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TRIPS and its possible impact on the Indian biopharmaceutical industry

By

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ABSTRACT

Many countries of the world, including India, have achieved self-sufficiency in knowledge intensive sectors by allowing for a loosely defined intellectual property regime (IPR). The implementation of TRIPS worldwide essentially represents a big step in the opposite direction as it refers to a tightening of national IPR systems. Its impact on the production and innovative capacity of developing countries, in knowledge intensive sectors is not at all clear. Taking India as a representative of a technologically advanced developing country, and biopharmaceuticals as an example of an emerging knowledge intensive sector, we examine the possible impact of TRIPS on the incentives to innovate. We conclude that TRIPS is not likely to have a significant impact on the incentives for innovation creation. The analysis is based on field interviews carried out by the authors.

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Introduction

Consider a developing country with an excess demand and a significant technological retard in a knowledge intensive sector. In order to provide the incentives for local firms to invest in R&D and either "re-engineer" or "independently develop" the knowledge intensive commodity, a necessary (but not sufficient) condition would be to provide for a weak intellectual property regime or IPR. The capacity of the developing country to realize its objective would then depend on its national system of innovation, including its existing scientific and technological competencies. Such a move towards a loosening of the IPR, might be *welfare enhancing*, if it leads to greater quantity being produced or a lowering of price in the final market. It might be welfare enhancing even at a global level, if other developing countries are able to thereafter obtain the generic versions of the knowledge intensive commodity more easily or at lower prices.

On the basis of arguments such as the above, many developing countries, including India, adopted a weak IPR in the latter half of the last century. This expedient was not something invented by the governments of developing countries, but a practise common to many developed countries as well during their periods of "technology catching-up". In the above context, TRIPS or the Trade Related Intellectual Property Rights System to be enforced by the World Trade Organization (WTO) on all its member countries from 2005, represents a move in the completely opposite direction. Its possible impact on welfare in developing countries is not at all clear. Thus, the objective of the present paper is to provide some insight on the above issue, by examining *the impact of TRIPS* on the *production and innovative capacity* of a developing country with a relatively strong national system of innovation[1], namely India, with respect to a highly knowledge intensive, emerging sector, such as biopharmaceuticals.

The case study of Indian pharmaceutical sector is particularly interesting for the debate on the impact on TRIPS on the innovative capacity of developing countries, because it has been clearly shown by many researchers (to be detailed later) that India could not have become self-sufficient and provided healthcare to its poor without changing its IPR system. India changed its patent law in 1970 to provide for process rather than product patents in pharmaceuticals and food products. This led to an augmentation of domestic capacity and competence, providing access to drugs at affordable not only within India, but also in other developing countries, which began to import from Indian firms.

Now the pharmaceutical sector itself is undergoing a revolutionary paradigm shift in all parts of the developed world --- from the creation of drugs based on chemical engineering to those based on biotechnology[2]. Biotechnology is expected to yield drugs for the maladies of the 21st century, such as cancer and AIDS as well as solutions to diseases plaguing the third world such as malaria and tuberculosis.

Given that the shift in the technology paradigm is coinciding with the equally significant change in the IPR regime, there is concern about whether TRIPS, a move totally in

[1] Countries in this set include those such China, India and Brazil, Cuba, Mexico, Tunisia etc. which have a strong scientific base.

[2] Modern biotechnology refers to techniques that involve an understanding, a mapping, a manipulation or a change of the genetic patrimony of a living organism (e.g. genetic engineering). These techniques have emerged since the last 25 years following breakthroughs in the biological sciences. They have led to the creation of new products, new processes and new methods of research in various industries among which the pharmaceuticals industry ranks as being the most prominent, the others being chemicals, agriculture and the environment.

reverse of the Indian Patent Act of 1970, will undermine the innovative capacity of the thriving Indian pharmaceutical sector or hinder its participation in the biotechnology revolution. On the other hand, some feel that it is equally plausible that the Indian national system of innovative has evolved sufficiently to take advantage of the strengthening of the IPR system. This view is particularly supported by the clear success of India, in market based, high-tech domains, such as generics and software.

In order to find out which of the above views is likely to be more probable, the present paper examines the following two questions:

- What are the different types of strategic positioning of Indian firms in the biopharmaceutical sector?
- For firms in the different categories, will TRIPS increase or decrease the incentives for the creation of new innovations?

We try to simply assess whether TRIPS will increase or decrease the incentives for investment in innovation in the Indian bio-pharmaceutical sector, without trying to estimate the order of magnitude of change. A more precise answer would require having data on the R&D strategies of a representative sample of firms in the Indian pharmaceutical sector, as well as information on the future strategies of potential entrants in the Indian pharmaceutical sector from the Western world. At the moment, such information is not available.

Our answer is also limited by the fact that the information used to formulate the arguments in this paper comes from about 40 interviews conducted by the two authors[3]. The companies interviewed included many leading firms, which are well known in the Indian market for their technological achievements. However, since the sector houses a set of very heterogeneous firms and is evolving rapidly, it is not possible to ascertain whether our sample is representative or not.

Our central proposition is that TRIPs is unlikely to have a significant impact, either positive or negative, on the creation of innovations by Indian biopharmaceutical firms (other than disallowing them to launch patented products on the market).

The contribution of the present paper to the literature dealing with the impact of TRIPs on the incentives for innovation creation may be viewed as follows. The existing studies on India pertain either to all manufacturing sectors or to the entire pharmaceutical industry. While they have the advantage of providing some indicators for policy, it is not clear whether their conclusion should hold for all segments of the pharmaceutical industry. By identifying the specific product segments and their characteristics, we are able to conclude that with respect to the biopharmaceutical sector TRIPs is not likely to affect the incentives for innovation creation.

The paper is organized as follows. Section 1 sets the background by discussing the literature on the Indian pharmaceutical sector and the possible impact of TRIPS on the pharmaceutical sector of developing countries. Section 2 presents the specificities of the biopharmaceutical sector. Section 3 presents the answer to the first question. Section 4 contains the answer to the second question. Section 5 concludes.

[3] This paper uses the information generated by 30 interviews with firms in the biopharmaceutical sector conducted by Augustin Maria during the summer of 2002. This is part of a report that can be found on the website www.cerna.ensmp.fr/Documents/AM-JR-MHZ-BiotechReport.pdf. It also uses the information obtained from about 10 interviews conducted by Shyama V. Ramani conducted during 1998-1999.

1. Setting the background

1.1 Impact of the Indian Patent Law of 1970

Just after independence in 1947, in India, there was no pharmaceuticals industry to speak of. Thereafter, during the 1950's and 1960's, a pharmaceutical sector developed, consisting mainly of Western pharmaceutical giants and Indian public sector mammoths. However, even the Indian public sector combined with the Western pharmaceutical companies could not cater to the demands of the Indian population. Moreover, in order to ensure access to drugs, the government pegged prices at affordable levels, not lending much incentive for the expansion of the production base. In short, there was a crisis in terms of provision of health care.

There were two possible solutions to this health care emergency. Either medicine could be imported in large quantities as essential commodities or incentives could be provided for the development of the local pharmaceutical industry. The Indian Government opted for the latter. Following the strategy adopted earlier by Japan, China, Russia and Eastern Europe and Southern Europe, the existing intellectual property rights regime (IPR), which was based on the British model of that time, was changed. From 1970 onwards, instead of according product patents, the new IPR regime began to recognize only process patents. Initially, this was not opposed by the Western multinationals, as they did not view the Indian market to be capable of producing threatening competitors.

The impact of the change in IPR was simply tremendous. Many Indian pharmaceutical firms were able to produce essential drugs like antibiotics with a heavy slashing of prices. Indian consumers revealed themselves to be price sensitive rather than being brand loyal to Western brands. The market shares changed tremendously, bearing witness to the downfall of the previous market leaders, mainly Western multinationals. Most importantly, the public Indian health care system was finally able to stand up on its feet and there was a significant increase in the proportion of the poor who had access to basic drugs. Indian firms even entered into production contracts with the original multinational inventors and some medicines were provided at lower costs to the rest of the world. India also became an exporter to other developing countries. (Ramani and Venkataramani, 2001).

The above case study reveals that an IPR system favouring access to modern technology can have a significant impact on augmenting industrial competence in a developing country, albeit one with a strong scientific base.

1.2 TRIPS

A weak IPR regime in developing countries leads to losses from "re-engineered products" for the original innovators, namely the Western multinationals and lowers the incentives for local developing country firms to undertake basic R&D themselves. Thus, the countries of the triad, the U.S.A., Europe and Japan, have been working towards the global harmonization of IPR regimes since the last two decades. TRIPS is one of the culmination of their efforts.

The countries initiating TRIPS based their actions on the presumption that a strong IPR regime is a critical pre-condition for private investment in research and development, and hence economic growth. They contend that an expanded and strengthened protection of IPRs would bring about increased flows of foreign direct investment and technology transfer to developing countries. It would also stimulate local innovation. Finally, it would also enable the multinationals of the developed countries to recuperate markets from local imitators. The developing world is, on the other hand, not so confident about reaping benefits from this

global IPR regime, since having access to technological knowledge is perceived as being crucial for economic growth.

As a signatory to the Uruguay round of GATT, which concluded in 1994, India was obliged to meet all provisions of the Trade Related Aspects of Intellectual Property Rights (TRIPs) 4. A transition period was accorded to developing countries depending on their state of development. India availed itself of the complete term of this transition period i.e. 10 years, to set up an IPR system in compliance with TRIPS.

The main elements of change in the Indian patent system are :

- Enforcement of product patent protection in all branches of technology, including drugs.
- 20 years of protection instead of 14 or 7 in the case of the Indian patent Act.
- No discrimination between imported and domestic products.
- Accommodate compulsory licensing5 (though no country south of the equator has yet used this clause).

There exists an extensive literature on the possible impact of TRIPs on developing countries. They deal with this problem along different lines, examining the impact on: incentives for R&D for local firms, foreign direct investment, technology transfer through foreign collaborations, market demand, final prices in the market, policies for improving distribution etc. Here we mention only those articles dealing with the *impact of TRIPs on the innovative capacity of Indian pharmaceutical firms*.

Lanjouw (1997) presents the results of a field survey conducted in order to assess the impact of the introduction of pharmaceutical product patents in India and her main conclusions can be summarized as follows. First, the profits made from producing generic drugs will decrease for Indian firms, as they will probably have to pay some of royalty to the original innovators. Second, the incentives for investment in R&D in diseases pertinent to developing countries, as well as in the creation of innovations in general, is likely to increase. However, this may be simply due to the fact that the strategy of imitation is no longer available, rather than being a direct incentive effect. Third, stronger IPR would not augment the R&D activity of foreign firms in India, since in multinationals pharmaceutical R&D is a highly centralised process, where cost is not the paramount concern.

Lall (2003) reviews the case for uniform and strong IPR by developing country classifications using various measures of domestic innovation and technology imports. This indicates that for India, "it is possible to argue, however, that India has now reached a stage in pharmaceutical production where stronger IPRs would induce greater innovation by local firms (the benefits of which would have to be set off against the closure of other firms)".

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[4] WTO, 1994. TRIPS: Agreement on trade-related aspects of intellectual property rights. *Annex 1C of the Marrakesh Agreement establishing the world Trade Organization, 15 April 1994.*

[5] The Compulsory Licensing provision: it is stipulated in the TRIPs agreement that in certain situations of national emergency, certain patents can be subject to compulsory licensing. This means that the owner of the patent has the obligation to propose licensing for this patent at a reasonable cost. This provision is the cause of many uncertainties concerning the actual enforcement of intellectual property on certain drugs. Indeed, many people argue that AIDS epidemic in most developing countries should be considered as a situation of emergency. This would justify the enforcement of the Compulsory Licensing provision. More over, the judges of what is a “reasonable cost” should be the concerned states. Therefore, Compulsory Licensing could be a way for certain states to impose the selling of a license on recent AIDS therapies at a low cost to national pharmaceutical companies. More likely, the lack of agreement between the states and the companies would allow the state to neglect the protection on the patent and allow domestic company to produce a similar drug if they succeed in developing it.

Thus, the literature on TRIPs indicates that it is likely to have a positive impact on the incentives for innovation creation.

1.3 The nature of the biopharmaceutical sector

The biopharmaceutical sector refers to firms that have incorporated biotechnology either in their production processes or in their R&D programs or are selling biotechnology based pharmaceutical products.

There are basically three types of products in the pharmaceutical market: drugs, vaccines and diagnostics. The scientific and technological foundation of drug production is the most complex and the regulation is the most stringent. Vaccines are easier to create and produce, but these also have to pass stringent regulation. Diagnostics are easier to fabricate and since they usually only involve interaction of a body fluid or waste with the product (rather than being imbibed by a person), the approval process is less severe.

Creation of a new pharmaceutical product usually involves five steps:

(i) R&D, creation of the drug and getting IPR;
(ii) Pre-clinical and clinical testing;
(iii) Getting market approval from the regulatory authorities;
(iv) Scaling up the production;
(v) Marketing the new product.

Prior to the emergence of the first biotech firms leading innovators in the pharmaceutical sector created their innovations in-house. In other words, step (i) was internalized, though they did have research contracts with public laboratories.

The first biotech firms, were dedicated biotechnology firms (DBFs) created during the late 1970's in the U.S.A. By "dedicated" they signaled that their production processes involved only biotechnology. The two dominant technologies available during the 1980's were rDNA and monoclonal antibodies technology. This basically meant that the DNA corresponding to a protein was implanted in a living organism (say a bacterium). Then the living organism was multiplied in vats called bioreactors, and finally, the protein was then extracted from them. In other words, living organisms were used as factories to produce proteins that could either not be produced before, or could not produced with a such a high degree of purity or low costs.

During the 1980's the biotechnology industry emerged in the U.S.A. with the creation of many DBFs. Large pharmaceuticals initially adopted a "wait and see policy" and initiated contractual relationships with the DBFs. By the mid 1980's, many established pharmaceutical firms understood the power of biotechnology. They began to have their own in-house R&D labs and they starting acquiring dedicated biotechnology firms. They also continued to contract out research to dedicated biotechnology firms. The 1990's witnessed a spate of DBFs creation and integration of biotechnology by many large pharmaceutical firms in Europe also. The State played a crucial role in the development of the biotechnology sectors in the developed world, either through its support of public research or through initiation of public investment programs in biotechnology.

A second technological paradigm shift in biotechnology occurred with the launching of the human genome project in 1990. The entire process of drug discovery underwent a radical change. Now drugs could be designed using the information on genes. This developed a new upstream segment or the "drug discovery platform", referring to the activities of

companies that did not produce drugs, but either produced something or offered a service for a drug company interested in creating a new drug.

The drug discovery platform encompasses a diverse and constantly evolving range of technologies that are used to exploit the information available on the genome and proteome in order to identify potential targets for new drugs, design the potential drugs in new ways, test them, and predict their efficiency and risks for health. These technologies are often grouped under the names of genomics, proteomics, rational drug design, pharmacogenomics, etc. The constant evolution of these technologies is the driver of the orientation of pharmaceutical research. Thus, biotechnology ceased to be limited to the production of proteins through reproduction of genetically modified cells. Now, chemically synthesized drugs could be produced using biological information and the methods of rational drug design (The Economist, 2003).

A complementary sector called bioinformatics also developed. It formed a component in the drug discovery platform, offering its services to generate, compile and analyze biological information using computer software designed specifically for the purpose.

At present, the limits of biotechnology for new product innovation in the pharmaceutical sector cannot be identified. The methods that are most efficient technologically or in terms of costs of production cannot be predicted. Furthermore, no single firm can develop competence in all possible technologies or pursue research on all possible lines. Hence, a division of labour with cooperation between different kinds of firms is likely to persist till the dominant paradigm emerges.

1.4 Biopharmaceutical firms in the Indian context

Indian pharmaceutical firms began to take an interest in biotechnology from the beginning of the 1990's, once the commercial viability of this sector was firmly established in the West, but they appeared to be rather daunted by the high costs and uncertain commercial returns of venturing into biotechnology.

The availability of technically competent manpower was not too much of a constraint. The most serious bottleneck was the financial constraint, both for the Indian Government and for the Indian companies. The sums that they could invest in biotechnology were lower than that spent by any of the major multinationals in their home countries. A second major problem was the virtual absence of networking among the actors of the biotechnology sector: the government, public research laboratories, firms and financial institutions. Given the absence of the requisite financial resources and alternatives to sharing risk and costs through financial markets, it was not clear whether self-organized or government engineered strategic alliances between firms and between firms and universities necessary for the integration of biotechnology could develop. This situation made it necessary for the Indian Government to narrow down carefully a few areas on which its financial resources could be concentrated. Thus, agriculture and plant biotechnology was targeted for Government aid and the pharmaceutical sector was more or less left to find its own way in biotechnology (Ramani, 2002; Ramani and Venkataramani, 2001).

According to Ramani and Venkataramani (2001), at the end of the 1990's five types of strategic positioning of Indian pharmaceutical firms could be distinguished with respect to biotechnology.

- **Wait and see:** A majority of pharmaceutical firms preferred to adopt the policy of "wait and see", with respect to biotechnology, as their counterparts had done in the West in the previous decade.

- **Marketing for Western firms:** Many established pharmaceutical firms marketed biotech diagnostic kits, vaccines and drugs for Western firms, in order to test the waters.

- **Producing diagostics:** A few large integrated pharmaceutical firms entered into the market for diagnostics.

- **Contract research :** Researchers from public laboratories or industrialists with venture capital or foreign capital backing created a handful of dedicated biotechnology firms. Most were into contract research, production of biological products or production of chemicals by rDNA techniques.

- **Speciality chemicals:** A few Enzyme producers got into biotechnology by producing chemicals using rDNA techniques.

The firms interviewed (during 1988) were also well aware of the coming of the TRIPs amendments and were in the process of examining different options for maintaining their competitive advantage in the post TRIPs era.

In a further study, Ramani (2002) identified the distinguishing features of the R&D strategies of the firms interested in integrating biotechnology and the relation between the different components of their knowledge base and their market performance. She found that in the Indian biopharmaceutical sector, R&D expenditure intensity is not linked to firm size, but to research orientation. Market sales were positively correlated to the knowledge base of firms as embodied in their qualified personnel outside of their R&D department. Firms doing research in biotechnology were usually young, with a high R&D expenditure intensity and more qualified people in the R&D department. Most importantly, internal R&D expenditure was found to be a strategic substitute for foreign collaborations.

Maria et al. (2002) have written a report on the Indian biotechnology sectors and they find that currently the main thrusts of Indian biotechnology firms are in the field of biogenerics, transgenic plants, building research platforms and bioinformatics.

As in the West, two types of firms are active in the bio-pharmaceutical sector. The first type refers to existing firms that have diversified into biotechnology and the second type consists of dedicated biotechnology firms. Among the former, we can find diversified pharmaceutical firms, producers of vaccines and producers of enzymes. Similarly, in the bioinformatics sector, there are established software firms that have diversified into bioinformatics as well as dedicated bioinformatics firms.

Each type of entrant new to the biotechnology industry has come with its particular competitive advantage but has had to develop a knowledge base in biotechnology in order to be active in the field. On the other hand, dedicated biotechnology firms entered the area with the required scientific expertise, but often lacked the knowledge of the scaling-up process and downstream competencies like marketing.

In developed countries, especially in the USA, the acquisition or the possession of technological knowledge is taken to be sufficient to ensure the creation of an innovation, since funds can be found easily (if it is commercially viable) for its commercialisation. In developing countries, the national system of innovation is not very developed. This means that barring exceptions, only large established firms have the luxury of being able to dream about innovations. Secondly, developing countries are characterized by greater informational problems and this in turn means that managerial vision is a critical determinant of the innovation strategy of a firm. Thus the business models of developing country firms are built to fit their financial constraints, their technological competence and their managerial vision.

2. Sample and Results

A sample of firms, about 30 in all, representing the different types of entrants and dedicated biotechnology firms were chosen for interviews. The objective of the interviews was to ascertain their product or service focus in the biopharmaceutical sector. The main advantages and shortcomings of the different types of companies are summarized in table 1.

As we noted, the innovation strategy of Indian firms is determined by the trio of managerial vision, knowledge base of firm and financial constraints, in the context of the Indian national system of innovation.

Table 1 : The firms considered in the study

Type of firm		Number of firms	**Strengths**	**Weaknesses**
Entrants from the pharmaceutical industry	Integrated Pharmaceuticals Company	8	• Knowledge of synthetic chemistry • Knowledge of industrial scaling up processes. • Marketing network and market force • Legal knowhow	Lack of knowledge of biotechnology
	Diagnostic reagents & vaccines manufacturers	**2**	• Downstream processing of natural proteins	Lack of knowledge of biotechnology
Entrants from the chemical industry	Enzyme manufacturers	**3**	• Acquisition of technical know-how through the production of recombinant products with non-therapeutic applications, • Expertise in fermentation process	Lack of knowledge of biotechnology
Entrants from the IT industry	IT firms	**8**	• Knowledge of software	Lack of knowledge of biotechnology
Dedicated firms	Dedicated start-ups	**9**	• Scientific know-how in biotechnology • Specialized and efficient technical management	Lack of techniques and infrastructure for industrial scaling up Lack of marketing force

2.1 Strategic positioning of Indian firms in biopharmaceutical sector

The central result that emerged from the interviews was as follows.

Result : The Indian biopharmaceutical firms envisage five main areas of activity to improve their competitive position in India and abroad :

- *Entry into the biogenerics market and the market for off-patent diagnostics and vaccines;*
- *Contract research;*
- *Creation of new pharmaceutical products;*
- *Bioinformatics;*
- *Clinical trials.*

The specificities of these segments are now detailed.

2.1.1 Recombinant Drugs, Vaccines and Diagnostics that are off patents or soon to be off patents

Biogenerics refers to therapeutics products based on genetically engineered or recombinant technologies that are already on the market at least in some industrialised countries. The first therapeutic protein produced through rDNA technology to be in the market, was Genentech's human insulin, introduced in 1982. The total amount of recombinant therapeutics molecules approved throughout the world is now around 30. In 2000, nearly 86 percent of the 77 biotechnology medicines approved by the FDA (Food and Drug Administration of the U.S.A.) constitute recombinant human proteins. (Maria et. Al., 2002) The approved products can be categorized into blood factors, hormones, growth factors, interferon, interleukins, vaccines, and other products. The estimated worldwide sales of recombinant products was US$ 1.4 billion in 1990 and US$ 6.6 billion in 2000. (TIFAC, 2002)

Over the next five years, more than $10 billion worth of products will come off patent. Many treatments for diseases like Diabetes, Gaucher Disease, Hepatitis B&C, Sclerosis, Growth Hormone deficiency relying on biotechnology will face patent expiration between 2001 & 2005. In India, the market of approved recombinant therapeutics in 2001 was estimated to be about US$ 109 millions, which represents 3.2 % of the total Indian pharmaceutical market, and 1.6 % of the world market for recombinant therapeutics. (TIFAC, 2002)

The recombinant products market in India has been led until recently, by imports of established global brands, and marketing of the products either by local subsidiaries (*SmithKline Beecham (SKB)*, *Novo*), or through marketing arrangements with local firms (as in the case of *Nicholas Piramal* and *Roche*). This trend is changing thanks to the massive entry of local competitors with a critical cost advantage. The first Indian players in the sector were in fact new companies created specifically to exploit the opportunity offered by recombinant therapeutics. When *Shantha* first introduced its locally developed recombinant Hepatitis B vaccine (first recombinant therapeutic to be produced by an Indian company), it forced down *SKB's* local selling price of $10 per dose down to 50 cents per dose. The market of recombinant Hepatitis B vaccine now counts four local players: *Shanta*, *Bharat*, *Panacea* and *Wockhardt*.

This segment has now attracted several types of companies with related activities such as pharmaceutical companies and industrial enzyme producers. The first type of company benefits from an established brand and marketing force; whereas the second type of company comes with a mastery of the fermentation and downstream processing technology that other companies such as pharmaceutical firms producing classical chemical drugs have to acquire in order to enter the market.

Even if from a technological point of view, there is no doubt that Indian companies have the potential to be international players in the field of generic recombinant therapeutics, the legal process of certification of biological equivalence in the main markets of U.S., Europe and Japan may still be too costly and time-consuming for them to access those essential markets in the next years. However, the domestic recombinant therapeutics sector seems to be large enough to support the Indian firms, and tremendous opportunities exist in the international market for off-patent products. Therefore, we can consider it as a field where technological activity in the field of biotechnology will develop strongly in the next years in India, even in an environment characterized by stronger patent protection.

2.1.2 Contract research

Several Indian companies are attempting to insert themselves in international networks of drug discovery. The basic model for an Indian company entering this sector is to constitute a technological platform allowing it to perform contract research on a service basis, and then use the cash flow generated and the competency acquired through the first type of activity to conduct its own research project with patenting as the primary goal.

2.1.3 Creation of new pharmaceutical products

For new product creation, in addition to the myriad of technologies to choose from, there lies the obstacle of finding the resources to invest in research, run the clinical trials and cross the legal hurdles. Finally, any Indian firm wanting to get credible IPR has to not only file a patent in India, but also with the US patent office or the European patent office, which increases the cost of new product creation considerably.

Given the twin problems of technology acquisition and the costs of the jumping the legal and IPR hurdles, the innovation strategy of Indian firms is highly dependent on managerial vision (there must be certain beliefs regarding the probability of success!) and the financial constraints. Thus, the creation of the new products is really reserved for the mighty or the enterprising, that can generate a cash flow through venture capital, contract research or selling a generic product. Some companies backed by powerful trusts can dedicate themselves directly to research with long term objectives, as it is the case of Reliance Life Science which benefits from the support of Reliance (Indian largest industrial trust). Some other companies such as Aurigene, backed by Indian Pharmaceutical company Dr Reddy's, have chosen to develop a large scale platform dedicated to contract research, with the goal of developing its own research project and accessing intellectual property. There are other examples of small start-ups founded by former scientists and oriented towards innovation, which offer technical services as a way to generate cash flow. Ten companies involved in this type of activity were identified during the 2002 survey (excluding established pharmaceutical companies). Among them, at least three of them are developing their own projects of biotech-based drug discovery (Dr Reddy's, Ranbaxy, Wockhardt).

2.1.4 Bioinformatics is defined as the application of computer technology to the management of biological information. It involves the development of software tools for the management and treatment of biological information. The explosion of information resulting from the Human Genome Project (HGP) has propelled the rapid development of bioinformatics as a discipline. The HGP's information management challenge involves tracking the sequencing of the entire human genome - approximately three billion base pairs of DNA that make up our 23 pairs of chromosomes - and the precise mapping of the 100,000 or so genes that are interspersed on these chromosomes. The amount of public DNA sequence

data doubles every 12-14 months and will increase even more dramatically in the coming years.

The Consortium of Indian Industries (CII) estimates the global turnover of the bioinformatics industry to be around $ 2 billion in 2001 and predicts a market of $60 billion by 2005. Identifying an objective of a 5% global market share for the Indian industry, the CII presents bioinformatics as a good candidate for becoming a high-growth niche in the next decade, like Software outsourcing during the 1990's (Tewari, 2001). More recently, the Nasscom, the powerful association of Indian IT companies has announced a strategic focus on bioinformatics.

At this stage of emergence, the business model is strongly determined by the financial constraints of the bioinformatics firms. Whereas firms with a strong corporate backing can allow themselves to adopt a long term strategy of competency building, small independent firms must cope with the requirement of external funding, i.e. rapid generation of cash flow.

2.1.5 Clinical research is defined as the management of the last stages of drug development which implies recruiting of patients for the testing of new drug candidates. On an average basis, this process accounts for more than 50% of the total cost of development of a new drug. (Tufts Center for the Study of Drug Development) The process of clinical testing of drugs is being normalized with the elaboration of common standards by the International Conference on Harmonization. Complying with the standards so defined could allow India-based clinical research organizations (CROs) to perform clinical research for foreign companies.

With its large patient pool benefiting from an exceptional biodiversity, along with a long tradition of excellence in Medicine sciences, India has the potential to become a major player in this new form of outsourcing. The evolution of this segment will depend on the rate of convergence of the Indian clinical test procedures toward the international standards. After years of sluggish evolution, the government is taking proactive measures with the clear goal of making the Indian standards converge towards the US-FDA standards. Some ethical considerations may also be raised to oppose what could be considered as the exploitation of the Indian poor as "guinea pigs" for medical research. Nevertheless, in order to be internationally accepted the research would have to follow strict rules (good clinical practices) that includes having the prior consent of patients.

The management of clinical trials cannot be considered in itself as an economic application of biotechnology. Nevertheless, clinical trials are the most expensive stage of the drug development chain and India possesses resources that should allow the country to offer clinical research services at a very competitive cost. Several companies have already taken the initiative to develop an activity of contract-driven clinical trials in India. For example the global major Quintiles has already settled three centres in the country and some Indian companies having activities in Biotech and pharmaceuticals have launched their own division for contract clinical trials. Indeed, the enzyme manufacturer Biocon has set up a new subsidiary, Clinigene to conduct clinical research under contract, so did the pharmaceutical companies Nicholas Piramal with its subsidiary WellQuest, and Ranbaxy with SRL Ranbaxy. Siro Research was founded in 1995 as a clinical research organisation. Catalyst Clinical Services is another clinical research organisation settled in India. All these companies are looking for large scale contracts with foreign partners and they are working on their practices in order to comply with the international standards such has the Good Clinical Practices defined by ICH.

2.2 Likely impact of TRIPS

The previous section described the strategic positioning of the Indian biopharmaceutical firms. Using the results obtained, we propose to show in this section that TRIPS is not likely to have much impact, either positive or negative, on the incentives for new technology creation. This is because the

First, in the post TRIPS era the biggest focus of the Indian biopharmaceutical firms is going to be on bio-generics, off-patent vaccines and off-patent diagnostics, which are totally outside of the purview of TRIPS. As important recombinant drugs come off patent, the winners in corporate India will be the firms that re-engineer them first or at the lowest cost. Even if Indian firms concentrate on this, it is not clear if the biggest beneficiaries will be Western Multinationals or Indian firms. Indian firms do not have the established brand image at the international level to be able to sell even a generic under its own name worldwide. There is no Sony, Mitsubishi or Daewoo among the pharmaceutical leaders. The international pharmaceutical market is dominated by well established American, British or European firms, with strong brand loyalty. Any Indian winner will make its money by licensing its technology or exporting the base to Western multinationals, besides dominating the Indian market.

Second, Indian firms are going to be active service providers in the international biopharmaceuticals market. They are going to be part of the *international division of labour* of the innovation creation process by Western firms. This has nothing to do with TRIPs but everything to do with their increasing technological competence and the evolution of the biotechnology sectors themselves. Their main services will be contract research on biotechnology, bioinformatics software providers and clinic research managers.

Third, TRIPs is not going to level the field of play or increase incentives for Indian firms in the area of new drug creation. In this case, the Indian firms start with a handicap, even before the start of the game, simply because they do not have the deep pockets necessary to create international blockbusters. Even, in the event that an Indian firm creates a blockbuster, it is more likely to patent it directly in the USA rather than go through the Indian channel. TRIPS has no impact on Indian firms patenting in the USA.

Fourth, TRIPs is not likely to increase incentives for multinational pharmaceutical firms to invest in, or to collaborate with research and production unities based in developing countries. This is simply not likely to happen and it is not happening, because of the other problems associated with having access to infrastructure (especially power), getting credible information quickly and ensuring commitment to contracts undertaken.

Fifth, The TRIPs convention will not increase incentives for the accumulation of technological competence in areas not of interest to Western pharmaceutical firms. There are a number of tropical and water borne diseases that seriously need attention. There are diseases such as malaria, which kill more people than AIDS every year in India. The TRIPS convention is not going to improve the incentives for investment in the finding of treatment for these diseases.

Therefore, the impact of TRIPs will be restricted to an elimination of the production of patented products. It will not have a deleterious or a positive impact on their levels of inventive activity. Even more importantly, TRIPs is not likely to create any incentive to

increase technological knowledge or create innovations other than that provided by the national system of innovation.

3. Conclusion

This objective of this paper was to give some insight on the impact of TRIPS on the innovative capacity of developing countries, by taking India as a representative of a technologically advanced developing country and biopharmaceuticals as an example of a knowledge intensive industry. The choice of India was motivated by its success in two different knowledge intensive fields : pharmaceutical generics and software outsourcing. The selection of biopharmaceuticals is justified by its role as a key driver in the creation of current and future innovations in human health care.

The two central results of the paper can be summarized as follows. First, given the present state of the competencies of Indian pharmaceutical firms and the national system of innovation, the major focus of innovative activity is going to be either on “racing to be the first or lowest cost producer” of off-patent products or being a link in the international division of labour supporting the creation of innovations by Western multinationals. Second, TRIPS is not going to have a significant impact on the two segments given above or on the other preoccupations of Indian pharmaceutical firms. Hence, the major effect of TRIPS would seem to be to force Indian firms to put their re-engineered products on the market only when they get off patent.

What about the impact of TRIPS on consumer welfare in the pharmaceutical sector? Consumers in India and abroad are likely to benefit in the future from lowered prices of biogenerics. The availability of drugs targeting tropical diseases is not likely to change. Indian markets will offer lower quantities of pharmaceutical products that are patented now and that are going to be patented by Western pharmaceuticals in the future. With the elimination of substitutes to patented products, the Indian consumers have to exclusively depend on Western pharmaceutical firms. Given the strict price controls imposed by the Indian government to ensure accessibility of drugs to the poor, Western companies do not have the incentives to increase sales. Then we may witness the repeat of the "McDonalds phenomenon". In the U.S.A., the McDonalds restaurants are more frequented by the poor than by the richer sections of society. In India, however, McDonalds is present in every major city and it mainly caters to the more affluent sections of society. Just like this, foreign multinationals selling patented drugs, vaccines or diagnostics are more likely to cater to the more affluent sections of society. Thus, the impact of TRIPs on the consumer welfare will be mixed in terms of availability of pharmaceutical products in the Indian market. Much will depend on how the clause of compulsory licensing is used.

In the light of the above, two recommendations can be offered to increase the production and availability of biopharmaceuticals in India and in other developing countries.

First, the national system of innovation can be strengthened. Besides the traditional instruments of the State, like subvention and fiscal benefits to firms and public laboratories, there is a need to augment the culture of entrepreneurship. Incentives have to provided for transfer of technology from public laboratories and creation of new firms by public researchers. At present venture capital funds as too risk adverse, and lack the technical knowledge that would enable them to propose good conditions of funding. Only a few states have taken the initiative to create technology parks and this can be increased. There is also a useful asset in the form of non-resident Indians (NRIs) who are skilled scientists or entrepreneurs with international experience in development. This group has played a

significant role in the creation of biopharmaceutical firms and products in India. This Diaspora of NRIs can be better tapped.

Second, if the developing countries are to participate in the biotechnology revolution in the pharmaceutical sector, with TRIPs they will need to collaborate more and more with Western pharmaceutical companies, since they cannot compete with them. If such collaboration is take place, the conditions for contract enforcement and protection of intellectual property must be created within the developing countries themselves and this can be greatly helped if there is financial and organizational support from international agencies. Cooperation between developed and developing country firms is blocked mainly due to problems of strategic interaction such as cheating on contracts or commitment (moral hazard) or misleading of beliefs through omission or falsification of information (adverse selection). TRIPS at present has no bearing or impact on such problems. The success of collaboration depends on the building of trust between the concerned partners, improved professionalism and the ability to redress through local or international courts any breaches of contracts. However, TRIPS will not have any impact on the parameters determining the initiation or the evolution of international R&D or technology collaboration in the biotechnology sectors. Therefore, establishing efficient courts to settle IPR disputes may do more to stimulate patent applications from Indian firms and cooperation between Indian and foreign firms than TRIPs.

References

Basant Rakesh, (1997), 'Analysing Technology Strategy Some Issues', *Economic and Political Weekly,* 32(48), P:M 111-120.

Chaudhuri Sudip., (2002) 'TRIPs agreement and Amendment of Patents Act in India'. *Economic and Political Weekly* Vol. 37, No. 32, 3354-3360.

Ernst & Young, (2002). *Beyond borders, the biotechnology industry report*. Report edited by E&Y in 2002.

Lalitha N. (2002), Indian Pharmaceutical Industry in the WTO Regime: A SWOT Analysis, *Economic and Political Weekly,* 32(48), P:M 111-120.

Lall Sanjaya, (2003) Indicators of the relative importance of IPRs in developing countries, Forthcoming in *Research Policy*.

Lanjouw J. O., (2002) Intellectual Property and the availability of pharmaceuticals in poor countries, *Center for Global Development Working Paper No. 5*¤ April, 2002.

Lanjouw, J.O. and Cockburn, I. M. (2001) New pills for poor people? Empirical evidence after GATT, *World Development*, Vol. 29, No. 2, pp. 265-289.

Maria A. et. al. (2002) Biotechnology in India, *Report prepared for the French Embassy in NewDelhi.* www.cerna.ensmp.fr/Documents/AM-JR-MHZ-BiotechReport.pdf

Prasad Ashok Chandra and Bhat Shripad (1993), Strengthening India's Patent System, Implications for the Pharmaceutical sector', *Economic and Political Weekly,* 28(21), May, 1037-1058.

Ramani, S.V. (2002) Who's interested in biotechnology : R&D strategies, knowledge base and market sales of Indian biopharmaceutical firms, *Research Policy* vol. 31, 381-398.

Ramani, S.V. and M.S. Venkataramani, (2001) Rising to the technological challenge: Integration of biotechnology in the Indian Pharmaceutical Industry, *International Journal of Biotechnology* , vol 3, no. ½, 95-115.

Tewari S. (2001) Genomics and Bioinformatics: The way for the future. In *CII ed. Business Opportunities in Biotechnology.*

The Economist, Patents and the poor: The right to good ideas, *The Economist*, (2001) pp. 25-30.

The Economist, Biotechnology A survey, *The Economist*, (2003).

The Human Development Report *Global initiatives to create technologies for human development,* (2001), http://hdr.undp.org/reports/global/2001/en/.

TIFAC 2002, Recombinant DNA Products, *TIFAC Report*

TCSDD 2002, Tufts Center for the Study of Drug Development Impact Report.

Watal, J. (2000). Access to Essential Medicines in Developing Countries: Does the WTO TRIPS Agreement Hinder It? Science, *Technology and Innovation Discussion Paper No. 8, Center for International Development,* Harvard University, Cambridge, MA, USA.