produced by domestic patent reform and liberalization. The focus is on assessing firm strategy where firm-specific deployment of capabilities, entrepreneurship and ad hoc problem solving skills determine the winners of the race for market shares, as new or untapped economic opportunities emerge. Athreye *et al*. (2009) illustrate this approach. They assess post-TRIPs radical regulatory changes as tantamount to technological revolutions which are making a major impact on domestic pharmaceutical firms' strategies, and how the winners and losers are being determined. Since the policies that latecomer countries have had to adopt on

account of trade liberalization have elicited diverse responses and produced diverse impacts on developing Indian pharmaceutical firms' capabilities, their attention is limited to assessing the impact on achieving competitiveness. They do not examine the impact of radical institutional changes on the realization of public health goals.

Their assessment of the co-evolving industry scene is that radical regulatory changes such as the Indian Patent Act of 1970, the New Industrial Policy of 1991 and the signing of TRIPS in 1995 have served to open up new economic opportunities and constraints in the wake of which the winners and losers were selected as a function of the dynamic firm capabilities most appropriate for the new market environment. The results of their assessing the impact of learning and innovation strategies of four major domestic pharmaceutical firms is that there exist clear relationships between existing capabilities, their response to new opportunities, development of targeted capabilities and the firm being likely to capture competitive advantages. They understand the co-evolution of firm strategy and capability having been determined by three main factors: the historical trajectory of the firm and existing capabilities, firm-specific managerial vision and learning by observing the successes and failures of other compatriot firms. Their limited observation on the development of 'second order' capabilities (those having the potential to provide lasting competitive advantage in the context of Indian pharmaceuticals) is that domestic firms are still uncertain about the payoffs of strategy to be adopted while integrating the drug discovery model. They have not questioned whether a different policy design could have been followed and neither therefore, what impact this might have had on developing 'second order' capabilities.

Arora *et al*. (2008) have a different starting point within this perspective, holding that strong intellectual property rights would create 'markets for knowledge' and are better for learning, competence building and innovation making. This way the firms of developing countries would be able to improve their access to knowledge and technology and would have a stronger incentive to develop new products. Consequently this view was favourably disposed to transitioning towards the implementation of TRIPs at the earliest possible date. It suggests too that once the larger Western economies are governed by effective patent systems, all inventors in a global trading economy have significant incentives to develop new products, patenting them in the major markets with strong protection. Preferring this position, they suggest that domestic patent reform based on TRIPs in India was wrongly identified as necessarily a suspect.

Moreover, they have recently claimed that the extent of progress made by the Indian pharmaceutical industry in respect of investment in R&D and innovation for exports, confirms their understanding. While they suggest that

we do not fully understand the transition process, their claim that domestic patent reform could even induce such a transformation process appears to fly in the face of conventional wisdom, as articulated in the received literature on the impact of stronger IPRs on invention in developing countries. They point out that if the changed patent regime in India did have an effect, it must be that by closing off the possibility of imitation, it increased the payoff to research. In principle, Indian firms already had the option of developing new compounds, patenting them in much larger markets, and licensing the compounds or selling drugs directly in the West. They suggest that what we need to explore is why the impact on research activity in India was so significant and under what circumstances transition to stronger intellectual property rights could stimulate domestic innovative activity. They hold that India's size, its vast potential human resources, and the possession of a common language with the United States raises some interesting possibilities for India's future role in the global pharmaceutical industry. They believe that India clearly has the potential to become more important. However, neither did they raise the questions as to whom India's potential has importance, and what kind of cost the Indian people would have to pay, nor what kind of impact all of this would have on the availability and prices of essential medicines.

The second important perspective on policy evaluation is embedded in an understanding that not all problems of development in developing countries can be solved solely via economic competitiveness policies, for these policies may be instrumental – if so designed – in promoting sustainable social, environmental and political development. In this perspective, for competitiveness policies to play this role, developing countries must actively pursue sustainable development goals, and not just increasing exports. Corrales-Leal (2007) have included in the basic proposals of this perspective the measures which must be taken to: develop local capabilities to permanently differentiate and diversify production; increasingly enhance productivity and add value to exports; and enhance the complementarities and linkages between economic sectors by putting in place ultimately a process in which technology is continuously intensified and productivity is increasing to realize employment and knowledge spillovers from trade liberalization. However, as a detailed evaluation is yet to be undertaken of the contribution that the policy measures belonging to all these strategies make to the goal of sustainable development, there exists at the moment a variety of views on how the developing countries have to handle policy design for the implementation of trade supported strategies of learning and innovation.

Post-TRIPS approach in the drugs and pharmaceuticals sector has been reflected in the works of Abrol (2004), Dhar and Gopakumar (2006) and Chaudhuri (2005), where assessments undertaken of post-TRIPs pharmaceutical industry performance have been largely clear on the fact that there are also

costs of product patent protection, which may also soon extend even beyond the adverse impact on prices of essential medicines. Warnings have been raised that consolidation of the Indian pharmaceutical industry may occur in a way to benefit more global pharmaceutical firms. Recently this apprehension has been articulated in the official paper of India's Department of Industrial Promotion and Policy (DIPP), raising issues such as whether the policy of automatic clearance of 100% FDI should be revoked, and why domestic pharmaceutical firms and government should not be thinking of using the route of compulsory licensing and invoking competition law. So far the policy design has been known to encourage more the pathways of growth preferring dependent routes. As by using the contract research and manufacturing services (CRAMS) and the route of exports of simple generics, leading domestic pharmaceuticals firms have been allowed to follow dependent routes for their growth, in this perspective scholars have been aware of a need to change the policy design and have made their suggestions to government.

For example, Abrol (2004, 2006) had earlier articulated that global pharmaceutical firms are trying to carve out a new international division of labour, using India to access the supply-side factors and markets by imposing the regime of strong intellectual property. Following this assertion, Abrol (2004) further argued that the introduction of strong IPRs would provide global pharmaceutical firms with enormous advantage to control knowledge diffusion and integrate India's local capabilities. This follows the reality of domestic firms, who are faced with a serious lag in their capability building structures, and subordinated by myopic and narrowly benefiting innovation strategies. As such, introduction of IPRs would increase their vulnerability. In light of this, the policy design challenge should be framed in ways that strategically delay the processes of external liberalization while accelerating the processes of learning, competence building and innovation by establishing a clear national strategy with the aim of strengthening the place of domestic pharmaceutical firms, and enhancing the systemic autonomy and coherence of a national system of innovation.

Similarly, today in this stream comes the work of Chaudhuri (2007), who holds that the primary incentive to invest in R&D, whether for New Chemical Entities (NCEs), modifications or development of generics, has not been the new TRIPS-compliant product patent regime in India, but the Hatch-Waxman Act based IPR regime in developed countries that was in place well before TRIPS. TRIPS may have accelerated the trend towards such R&D because of the anticipated shrinkage of domestic opportunities. Such analyst's view is that while R&D activities have diversified, Indian pharmaceutical firms have yet to prove their competence in innovating new products. No NCE has yet been developed. There have been several setbacks and the partnership model has not always worked properly. Accordingly, little has changed to dispute the

traditional wisdom that developing countries should not grant product patent protection (Chaudhuri, 2007). Recently, Chaudhuri (2010) explored the issue of policy options in the light of the Indian private sector's experience and of the public-private partnerships initiated for developing new drugs. He suggests the expansion of public-private partnerships to include organizations from other innovative developing countries such as Brazil and China.

Dhar and Gopakumar (2006) analyze the Indian generic pharmaceutical industry's performance on a far more hopeful note. They indicate that both Ranbaxy and Dr Reddy's have developed improved generics and Novel Drug Delivery Systems (NDDS), which have opened the doors for collaboration with the pioneer producers, and that India is fast emerging as the hub for contract research and manufacturing with a number of pharmaceutical majors establishing joint ventures with Indian generic producers. However they are aware that as Indian firms are yet to make a mark in the area of new drug discovery, this activity could be strengthened through the government's increasing efforts to participate in R&D activities involving the industry. When suggesting that efforts taken with a view to strengthening the Indian pharmaceutical industry's technological sinews should stand the industry in good stead as it evolves strategies to meet the challenges posed by the post-TRIPS patent regime, they did not forget to advocate that these successful forays by Indian pharmaceutical firms would have to be assessed in the context of their role in accessing medicines at affordable prices.

We have indicated that the problem of innovation faced by domestic pharmaceutical firms is inherent in the choice of growth pathways. Penchant for patenting, involving incrementally modified drugs tends to focus on the bleak side of the industry. Besides, R&D priorities are being increasingly set in tune with global trends, especially since local firms have enhanced their level of collaboration with foreign ones. Particularly affected in this process would be the 'neglected diseases' and capability building for the development of NCEs.

While the two differing perspectives discussed above continue to pursue their own respective aims, even this scholarship is geared to taking different stance with regard to the achievements and limitations of ongoing processes of learning, competence building and innovation making. Their assessments differ particularly in respect of the role of chosen pathways of growth and of policy design in the evolution of capability development for drug discovery and development. Both sets of scholars have only studied the strategies of selected leading firms in order to arrive at their findings and recommendations. Consequently their assessments appear to differ over the nature of policy changes to be brought about at this stage within the country and in the TRIPs Agreement. Similarly, even those who have covered the progress being made with regard to the development of complementarities and linkages on the basis

of the assessment of public-private partnerships have also produced a different take on the limitations and achievements of competencies created in the Indian case during the post-TRIPs period (see Abrol, 2006, Dhar and Gopakumar, 2006; Pradhan, 2006; Mani, 2006).

In order to resolve the different views on future strategies, we need to make a more systemic assessment of the potentials of global integration pathways. In order to assess the contribution of policy actions and instruments used in implementing the trade supported strategies for technological learning and innovation and creating the linkages and complementarities, scholars need to go beyond anecdotal information on R&D outcomes. They need to take an industry-wide view, assess second order capabilities and evaluate the complementarities and linkages developing within the national system of innovation.

3. Emerging Evidence on Innovation

Evidence built on the basis of industry-wide patenting activity itself clearly shows that as far as investment orientation toward in-house R&D of domestic pharmaceutical companies is concerned, work seems to have been mainly focused on developing capabilities, innovations and technological know-how for off-patent generics that the industry thought could be exported to regulated markets of Europe and USA. See Table 1 for the historical time line of capability development profile mapped by the authors on the basis of patents

Table 1: Emerging Patterns of Pharmaceutical Innovations, 1992-2007

No.	Nature of patent	1992-1995	1996-1999	2000-2003	2004-2007	Total
1	Process patent	1	8	62	149	220
2	Product patent		6	18	38	62
3	NDDS patent			11	20	31
4	NCE patent		2	10	23	35
5	Dosage/formulation/ composition of matter patents	2	43	228	285	558
6	Method of treatment		1	19	16	36
7	New form of substance		5	85	195	285
Total		3	65	433	747	1227

Note: NDDS – Novel Drug Delivery System; NCE – New Chemical Entity.

Source: Data of emerging pattern of patenting activity of domestic (30) and foreign (5) companies active in India (process, product, NDDS, NCE, dosage/formulation/ composition, salt/polymorphs/derivative) data collected from USPTO 1992-2007. USPTO website URL http://www.uspto.gov/

filed by the Indian pharmaceutical industry with the United States Patents and Trade Mark Office (USPTO).

Table 1 shows that the chemistry driven process research leading to non-infringing processes for active pharmaceutical ingredients (APIs), introduction of cost effective routes, identification and characterization of impurity profiling pertaining to APIs, reduction of impurity levels, acceptable dosage forms and formulations came to be pursued as the main priority in the Indian pharmaceutical industry during the post-TRIPS period. This emphasis has continued to date. The other area of R&D pertains to formulations where NDDS based products are introduced. Our analysis also confirms that the economic opportunity created by the Hatch-Waxman Act of 1984 has been the most important stimulus for the domestic pharmaceutical firms to invest in the processes of learning, competence building and innovation making activity.

Another major area of competence building has been related to the improvement of good manufacturing practice. Table 2 clearly shows the key areas of competence building in the case of domestic pharmaceutical firms in relation to the registration of Drug Master Files (DMFs) and Abbreviated New Drug Applications (ANDAs) prior to registering products (generics) in EU, USA and other developing countries. The new drug applications (NDAs) filed with United State Federal Drug Regulation Authority (USFDA) have still been few and far in the Indian pharmaceutical industry.

Assessment clearly shows that the face of the Indian pharmaceutical industry has gradually changed during the post-TRIPS period. It is now an R&D based industrial segment competent to participate in the processes of learning, competence building and innovation for the supply of off-patent generics to regulated markets. However, in the field of product development, the bulk of 'innovative outputs' still belong mainly to the areas of dosage/formulation/composition of matter related R&D work.

The story of Indian new drug discovery through the private sector started in 1994 with Dr. K. Anji Reddy of Dr. Reddy's Laboratories (DRL), earlier

Table 2: DMFs, ANDAs and NDAs Received by the Top Fifteen Indian Companies

Company	No. of DMFs	No. of ANDAs	No. of NDAs	Sales turnover as of 2008 in CMIE Prowess Database (in Crores)
Total (Top Fifteen Companies)	1242	1129	19	78963.13

Source: Data collected from each company's website.

Table-3: Pattern of Phase-wise Clinical R&D Activities in the Case of Domestic and Foreign Pharmaceutical Firms Active in India, 1999-2009

Companies	1999-2001			2002-2004			2005-2007			2008-2009			
	Compound Status/Phases												
	I	II	III	I	II	III	I	II	III	I	II	III	Total
Foreign (8 Companies)	1	2	1		1	1	2	4	2	10	23	69	116
Domestic (15 Companies)	1			9	3	1	19	17	12	27	21	47	157
Grand Total (23 Companies)	2	2	1	9	4	2	21	21	14	37	44	116	273

Sources: Data collected from each company's website and latest annual report of individual pharmaceutical companies and CTRI Clinical Trial Registry India (CTRI).

a technocrat in the leading public sector firm namely Indian Drugs and Pharmaceuticals Limited (IDPL). DRL was responsible for setting up the first new private sector drug lab at Hyderabad as a distinct facility. Table 3 gives the phase-wise status of compounds under development in the case of active domestic and foreign pharmaceutical firms for the period 1999-2009.

Evidence is clear that investment in product development activity is unevenly developing in respect of the use of national S&T infrastructure of hospitals and medical colleges. Foreign firms are far more able to use the S&T infrastructure developed during the past sixty years. Further, it is also a matter of concern that the clinical R&D activity is concentrated in phase III stage where the gains of competence development are extremely limited. An estimated 60 new compounds are also known to be in various phases of development and testing for the domestic firms. Some of these compounds have been licensed by the domestic companies from foreign firms. Needless to say, the activity of compound development and testing by domestic companies is quite small compared to world standards. Domestic pharmaceutical firms are just starting to pursue their phase I clinical trials in India. Much of the efforts of foreign pharmaceutical companies in clinical trials are in phase III. This means that the clinical research part of the national system of drug innovation is being far more valued for the patients India can provide, rather than for competencies that the system built on the basis of competencies of clinical research organizations (CROs), medical practitioners, colleges and hospitals is usually known to be accomplishing in the case of cutting edge drug innovation.

Furthermore, it is becoming evident that neither the domestic firms nor the above described system can really claim to have developed during the post-TRIPS period, accumulate enough resources to pursue cutting edge drug innovation and take a new compound through all stages up to marketing. India is still weak in early stage drug discovery. Large domestic companies have been pursuing those areas of drug discovery and development in a bigger way that lowers their costs and risk factors. This can be illustrated through the case of one of the DRL compounds. DRL is still one of the most determined domestic companies working on the national scene in the area of drug discovery and development. Their strategy is to find a new drug within an existing family that has been discovered, finding a compound analogous to an existing one like DRL, where originally Sankhyo was doing work on Giltazones. This strategy cuts down on the risk. A company can reduce some of the uncertainties of new drug research though this may not produce a drug as big as a blockbuster. The second strategy is out-licensing where the Indian company takes some leads to pre-clinical stage. Then it may strike a deal with an MNC which will have the right to market the compound in a particular

market if all tests are cleared. The Indian company gets milestone payments for each stage of clinical trials the compound clears. All the big companies namely, Ranbaxy, DRL and Glenmark have followed the out-licensing route to developing new drugs. DRL has tried a deal with Novartis too, for further work on an anti-diabetic compound DRF 4158. Ranbaxy entered into a deal with Bayer for Cipro NDDS and RBx 2258 (BPH). Glenmark has tried a deal with Forest of North America and Tejin of Japan for compounds that could provide treatment for asthma. But the level of success obtained by these companies through the routes currently under perusal has not yet yielded the desired results in respect of new product development.

Evaluating innovation directions, Tables 4 and 5 provide details of disease focus of the new drugs under development in India and their current status. It should be noted that all the important developments that we see in the creation of R&D capabilities for new drug discovery and development within the Indian firms, have a global market favouring R&D orientation. Under the emerging conditions of competition in the 'global' pharmaceutical industry locally bred firms of developing countries are likely to be lured by the multinational corporations to work for the western markets.

It is evident that only a handful of firms have been able to increase their R&D investments in a significant way. R&D expenditure of the top fifteen Indian pharmaceutical firms is nowhere near the expenditure being incurred by the generic companies of Israel and Europe. But the top ranked domestic company Ranbaxy is now no more a domestic company. It has been sold by its Indian promoters to Daichi Sankhyo, a Japanese MNC. Moreover, even the other leading companies *viz*. Dabur, Nicholas Piramal, Wockhardt and Shanta Biotech have divested important parts of their pharmaceutical business to foreign companies. In many cases these divestures have also involved R&D based segments. The latest news is that Cipla is also negotiating the sale of its assets with foreign firms. While it is true that DRL, Glenmark, Lupin, Cadila, Wockhardt, Sun Pharma and Torrent are still around as integrated Indian pharmaceutical companies that have substantial foreign sales, an analysis of the current status of their new drug development clearly indicates that most molecules have not progressed very far. Many of them have been completely abandoned by the firms. In spite of 16 years of investment in research, no new drug has made it out of Indian domestic pharmaceutical firms. See Table 5 for the changing status of NCE based drug discovery pipeline of pharmaceutical firms active in India.

Analysis undertaken of the disease focus and the status of progress confirms that the Indian companies consider the size of the domestic market as small and not sufficiently attractive for taking up the development of new products in the drugs and pharmaceutical sector. In recent years, ambitious

Table 4: Disease Focus of New Chemical Entities' based Drug Discovery Pipeline

Companies	Cancer	Metabolic disorders	Brain/ Nervous system	Bone diseases	CVS	TB	Malaria	Skin	Multiple infections	Total
Lupin Ltd		1	1	1		1		2		6
Dr Reddy's Laboratories	3	5		1	2				1	12
Wockhardt Ltd								1	5	6
Glenmark Pharmaceutical		2			1				1	4
Torrent Pharmaceutical		1			1					2
Orchid Pharmaceutical		1								1
Zydus Cadila		6								6
Piramal Healthcare	1								1	2
Alembic Ltd			3						1	4
Biocon Ltd	1	1								2
Sun Pharmaceutical Industries									1	1
Ranbaxy Laboratories							2		6	8
GSK Pharmaceutical	1		1						1	3
Total	6	17	5	2	4	1	2	3	17	57

Source: Companies' annual reports and websites, accessed in December 2009.

Table 5: Current Status of NCE based Drug Discovery Pipeline

Companies	Compound Continuing				Compound Abandoned				Total
	Preclinical	Phase I	Phase II	Phase III	Preclinical	Phase I	Phase II	Phase III	
Dr. Reddy's Lab		1		1	5	2	1	2	12
Glenmark	1	5	1					1	8
Lupin	2		3	1					6
Orchid			1						1
Piramal Healthcare	3	2	4						9
Ranbaxy				1	2	2	1	2	8
Torrent								1	1
Wockhardt			1		1				2
Total	6	8	10	3	8	4	2	6	47

Source: Compiled on the basis of reported information in "Death of a dream", cover story in *Business World*, 30 January 2010. Available at: http://www.businessworld.in/bw/

new start-up discovery firms backed by private equity investors such as Pune-based Novolead and Indus Biotech have also come up. They could succeed where Indian pharma's Goliaths wandered into and faltered (*Business World*, 30 January 2010). These discussions about where the hopes lie for new drug development have led some to suggest that India's first innovative drug could come instead from a new generation of pharmaceutical companies, but is this the end or the beginning of the story? Whether the dream can be revived for the Indian domestic pharmaceutical firms is in need of rigorous analysis if the policy design is to be worked out appropriately.

4. Process Evaluation of Post-TRIPS Innovation Routes

An important claim by advocates of the TRIPS Agreement which formed the basis of path construction and innovation policy of post-TRIPS period was that India would be attracting high quality FDI, technology transfer and overseas R&D in the field of drug innovation. Based on this expectation, the policymakers were upbeat about the Indian pharmaceutical industry's prospects and its potential contribution to processes of drug innovation. There is evidence that while most analysts were clear about predicting the loss of welfare and wealth as a key consequence of implementing the TRIPs Agreement, however, their conclusion remained positive on the likely impact of TRIPS on drug innovation and the economy.

Lall and Albaladejo (2002) assessed the case for uniform and strong IPRs for developing countries as a whole by classifying them using various measures of domestic innovation and technology imports. Their generalized analysis suggests that it is possible to argue that India has now reached a stage in pharmaceutical production where stronger IPRs would induce greater innovation by local firms, though the benefits of which would have to be set off against the closure of other firms. Keely (2000) similarly concluded that the TRIPs Agreement will continue to negatively impact social welfare in most developing countries.

Analysts of pro-TRIPs Agreement have followed the route of global integration of pharmaceutical industry to make a case for the upgrading of the innovation system that will be made possible through acceptance of TRIPs. For example, Lanjouw (1998) notes that for an Indian firm taking the first steps towards new molecule discovery, the ability to lower costs by sub-contracting or by joining up with foreign firms in research joint ventures, is particularly important. Similarly, Granville and Leonard (2003) claim that since research, innovation and generics production arise from knowledge distribution and spillovers as well as property rights protection, neither trade liberalization nor TRIPs requirements are likely to suppress their spread.

Revisiting Policymaking with the Post-TRIPS Evidence on Performance

The challenge of TRIPS was tackled by policymakers in the midst of delayed external liberalization and postponement of implementation of product innovation until 2005. The observers of industry expected consolidation and predicted that there would be fewer players in the market after some time. But very few had ventured to predict the sellout of large domestic firms. This idea was entertained only in the camp that was opposed to the early implementation of TRIPS agreement and did not agree to the rosy picture being painted in respect of flows of investment in new manufacturing, transfer of new technology and R&D. This camp was in favour of strengthening the domestic demand and gearing the innovation system to undertake more of product innovation based on national strengths and needs (Abrol, 2004).

Contrary to the above discussed predictions on strong IPRs before the implementation of TRIPS, our analysis of the evidence of the post-TRIPS behaviour of Indian pharmaceutical industry seems to be clearly confirming more the apprehensions of not-for-TRIPS interest groups. Strong IPRs have not favored India with the claimed benefits of increased access to good quality FDI, technology transfer, overseas product R&D and stimulation of domestic investment in R&D for product innovation for local needs. Evidence is also how as of today domestic and foreign pharmaceutical companies do not have plans to invest in R&D on the development of medicines related to local needs of India. Their incorporation in to the emerging international division of labour is leading the domestic pharmaceutical production and the linked innovation systems to move only further away from the goal of development of medicines for developing countries health conditions.

Impact of TRIPs on FDI, Technology Licensing and R&D

While many TRIPS opponents focused strongly on access and protection of domestic market and industry, there is excitement among policymakers regarding the prospects of higher rate of growth of pharmaceutical production on account of the likely opportunity to export generics to the regulated markets. To what extent the TRIPS Agreement would offer an advantage in respect of incentivization of technology transfer or investment in manufacturing and R&D was not rigorously debated. Not much discussion was taking place regarding the kind of learning, competence building and innovation that would be encouraged should the country choose to focus mainly on the opportunity available in the regulated markets. But we are now in position to take a deeper view based on empirics. We analyze below, emerging evidence about claims made with regard to the gains that would accrue from the pathways relying on FDI, technology transfer and R&D investment from overseas.

5. Foreign Direct Investment

Contrary to the expectations of pro-TRIPS policymakers, the pharmaceutical sector's performance is worst among the sectors expected to be positively impacted in terms of FDI inflows on account of the acceptance of strong IPRs. Pharmaceuticals' ranking declined from 8th in 1991 to 13th position in 2009.[1]

Furthermore, regarding patterns of investment by global pharmaceutical firms in the Indian pharmaceutical industry, a large part of the newer investments of foreign firms in manufacturing activity has expanded formulation activity. Newer investments in the bulk drug were few and far between. The post-1999 situation is certainly now a far more permissive environment for imports. Global pharmaceutical firms have been able to increase their operating freedom. They are able to shift to import based production for a number of product segments (Abrol, 2005). Their preference for the establishment of new operations through the incorporation of wholly owned subsidiaries is also now a well confirmed tendency.

New FDI in pharmaceuticals has largely been devoted to mergers, acquisitions and takeovers to facilitate the parent firms increasing their control over the operations located in India (Abrol, 2004). Global mergers have affected the foreign pharmaceutical industry on familiar lines. Stronger control over the ownership of investments continues to be the main driver of merger and acquisition activity for the pharmaceutical MNCs in India. Bhaumik *et al*. (2003) also confirmed the same for the pharmaceutical industry in their survey of FDI in India when they suggest that MNCs investing in the pharmaceutical sector prefer green-field investment to joint venture. The government has been made to relax its laws with regard to the control of FDI. For example, earlier the Indian government used to grant permission for the establishment of 100% wholly owned subsidiaries only on the condition that the industry would be willing to take up the production of pharmaceuticals right from the basic stage of manufacture of bulk drugs involved. This is no longer a requirement.

Analysis of Activity-wise FDI

Table 6 shows that recently, research and development activities accounted for the highest number of projects carried out amongst a range of business activities, registering 36 of the overall total of 86.

However, more complete analysis of the purposes of FDI transactions shows that a large number of foreign R&D investment projects are focused on developing facilities for phase III clinical trials and other such modules that only integrate Indian talent and facilities into foreign pharmaceutical firms' global objectives. As such, these R&D projects have little to do with

Table 6: Industry Analysis – Number of Projects by Activity

Business Activities	2003	2004	2005	2006	2007	2008	2009	Total
Research & Development	2	4	10	5	8	5	2	36
Manufacturing	3	8	6	3	3	5		28
Sales, Marketing & Support		2	2	3	1	1	1	10
Design, Development & Testing		1	1		2	1		5
Business Services			1					1
Headquarters				1				1
Logistics, Distribution & Transportation					1			1
Retail		1						1
Overall Total	5	16	20	12	15	12	3	83

Source: FDI Markets Intelligence. Available at: http://www.fdimarkets.com

Table 7: Sample Characteristics of Selected Pharmaceutical Companies

Total number of listed companies in prowess database of (CMIE)	Number of selected companies in the sample		Total sales of 134 pharmaceutical companies	Total sales of selected companies	%
134	(Domestic+ Foreign)	50	55214.06 (50 Companies)	50397.46	91.27
134	(Domestic)	41	55214.06 (41 Companies)	39745.47	71.98
134	(Foreign)	9	55214.06 (9 Companies)	10651.99	19.29

Source: CMIE Prowess Database, 2009. Available at: http://www.cmie.com

the needs of local populations. Thus, the quality of FDI being attracted into pharmaceutical R&D cannot be characterized as very high.

5.1 Evidence on Technology Transfer from MNCs

During the pre-TRIPS era foreign pharmaceutical firms often exhibited in India an almost near complete aversion to technology transfer in bulk drug production. Evidence collated on the recent patterns of technology transfer from foreign firms to domestic companies shows that the results are not very encouraging for pharmaceuticals. Table 7 shows the sample characteristics for which knowledge accumulation expenditure was undertaken by the authors.

Evidence obtained on the intensity of R&D and royalty payments made by the domestic pharmaceutical and the foreign pharmaceutical firms to their own parents and local sources is also quite clear and shows that royalty figures have been extremely small for the domestic firms until now. In Table 8, it is discernible that foreign firms are still spending much less on R&D as compared to domestic firms.

Table 8: Intensity of R&D, Royalties and Marketing and Advertising, 2006-2008

CMIE Rank	Companies	R&D Intensity	Marketing & Advertising	Royalties Paid
	Foreign Companies			
	Integrated companies			
3	Ranbaxy Laboratories Ltd.	12.65	11.08	0.01
35	Merck Ltd.	0.40	5.51	3.07
	Formulation			
16	Aventis Pharma Ltd.	0.43	4.21	0.00
8	GlaxoSmithKline Pharmaceuticals Ltd.	0.47	4.61	0.01
20	Pfizer Ltd.	3.23	6.26	1.56
24	Abbott India Ltd.	0.56	3.12	0.00
28	Novartis India Ltd.	0.19	7.91	1.97
	Bulk drug			
10	Matrix Laboratories Ltd.	10.70	1.49	0.04
	Domestic Companies			
	Integrated companies			
2	Dr. Reddy'S Laboratories Ltd.	9.87	7.01	0.00
4	Lupin Ltd.	6.90	8.30	0.00
5	Aurobindo Pharma Ltd.	4.75	0.81	0.00
6	Sun Pharmaceutical Inds. Ltd.	8.98	4.23	0.00
12	Ipca Laboratories Ltd.	3.88	6.32	0.01
44	Natco Pharma Ltd.	0.00	1.64	0.00
45	Fresenius Kabi Oncology Ltd.	10.66	7.50	0.00

Table 8: (continued)

CMIE Rank	Companies	R&D Intensity	Marketing & Advertising	Royalties Paid
49	Marksans Pharma Ltd.	1.36	3.07	0.00
50	Wanbury Ltd.	3.03	3.88	0.00
	Formulation			
1	Cipla Ltd.	5.11	9.33	0.00
7	Piramal Healthcare Ltd.	4.48	4.68	0.03
9	Cadila Healthcare Ltd.	9.42	9.33	0.04
11	Wockhardt Ltd.	9.87	3.99	0.21
15	Alembic Ltd.	4.45	6.51	0.03
17	Ankur Drugs & Pharma Ltd.	0.00	0.00	0.65
19	Glenmark Pharmaceuticals Ltd.	5.24	5.64	0.00
25	J B Chemicals & Pharmaceuticals Ltd.	2.19	12.11	0.27
26	Unichem Laboratories Ltd.	4.15	10.84	0.00
27	Elder Pharmaceuticals Ltd.	0.72	5.24	0.00
29	Strides Arcolab Ltd.	8.17	2.49	0.00
30	F D C Ltd.	1.78	5.56	0.00
32	Ind-Swift Ltd.	1.56	3.37	0.00
34	Plethico Pharmaceuticals Ltd.	4.28	5.03	0.00
40	Twilight Litaka Pharma Ltd.	0.08	0.92	0.00
41	Indoco Remedies Ltd.	5.17	6.09	0.00
42	Ajanta Pharma Ltd.	6.50	6.14	0.00
47	Granules India Ltd.	0.81	1.88	0.00
	Vaccine			
22	Panacea Biotec Ltd.	11.21	3.93	0.09
	Fine chemical / biotech			
18	Biocon Ltd.	6.06	2.03	0.10
	Bulk drug			
13	Divi'S Laboratories Ltd.	1.46	0.29	0.00
14	Orchid Chemicals & Pharmaceuticals Ltd.	6.36	2.07	0.07
21	Nectar Lifesciences Ltd.	0.00	0.84	0.00
23	Surya Pharmaceutical Ltd.	3.40	0.41	0.00
31	Ind-Swift Laboratories Ltd.	13.16	1.10	0.00
33	Shasun Chemicals & Drugs Ltd.	5.50	2.40	0.12
36	Dishman Pharmaceuticals & Chemicals Ltd.	4.21	0.00	0.00
37	Sharon Bio-Medicine Ltd.	0.00	0.00	0.00
38	Aarti Drugs Ltd.	1.24	0.89	0.00
43	Neuland Laboratories Ltd.	9.09	1.41	0.00
46	S M S Pharmaceuticals Ltd.	4.47	0.80	0.00
48	Themis Medicare Ltd.	0.82	2.13	0.00

Source: Compiled from the Prowess Database of Centre for Monitoring of Indian Economy (CMIE). Available at: http://www.cmie.com

5.2 Overseas R&D

Evidence is again quite clear that the agreement on TRIPs has not succeeded in inducing the foreign firms to take up overseas R&D for the discovery and development of drugs where the Indian markets could be large. In those cases where some MNCs had located part of their global R&D outfit in India, activities have been on the decline. For instance, Barring Hoechest and Astra that carry out limited drug discovery operations still remain, while others have closed down the units that had the mandate to develop products for the benefit of local markets. Moreover, Ciba-Geigy that earlier had a large presence in R&D has now closed its R&D centre India. Similarly, Hoechest has also been reducing its R&D involvement in India. Their current strategy is to reduce the locally oriented in-house R&D investment. They are now building on the work done at these centres on natural products in European laboratories.

There is also evidence that R&D activities of MNC subsidiaries reflect more thrust on formulation R&D (or product development) compared to bulk drug R&D related process development. Their focus remains on conventional dosage forms. Although few of them manufacture NDDS, no research on NDDS is being undertaken at the subsidiaries. Tables 9 and 10 provide details of contributions made to the pattern of innovative activities undertaken for the benefit of domestic markets by foreign pharmaceutical firms from Indian soil.

India does not seem to figure much in the increased strategic R&D alliance activity of the global biopharmaceutical and biotechnology firms. Saberwal (2009) showed in her survey of alliance activity that only eight companies were involved from India *viz*. Gland Pharma, GVK Bio, Odyessey (US entity), Advinus Therapetuics, Bharat Biotech, Serum Institute, Stride, Shantha Biotech. An explanation for this trend is simple because in biopharmaceutical research the distribution of capabilities is the major determinant of the partner and the mode of alliance.

Further, at present under the route of a wholly owned subsidiary, Astra-Zeneca is the only example of drug discovery operations for tuberculosis (TB), a Type II disease. Of course, here too one needs to keep in mind that these operations were started when Astra was an independent company. In fact the Indian government induced Astra to start its operations as a joint venture with the government to work on TB related drug discovery and diagnostic work. After its merger with Zeneca the Indian operations are now taking place under the direct control of Astra-Zeneca. This is still an isolated case. Foreign firms are unlikely to establish integrated drug discovery facilities for the diseases that disproportionately affect India.

Therefore, the policy design related question is whether the MNCs should be allowed to use India merely as a cheap source of S&T manpower, and patients as a ‘listening post’. Foreign pharmaceutical firms are unlikely

Table 9: Directions of Innovative Activities of Foreign Firms, 1999-2009

Foreign companies		CMIE Rank	Compounds Commercialized	Process Patents	NDDS	NCE	MOT	New Forms of Substances	Other Products
1	Ranbaxy Laboratories*	3	71	88	20		4	109	239
2	GSK Pharmaceutical	8	4						
3	Astrazeneca Ltd	59	4						
4	Pfizer Ltd	28	3						
5	Shanta biotech	137	5						
6	Novonordisk			1		2			1
7	Alfred								1
8	Hindustan Lever/Unilever**			30			18	18	363
9	Johnson & Johnson								3
Grand total			87	119	20	2	22	127	607

Notes: CMIE – Centre for Monitoring of Indian Economy; NDDS – Novel Drug Delivery System; NCE – New Chemical Entity; Method of Treatment (MOT); Other Products included – skin products, cosmetics, oral dental care, toiletries products, antifungal, antibacterial, antimicrobial products.

* Until recently, Ranbaxy was a domestic firm.

** Pharmaceutical activities of Hindustan Lever are rather low and focuses on cosmetics.

Sources: Data on commercialization and launched compound collected from news archive search of individual pharma companies from 1999-2009, and emerging patterns of pharmaceutical innovations (process, product, NDDS, NCE, dosage/formulation/composition, salt/polymorphs/derivative) data collected from USPTO of 1992-2007. Available at: http://www.uspto.gov/

Table 10: Disease Type-wise Product R&D Activities of Foreign Firms Active in India, 1999-2009

Foreign Companies (8 Companies)	1999-2001			2002-2004			2005-2007			2008-2009			
	DISEASE TYPE												
	I	II	III	I	II	III	I	II	III	I	II	III	Total
Grand total	5			2			8	1		98	1	3	118

Notes: Type I – Cancer, cardiovascular, diabetes, metabolic diseases and so on.
Type II – Tuberculosis, malaria and so on.
Type III – Leishmaniasis, trypanosomiasis, lymphatic filariasis, leprosy, diarrhoea.

Sources: Data collected from individual website and latest annual report of individual pharma companies and Clinical Trial Registry India (CTRI). Available at: http://www.uspto.gov/

to promote India as a location for the development of system integration capacity. Since in the new drug discovery paradigm the system integration capacity is going to finally count[2] and if the development of this capacity cannot be expected to take place automatically, it is obvious that the foreign subsidiary mode in which the MNCs are now restructuring their investments should not be encouraged at all by the government in India.

But the current expectations of global pharmaceutical firms are clear. They will prefer to invest in the selected R&D operations namely bio-informatics and clinical research where, by relocation it is possible for them to cut down the R&D costs without increasing information spillovers. Available evidence from India suggests that in many cases the MNCs appear to have preferred the route of outsourcing of R&D from fully dedicated companies to reduce costs in respect of clinical trials and bioinformatics related R&D work. Presently, the choice of MNCs has been to establish fully owned R&D subsidiaries only for healthcare management and pharmaceutical services. Establishment of operations for the implementation of clinical trials, data management and biostatistics by Quintiles, a leading pharmaceutical service provider, is an example.

6. Technology Acquisition by Domestic Firms

The claimed benefit of increased technology transfer to domestic firms is also yet to accrue in the case of India. Foreign technical collaborations have not been important for export, yet many small and medium scale firms have entered into collaborations with foreign firms primarily to cater to the domestic market. Production capabilities can certainly improve on account of enforcing Good Manufacturing Practice (GMP) in the case of some firms. Analysis indicates that though players like Matrix Laboratories, Divi or Shasun Chemicals or Cadilla have made much use of this opportunity to grow, their technological capabilities have not been upgraded through the provision of contract manufacturing services. Recently the USFDA warned the third drug company working from India for the US market, Matrix Laboratories, about their manufacturing practice.[3]

There is also evidence that as far as terms and conditions of contract manufacturing of bulk drugs are concerned, in the post-TRIPS scenario deals being entered into by Indian firms are far from mutual. Ranbaxy Laboratories and Lupin Laboratories were among the first Indian companies to bag manufacturing contracts from multinational companies-Ranbaxy from Eli Lilly and Lupin from Cynamid. Pre-TRIPS, contracts for manufacturing came through when Ranbaxy developed an alternative process for manufacturing 7 ACCA, Eli Lilly's intermediate for its patented drug Cefaclor. The American Company had sensed it would lose its markets to Ranbaxy's low

Table 11: Pharmaceutical Companies in CRAM Activities in India

Companies in Contract Research (excluding Clinical Trials)	Clinical Trials
Nicholas Piramal	Clingene (Biocon)
Aurigene (Dr. Reddy's)	Jubilant Clinsys (Jubilant Organosys)
Syngene (Biocon)	WellQuest (Nicholas Piramal)
GVK Biosciences	Synchron
Jubilant Organosys	Vimta Labs
Divi's Laboratories	Lambada
Suven Lifesciences	Siro Clinpharm
Dr. Reddy's Laboratories	Relience Life Sciences
Vimta Labs	Asian Clinical Trials (Suven Life Sciences)

Source: *Annual Report of International Disease Management Alliance (IDMA) 2007*. Available at: http://www.idma-assn.org/

cost substitute in countries that did not recognize product patents and acted so as to make the best of a bad situation. But of course Ranbaxy is no more an Indian company, having been sold to Daichi Sankhyo, a Japanese MNC. Today the situation is changed due to the implementation of TRIPs. Take the example of Nicholas Piramal, which entered a joint venture (49:51) with Allergan Incorporated, USA to earn business for the manufacturing of bulk drugs. It is also carrying out negotiations with the UK based Baker Norton to earn business in the form of contract manufacturing. So it seems that growth in contract manufacturing will come from the efforts of companies such as Divi, Sashun and Nicholas Piramal India (now taken over by Abbot Laboratories, USA), which have been willing to accept even 'subordinate relationships' in their collaborations for contract manufacture. Table 11 provides a glimpse into the pattern of CRAM activities being undertaken by large domestic pharmaceutical firms since India's adoption of the TRIPS Agreement.

Indian pharmaceutical firms cannot assume the traditional pharmaceutical generics opportunity will fall in their lap. As the evidence shows, even in bio-generics a tough fight is waiting for the industry. The recombinant products market has been led so far by imports of established global brands and marketing of the products either by local subsidiaries (SmithKline Beecham, Novo), or through marketing arrangements as in the case of Nicholas Piramal and Roche. Though changes have come due to the recent introduction of local firms, such as Shanta, Bharat, Panacea and Wockhardt in the Indian market for products like Hepatitis B Vaccine, Interferon-alpha, insulin and EPO,

the situation was to change quite radically after January 1, 2005. As already discussed earlier, the Indian policymakers should expect litigations to grow in the case of bio-generics. The Indian industry is getting a taste of this at an early stage. Almost all the export oriented Indian firms have recently faced this challenge in the US.

Domestic Firms' R&D

Studies differ in their degree of optimism with regards to positive effects of stronger patents on product development by local firms based on disclosed foreign patents and on additional R&D efforts. Only a handful of domestic firms have been able to increase their R&D investments. Some of these have earlier demonstrated that with the help of public sector research they can devise their expertise in creating new processes for patented products. Dr. Reddy's domestic Group was the first company in filing two product patent applications for anti-cancer and anti-diabetes substances in the US. But it is also clear that Dr. Reddy's Group does not want to engage autonomously in drug development. It is interested in selling its rights to partners abroad because it does not have capacity to invest beyond the stage of drug discovery work. Examples of Wockhardt joining hands with Rhein Biotech GmbH, Germany, and Ranbaxy shaking hands with Eli Lilly for development work, Cipla undertaking custom synthesis, collaborations with Japanese and Swiss firms, indicate the limitations of and opportunities available to Indian firms.

Today as the situation stands in India the in-house industrial pharmaceutical R&D is largely directed to the needs of the western markets and much less to undertaking Type III R&D meant for neglected diseases of the poor in developing countries. This is clear from the overwhelming nature of evidence available at a glance in Tables 12, 13 and 14. But there is more to the evidence available here. These Tables also show that while all the important developments that we see in the creation of R&D capabilities for drug discovery and development within Indian firms have a far more global market favouring R&D orientation, the pattern of their R&D activity apparently indicates that their inventive activity is still better distributed in favour of domestic burden disease as compared to foreign firms.

At the moment, biotechnology dynamics in India seems to be much dependent on the overall movement of internationalization of R&D. Contract research is becoming one route through which domestic pharmaceutical companies are trying to build their competence in drug discovery and clinical research. Outsourcing markets in clinical trials are growing rapidly. The contract research scene is also livening up in drug discovery. Because of very many short-term benefits it is obviously quite tempting to direct the industry totally or mainly for these markets in countries like India.

Table 12: Disease Type-wise Product-Specific R&D Activities of Domestic Firms Active in India, 1999-2009

Domestic Companies	1999-2001			2002-2004			2005-2007			2008-2009			
	DISEASE TYPE												
	I	II	III	I	II	III	I	II	III	I	II	III	Total
Orchid Pharmaceuticals Ltd				2			6			2			10
Sun Pharmaceutical Ltd							2			7			9
Biocon Ltd				2			4			6			12
Glenmark Pharmaceuticals Ltd				1			5		1	7			14
Bharat Biotech Ltd								1	1	3		2	7
Alembic Ltd													–
Dr. Reddy's Laboratories Ltd				7			2	1		15			25
Lupin Ltd	1				1		4	4		4		1	15
Cadila Healthcare Ltd							3	1		9			13
Piramal Healthcare Ltd							7			5			12
Wockhardt Ltd							1			2			3
Ipca Laboratories Ltd										2	2		4
Aurobindo Pharmaceutical Ltd													-
Torrent Pharmaceuticals										1			1
Ajanta Pharma										7			7
Natco Pharma										2			2

Table 12: (continued)

Domestic Companies	1999-2001			2002-2004			2005-2007			2008-2009			
	DISEASE TYPE												
	I	II	III	I	II	III	I	II	III	I	II	III	Total
Granules India Ltd										1			1
SMS Pharmaceutical										10			10
Shanta Biotech							3		2	10	1		16
Panacea Biotech												2	2
Matrix Laboratories										3			3
Grand total	1			12	1		37	7	4	96	3	5	166

Notes: Type I – Diabetes, cancer, metabolic diseases, hepatitis, influenza, cardiovascular, infectious diseases, inflammatory diseases, allergy, respiratory diseases.
Type II – HIV/AIDS, tuberculosis, malaria.
Type III – Leishmaniasis, trypanosomiasis, lymphatic filariasis, leprosy, diarrhoea.

Sources: Data collected from individual website and latest annual report of individual pharmaceutical companies and Clinical Trial Registry India (CTRI).

Table 13: Clinical Phases of Compound for Various Diseases by Foreign and Domestic Pharmaceutical Industry, 2007-2009

Company	Disease Type			Status of Trial/Phases			
Domestic Firms	Type I	Type II	Type III	Phase I	Phase II	Phase III	Phase IV
(16 Companies)	65	3	2	5	20	35	9
Foreign Firms	Type I	Type II	Type III	Phase I	Phase II	Phase III	Phase IV
(9 Companies)	110	3	3	12	23	12	9

Notes: Type I – Diabetes, cancer, metabolic diseases, hepatitis, influenza, cardiovascular, infectious diseases, inflammatory diseases, allergy, respiratory diseases.
Type II – HIV/AIDS, tuberculosis, malaria.
Type III – Leishmaniasis, trypanosomiasis, lymphatic filariasis, leprosy, diarrhoea.
Phase I, Phase II, Phase III, Phase IV – Status of involvement of domestic and foreign firms in the trials.

Source: Clinical Trial Registry Analysis (CTRI) 2007-2009. Available at: http://ctri.nic.in/Clinicaltrials/index.jsp

Table 14: Pharmaceutical Projects and Patents and the Pattern of Matches with the National Burden of Disease, 1992-2007

No.	Major Therapeutic Areas/ Disease/ Health Conditions	Share in the Total Burden of Disease (%)	Domestic Companies Pharmaceutical Project (%)	Foreign Pharmaceutical Project (%)	Domestic Pharm Cos. Patents as (%) of Total Domestic Patents	Domestic Pharm Cos. Pharmaceutical Patents Percentage (%) of Total Patents	Foreign Cos Pharmaceutical Patents Percentage (%) of Total Foreign Patents	Foreign Cos Pharmaceutical Patents Percentage (%) of Total Patents
1	Diabetes	0.7	17.15	16.36	5.94	5.91	20	0.084
2	Cancer	3.4	10.05	8.81	5.6	5.57		
3	Tuberculosis	2.8	1.18		0.50	0.50		
4	Malaria	1.6	2.36		0.93	0.92		
5	Metabolic disease	–	7.36	0.9	6.79	6.76	20	0.084
6	HIV/Aids	2.1	0.59	0.23	0.84	0.84		
7	Inflammatory diseases		3.55	0.67	5.6	5.57		
8	Infectious disease/Injuries	16.1	8.28	4.54	38.96	38.79		
9	Respiratory diseases	1.5	4.73	5.61	1.1	1.09		
10	Arthritis	–						
11	Bone disease	–	4.73	6.63	1.27	1.26		
12	Brain disorders	8.5		0.56	10.18	10.14	40	0.16
13	Ulcer	–			0.5	0.50		
14	Psoriases	–			0.33	0.33		
15	Cardiovascular	10.0	0.59		2.63	2.78	20	0.084
16	Maternal & prenatal problems	11.6	1.34		0.25	0.25		
17	Diarrhoea	8.2	1.77		0.08	0.084		
18	Heart Disease	–			0.93	0.92		

Table 14: (continued)

No.	Major Therapeutic Areas/ Disease/Health Conditions	Share in the Total Burden of Disease (%)	Domestic Companies Pharmaceutical Project (%)	Foreign Pharmaceutical Project (%)	Domestic Pharm Cos. Patents as (%) of Total Domestic Patents	Domestic Pharm Cos. Pharmaceutical Patents Percentage (%) of Total Patents	Foreign Cos Pharmaceutical Patents Percentage (%) of Total Foreign Patents	Foreign Cos Pharmaceutical Patents Percentage (%) of Total Patents
19	Depression	–			3.56	3.55		
20	Hypertension	–		10.12	4.49	4.48		
21	Allergy	–			1.78	1.77		
22	Hepatitis	–		1.81	0.16	0.16		
23	Leprosy	0.1						
24	Childhood disease	5.4						
25	Otitis Media	0.1						
26	Blindness	1.4						
27	Oral diseases	0.5						
28	Prosthetic hyperplasia	–			1.01	1.014		
29	Others	25.4	30.17	18.18	6.45	6.42		

Source: USPTO from1992-2007, company websites and data available on the Burden of Disease from GOI. http://www.uspto.gov/

Emerging Relations of Public Sector R&D with Domestic Firms

On the issue of emerging relations of public sector R&D with industry, the main challenge is that public sector R&D institutions maintain a long term vision and strategy directed by public health priorities of the Indian nation whose citizens have a first claim on their outcomes. Table 15 shows the current status of matches and mismatches of R&D priorities under perusal with the priorities of burden of disease in the public sector. It appears there are too many mismatches to be taken care of. This reflects a clear systemic failure which is seemingly connected with the determination of disciplinary priorities of the Indian scientific community in the west and the decisions of the government to subject the public sector to short term demands of the private sector post-TRIPS.

Public-Private Partnerships (PPPs) is the latest buzzword in health research and technology development. In India, the New Millennium Indian Technology Leadership Initiative (NMITLI) of the Council of Scientific and Industrial Research (CSIR), the Drugs and Pharmaceuticals Research Programme (DPRP) and the Technology Development Board (TDB) of Department of Science and Technology (DST) and the Small Business Innovation Research Initiative (SBIRI) of Department of Biotechnology (DBT) constitute the main examples of public private partnerships. Strong experience has been gathered through these schemes in respect of the determinants of success in implementing PPPs. A large number of NMITLI-based PPPs have preferred to catalyze health innovations only as a vehicle for the domestic industry to attain mainly global leadership positions in selected niche areas by synergizing the best competencies of publicly funded R&D institutions, academia and private industry. In the last six years NMITLI has supported 42 R&D initiatives in various fields including new targets, drug delivery systems, bioenhancer and therapeutics for psoriasis, tuberculosis, pain management in osteoarthritis, insulin sensitization in diabetes mellitus type II and process of tamiflu and so on, with about 287 partners, 222 in public sector and 65 in private sector with an estimated outlay of over Rs300 crore. Analysis of SIBRI efforts (37 cases till May 2008) shows that there is not much focus on diseases of Indian interest though a couple of cases pertain to malaria and typhoid. Similarly, in the case of DPRP, it is also known that the government had to add a special grant-in-aid programme for the promotion of research on neglected diseases because in the earlier years the programme was unable to attract domestic companies to work on these areas.

Conceived in 2003 the Golden Triangle partnership is also now receiving special budgetary support for an integrated technology mission focused on the development of Ayurveda and traditional medical knowledge that synthesizes modern medicine, traditional medicine, and modern science. In this way efforts on traditional medicine have also picked up momentum.

Table 15: Comparison with Disease Burden of Public Sector Projects, 1992-2007

No.	Major Therapeutic Areas/Disease/ Health Conditions	Share in the Total Burden of Disease (%)	IMR Projects (%)	EMR Projects (%)	Public Sector Patents as Percentage (%) of Total Patents
1	Diabetes	0.7	2.08	8.29	5.96
2	Cancer	3.4	12.71	19.21	13.1
3	Tuberculosis	2.8	8.30	12.66	6.37
4	Malaria	1.6	10.38	5.24	9.87
5	Metabolic disease	–			4.73
6	HIV/Aids	2.1	8.43	10.26	9.85
7	Inflammatory diseases				2.05
8	Infectious diseases/ Injuries	16.1			24.27
9	Respiratory diseases	1.5		1.74	2.26
10	Bone disease	–		2.35	1.4
11	Brain disorders	8.5		4.71	2.26
12	Ulcer	–			
13	Psoriasis	–			
14	Cardiovascular	10.0	1.43	2.18	4.11
15	Maternal and prenatal problems	11.6	5.96	3.02	5.25
16	Diarrhoeal diseases	8.2	0.26	1.39	0.20
17	Heart Disease	–			
18	Depression	–			0.41
19	Hypertension	–			2.26
20	Allergy	–			
21	Hepatitis	–	3.37	5.02	2.44
22	Leprosy	0.1	4.15	3.93	2.24
23	Childhood disease	5.4	2.52	1.21	0.41
24	Otitis Media	0.1			
25	Blindness	1.4			0.2
26	Oral diseases	0.5			0.3
27	Prosthetic hyperplasia	–			
28	JE		3.11		0.61
29	Dengue		3.11	0.43	0.41
30	Leishmaniasis		9.86	4.80	3.29
31	Others	25.4	23.48		12.1

Source: Developed by the authors from the public databases on R&D projects and patenting activities being undertaken by the public sector R&D organizations in India, 2009.

The CSIR and ICMR are working with the Department of Ayurveda, Siddha, and Homeopathy to bring out safe, efficacious, and standardized classical products for identified disease conditions. New Ayurvedic and herbal products for diseases of national/global importance are also being pursued. Innovative technologies are being used to develop single and poly-herbal-mineral products, which have the potential for IP protection and commercial exploitation by national/multinational pharma companies. Areas identified are limited to mainly rasayana (rejuvenators/immunomodulators) for healthy aging, joint disorders, memory disorders, bronchial allergy, fertility/infertility, cardiac disorders (cardio-protective and antiatherosclerotic), sleep disorders, and diabetes. This ambitious multiagency programme proposes to spend more than Rs350 million in the next three years. Several areas have already been identified and research is underway.

Evidence collated as a part of the preliminary health research system analysis (HRSA) undertaken, has confirmed important gaps and mismatches in many specialties, narrow research bases in many areas, fragmentation of research effort, lack of coherence, development gaps, competence in biology for drug discovery work being inadequate, etc. Some examples of research imbalances are indicated here. The health research system is lacking in capacity for learning and reflection. Mechanisms must be created for a systematic health research system analysis to be undertaken on a periodical basis by the Department of health research. The government is yet to give attention to creating this capacity. Other issues also require addressing for the promotion of R&D-S&T departments' extra mural research priorities, stability of funding, network development and access-related IP management issues. It appears that besides the importance of increasing research efforts on neglected diseases in India, one can talk of underdevelopment of toxicology research, drug development for treatment of arsenic and lead. There are about 1,000 qualified occupational health professionals in India and only 100 qualified hygienists. The country needs close to 8,000 qualified occupational health professionals, a tremendous gap between need and availability.

Dependence of Neglected Disease R&D on External Factors

Recently India has also witnessed a spurt in research investments for neglected diseases. But much of this increase has resulted from external influences. Some of the international partners include (i) WHO Special Programme for Research and Training in Tropical Diseases (TDR), (ii) the Global Alliance for Tuberculosis Drug Development (TB Alliance), (iii) the Medicines for Malaria Venture (MMV) for Malaria vaccine, (iii) the International AIDS Vaccine Initiative (IAVI) for HIV/AIDS Vaccine, (iv) the Institute for One World Health (IOWH), (v) Drugs for Neglected Diseases Initiative (DNDi) for

sleeping sickness, Chagas disease, leishmaniasis, and malaria, (vi) Programme for Applied Technology for Health (PATH) for JE vaccine, (vii) Concept Foundation for microbicides, etc. The MMV is collaborating with Ranbaxy for developing anti-malarials. The IOWH is collaborating with the ICMR in the clinical trials of paromomycin for visceral leishmaniasis.

Earlier in 2003-2004, for the segment of neglected Type III diseases India had also taken another important initiative for developing new generation vaccines for cholera, malaria, tuberculosis, Japanese encephalitis and HIV/AIDS. Projects initiated as a part of Jai Vigyan programme of the Ministry of Science and Technology are known to be following a different route of PPPs where the collaboration in technology development involves collaborating with advanced world partners for technology transfer. Under this initiative the government had also signed a number of technology licensing agreements to obtain technologies required for tackling diseases of the poor. Although at the moment the future of pharmaceutical production innovation appears to be in a critical way in the hands of these companies' potential partners abroad, the outcomes of public sector R&D can be leveraged to align their priorities with public health goals if the pathways and models of innovation are redirected suitably. From the above analysis it is also clear that the leadership was so far quite willing to subject the priorities of public sector R&D organizations to short term priorities of the domestic industry during the post-TRIPS period. Leadership of the scientific community clearly only chose to give a higher priority to the R&D work to be undertaken on the problems of ageing disorders, psoriasis, rejuvenates and so on rather than putting money into products for neglected diseases (Type III).

7. Conclusion

Contrary to policymakers' expectations the pathway of growing global integration is failing to generate the 'best case conditions' predicted to be prevailing for upgrading the pharmaceutical sector for the benefit of public health in India. Even what was expected to be the responsibility of the institutional sector has not been realized for biomedical research during the post-TRIPs Agreement period. Progress in coordinating efforts for knowledge generation in the institutional sector for the benefit of drug innovation has been tardy. The main pathways to learning and innovation that Indian policymakers have constructed via the development of in-house capabilities of the pharmaceutical industry are yet to be subjected to monitoring and evaluation. Channels of interaction for learning, competence building and innovation are therefore, still mainly subject to the push and pull for innovation efforts arising out of the strategies of domestic and foreign pharmaceutical firms.

The industry is shown to be in urgent need of creating complementarities and linkages to establish new pathways of growth with a view to impacting processes of learning, competence building and innovation. Steps considered necessary to bring about a radical change in the impact of active policies under implementation include the tasks of domestic market building, dealing with information externalities arising out of weak institutional research base and remedying the coordination failure and various other such problems of promotion and regulation of technology development.

Despite recent developments, drivers of funding for health research in favour of Type III diseases and traditional medicine, the enabling environment to steer and coordinate, manage, appraise, articulate demand and appropriate IPRs is still missing. Strong IPRs is one of the most important institutional changes that Indian policymakers can expect to come in the way of knowledge diffusion. Their adverse effect on the size of market for local firms has to be suitably alleviated. Markets for knowledge and technology are by no means neutral space. Policy interventions for industrial upgrading have to take into account that there is an international division of labour being constituted through outsourcing. Innovation systems must stay clear of the traps that this division of labour is laying down for domestic firms.

There are limits to market growth through generics and contract work in research and manufacturing. These can be used to supplement the strategy of expanding the domestic market, but to mainly depend on them for further growth would take domestic firms away from real needs-based innovation. There would not even be much increase in the domestic private sector's R&D expenditure. In the face of more opportunities for short-term gains very few firms would have the incentive to compete with their international partners. It is likely that most would ultimately settle down to accept the role of junior partners in the new game of proteomics and genomics based innovation wherein the R&D platform/tools are already monopolized via strong IPRs.

Prospects for domestic R&D for neglected diseases and conditions would improve only under conditions where the constraint of market size has been suitably eased for the benefit of local pharmaceutical firms. To alleviate the constraint of small market size the Indian government must step in to also improve demand conditions. Recently health expenditure has been declining across the board in India, a direct consequence of the implementation of neoliberal fiscal strategy. It is too much to expect domestic pharmaceutical firms whose revenues are insecure, to contribute to R&D investment for neglected diseases under this situation.

Policymakers will have to also seek significant changes on the side of supply of innovation capacities if their new strategies for industrial upgrading are to obtain significant success. The private sector needs to coordinate with the public sector in creating a programme for upgrading innovation capacities

to play a positive role in developing drugs for the diseases of the poor. Direct support for R&D and facilities for clinical trials must be targeted. Domestic firms should not be incentivized for inappropriate product targets. Dependent relationships being forged through excessive reliance on low quality contract work in both manufacturing and research would have to be discouraged.

Finally, policymakers would have to try getting domestic firms to concentrate their efforts on real needs-based innovations and those strategies that would largely free Indian firms from getting into dependent relationships with foreign firms. With the intervention of public sector agencies the situation can change and head for the better. It is possible to conceive a route of public-private partnership to give momentum to pharmaceutical discovery and development research that would take care of national public health priorities and neglected diseases of the poor of the developing world as a whole. Experiencing the world-wide practice of negative innovation emanating from the pharmaceutical sector under the strategy of 'innovation for profit', the Indian policymakers have a social responsibility to ensure that health sciences institutions remain geared to producing more public goods rather than market goods. In particular, they have a duty to use the instruments of public sector R&D and governmental support for innovation to the private sector in a targeted way. It is essential to plan, monitor and evaluate public sector R&D institutions on the basis of public health priorities. The results would tend to benefit public health if the agency is determined to pursue the roadmap for developing products that are required locally and have the support of public health systems.

Notes

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1. Fact Sheet on FDI, August 1991 to April 2009, Annex – B, Department of Industrial Promotion and Policy, Government of India, pp. 8-10.
2. Nightingale (2000) emphasizes this by suggesting that the learning of system integration skills is a pre-condition of further competition in the development of innovative drugs in the global pharmaceutical industry today.
3. In the area of manufacturing, India ranks only second to the US in terms of the yearly number of global Drug Master Filings (DMF). DMF is the permission granted to enter the US bulk activity market with the objective of either supplying to a large US generics player or captive consumption. DMFs by Indian companies rose to 19 per cent of the world filings in 2003 compared to 2.4 per cent in 1991. For the April-June 2003, India accounted for 34 per cent of the world's filings.

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