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TRIPS: Its Possible Impact on Biotech Segment of the Indian Pharmaceutical Industry

Many countries of the world, including India, have achieved self-sufficiency in knowledge intensive sectors by allowing for a loosely defined intellectual property rights (IPR) regime. The implementation of TRIPS worldwide represents a step in the opposite direction and its impact on the production and innovative capacity of developing countries in knowledge intensive sectors is not at all clear. Taking India as representative of a technologically advanced developing country, and the biotech based segment of the pharmaceutical industry as an example of an emerging knowledge intensive sector, we examine the possible impact of TRIPS on the incentives and ability to innovate. The conclusion is that TRIPS is not likely to have a significant impact on incentives for innovation creation in the biotech segment.

Shyama V Ramani, Augustin Maria

I
Introduction

The creation of innovations in a knowledge intensive sector is essentially a dynamic process. A radical innovation is often followed by a second, third or subsequent version that constitutes an improvement of the original commodity, either in terms of quality or cost of production. An externality is necessarily generated in this process, in the form of unilateral spillovers from the first innovator to the subsequent ones, as the latter innovators benefit from the knowledge generated by the first innovator without having to incur the same research costs. The challenge of any intellectual property rights regime (IPR) is to provide the right incentives for both the first innovator and any subsequent innovator to invest in knowledge creation given these spillovers [Scotchmer 1991]. The first innovator must be rewarded for the knowledge created by his R&D undertakings and the subsequent innovator for any additional technological knowledge generated.

The broadening of an IPR regime shifts the incentives for innovation creation from the second innovator to the first innovator (where the term 'second innovator' is used to represent all generations of innovators other than the original one). When a patent system becomes broader, it leaves fewer loopholes around which second innovators can commercialise new products, without having to enter into some sort of a licensing agreement with the first innovator. A narrowing of the patent regime moves the incentives for innovation creation from the first innovator to the second one, as it permits the second innovator more opportunities to improve upon the original innovation, thereby eroding the market shares of the first innovator.

TRIPS or Trade Related Intellectual Property Rights, constitutes a broadening of the existing patent system of many developing countries, including India. It has been initiated by the triad countries, in order to preserve the incentives for innovation creation, for first innovators, namely western firms, who find their market shares eroded in many industries by second innovators from middle income country firms, with a strong scientific and technological base. In principle, TRIPS should generate incentives for any firm to be the first innovator. However, we all know that the conditions faced by developing country firms are different from those encountered by developed country firms. Hence, it becomes an open question as to whether TRIPS will have a positive impact on incentives for innovation creation by developing country firms. In order to give some insight on the above issue, the present article focuses on one specific knowledge intensive emerging sector, namely the biotech based segment of the Indian pharmaceutical industry (hereafter referred to as the biopharmaceutical industry or sector in this paper). It examines whether the impact of TRIPS on the incentives to innovate by Indian biopharmaceutical firms will be positive or negative. By the biopharmaceutical industry, we refer to firms that have incorporated biotechnology either in their production processes or in their R&D programmes or are selling biotechnology based pharmaceutical products.[1]

We start with the basic hypothesis that the creation of innovations in any sector and in any country depends on its national system of innovation (NSI), which refers to all the institutions in the country, involved in the creation, adoption and diffusion of a new technology. This approach was spearheaded by the seminal work of Lundvall (1992), Nelson (1993) and Freeman (1995), as a possible alternative to the macroeconomic models of growth. The advantage of the NSI approach is that it is useful for policy-makers, because an understanding of national specificities in terms of knowledge production helps them to "develop approaches for enhancing performance in the knowledge based economies of today" [OECD 2001]. However the NSI approach suffers from the drawback of being a conceptual

framework rather than a theory, open to many forms of interpretation, and many forms of investigations [Edquist 2001; Lundvall 1998]. Nevertheless, following this method, the present paper takes the liberty of sharing with its readers the inferences made by the authors on the basis of a large set of interviews, about 40 in all, with executives of leading firms, patent officers and scientists in the Indian biopharmaceutical sector.[2] The sample set is considered to be representative, though not comprehensive of the sector. The interviews were designed to obtain information on the areas and types of innovative activity pursued by the firms at present and the problems so encountered. This information was then used to answer the following central question: Given the present state of the Indian national system of innovation, what will be the impact of TRIPS on the creation of innovations in the Indian biopharmaceutical sector?

Our main finding is that TRIPS is unlikely to have a significant impact, either positive or negative, on the incentives for the creation of innovations by Indian biopharmaceutical firms. The contribution of the present paper to the literature dealing with the impact of TRIPS on the incentives for innovation creation, is the following corollary of the above inference. TRIPS cannot be justified on the basis of the argument that it increases the incentives for new technology creation by local firms in all knowledge intensive sectors and in all developing countries. Our case study provides a contradiction by being an example of a sector, in which TRIPS is unlikely to have any incentives for local firms to become first innovators. This is, of course, subject to certain caveats that will be detailed further.

The paper is organised as follows. Section II 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 III presents the specificities of the biopharmaceutical sector. Section IV contains our results. Section V concludes.

II
Setting the Background

How IPR Can Influence Creation of Innovation

Just after independence in 1947, in India, there was no pharmaceuticals industry to speak of. Thereafter, during the 1950s and 1960s, a pharmaceutical sector developed, consisting mainly of western pharmaceutical giants and Indian public sector mammoths. However, even the Indian public sector combined with 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 healthcare.

There were two possible solutions to this healthcare 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 solution. Following the strategy adopted earlier by Japan, China, Russia and eastern and southern Europe, the existing IPR, the Indian Patent and Design Act of 1911 was changed. From 1970 onwards, instead of according product patents, the new IPR regime began to recognise 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 Indian Patent Act of 1970 thus constituted a ‘narrowing’ of the IPR regime (in opposition to TRIPS), increasing the incentives for Indian firms as second innovators. 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 healthcare 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, permitting them also to enjoy lower costs, and a greater mark-up. India became an exporter of bulk drugs and final therapeutics, providing them to many parts of the developing and developed world at lower costs [Ramani and Venkataramani 2001].

The above case shows that in a developing country, with an excess demand and a significant technological retard in a knowledge intensive sector, a narrowing of the IPR can not only create industrial competence but also increase welfare. This is of course provided that the national system of innovation, including the existing scientific and technological competencies, is so developed as to permit the local firms to emerge as second innovators. It also shows that a narrowing or a loosening of the IPR, might be welfare enhancing, if it leads to a 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.

TRIPS

A weak IPR regime in developing countries leads to losses from 're-engineered products' for first innovators, namely western multinationals, and lowers the incentives for second innovators, i e, developing country firms, to undertake basic R&D themselves. Thus, the countries of the triad, US, Europe and Japan, have been working towards the global harmonisation of IPR regimes since the last two decades. TRIPS is one of the culminations of their efforts.

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).[3] 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:

– Product patent protection possible in all branches of manufacturing, including drugs.
– Twenty years of protection instead of 14 years or seven years, as in the case of the Indian Patent Act.
– No discrimination between imported and domestic products. – Accommodation of compulsory licensing.[4]

Clearly, TRIPS represents a move totally opposite to that of the Indian Patent Act of 1970. It broadens the Indian IPR system, shifting the incentives for any firm in India, to be a first innovator rather than a second innovator. It is felt that the national system of innovation of some middle income countries, like China, Brazil and India are mature enough to generate first innovators. This view is particularly supported by the clear success of India, in market based, high-tech domains, such as bulk drugs and software. Thus, TRIPS was initiated on the presumption that a strong IPR regime would stimulate private investment in research and development, and hence economic growth. It is also argued that an expanded and strengthened protection of IPRs would bring about increased flows of foreign direct investment and technology transfer to developing countries, including India. And, of course, it would prevent the erosion of market shares of western multinationals by developing country imitators.

The developing world, on the other hand, is 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. Given that the Indian healthcare system was developed mainly due to a 'narrowing' of the IPR system, there is concern about whether TRIPS, will undermine the innovative capacity of the thriving Indian pharmaceutical sector. This concern is expressed not only by Indian firms but also by Indian civic society, which is worried that TRIPS may have a deleterious effect on access to future innovations that could include essential drugs, like a vaccine for AIDS.

TRIPS and Indian Pharmaceutical Sector: A Literature Survey

There exists an extensive literature on the possible impact of TRIPs on developing countries. They tackle this problem along many 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 and; 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 and Cockburn (2001) present the results of field surveys and statistical analysis conducted in order to assess the impact of the introduction of pharmaceutical product patents in India. Their main conclusion is that a lack of a strong IPR in the past impeded the development of new treatments for classical tropical diseases like malaria, and that with TRIPS, incentives for investment in R&D in diseases pertinent to developing countries is likely to increase. However, this may be simply due to the fact that the strategy of imitation is no longer available, rather than it being a direct incentive effect.

Lall (2003) reviews the case for uniform and strong IPR by developing countries. He categorises countries according to technological activity, industrial performance and technology imports to illustrate that there exists a great heterogeneity among them and that any move towards the standardisation of norms, including TRIPS, should take into account this factor. With respect to India, his inference is, "…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)". Ganguli (1999) and N Lalitha (2002) also indicate that TRIPS is likely to induce greater innovation creation, more R&D expenditure, and more patents by both Indian and foreign firms in the Indian biopharmaceutical sector.

III
Nature of the Biopharmaceutical Sector

A Technico-economic Description

Since the last 15-20 years, in most parts of the developed world, the pharmaceutical sector has been undergoing a revolutionary paradigm shift – from the creation of drugs based on chemical engineering to those based on biotechnology. 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. Thus, the biopharmaceutical sector, i e, firms incorporating biotechnology either in their production processes, R&D programmes or marketing portfolios, is likely to contain the main innovators in the pharmaceutical industry.

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 its 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. The costs of creating a new drug are therefore much greater than those required to create a vaccine or a diagnostic.

The biotechnology revolution also had a profound impact on the organisation of innovation creation, and consequently, on industrial organisation in the pharmaceutical sector. Earlier, pharmaceutical innovations were basically created in-house. Some research contracts were initiated with public laboratories and clinical trials of a new chemical entity or product were usually outsourced. Biotechnology created a division of labour within the innovation process itself. Now, innovations in the pharmaceutical sector are created in a variety of organisational arrangements, in in-house laboratories of large pharmaceutical firms, small in-house teams of dedicated biotechnology firms (DBFs), strategic alliances, research consortiums, in public-private cooperative networks, etc.

The first biotech firms, were dedicated biotechnology firms (DBFs) created during the late 1970s in the US By 'dedicated' they signalled that their production processes involved only biotechnology. During the 1980s, the biotechnology industry emerged in the US with the creation of many DBFs. The two dominant technologies available during this period 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 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 such high degrees of purity or low costs.

Large pharmaceuticals at first adopted a 'wait and see policy' and initiated contractual relationships with 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 started acquiring dedicated biotechnology firms. They also continued to contract out research to dedicated biotechnology firms. The 1990's witnessed a spate of DBF creation and integration of biotechnology in many large pharmaceutical firms in Europe as well. 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 programmes in biotechnology [Pisano 1991].

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 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 synthesised drugs could be produced using biological information and the methods of rational drug design ['Biotechnology, A Survey', *Economist* 2003].

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

The genomic revolution has, in other words, increased the division of labour in the creation of innovations even more in the pharmaceutical sector. 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.

With respect to the biopharmaceutical sector in developing countries, we first note three features that distinguish them from those in developed countries. These comments hold for other high-tech sectors as well. First, the initial set up costs of infrastructure are much higher in terms of effort and time. This is because facilities like land, electricity and water have to be negotiated with local authorities and depending on the degree of efficiency and corruption of the local authorities, this process can be more or less difficult. Second, in developing countries, it is hard to find seed money for a high-tech venture. In developed countries, the viability of a potential innovation and the technological competence of a firm are taken to be sufficient to ensure the commercialisation of an innovation, since funds can be found relatively easily. This is particularly true of the US. Already, in Europe funding is more difficult to come by as compared to the US. In developing countries, this problem is even more exacerbated. This means that barring exceptions, only large established firms have the luxury of being able to dream about radical innovations requiring significant investments. Third, developing countries are characterised by greater informational problems, which means that managerial vision is a critical determinant of the innovation strategy of a firm. Thus, the business models of developing country firms are formulated as a function of three parameters: technological competence, financial base and managerial vision. Furthermore, since managerial vision refers to a subjective rather than objective probability (since there is little common knowledge and a lot of informational uncertainty), in developing countries, we find more heterogeneity of business models, fewer firms that are totally specialised in one product or service and less inter-firm cooperative networks (outside of partners in the value added chain-suppliers or downstream clients).

Indian Biopharmaceutical Industry in the 1990s

Indian pharmaceutical firms began to take an interest in biotechnology from the beginning of the 1990s, 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 the area. The availability of technically competent manpower was not too much of a constraint. The most serious bottleneck was the financial constraint. The sums that Indian firms 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-organised 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 diagnostics*: A few large integrated pharmaceutical firms entered 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.

In another study, Ramani (2002) identified the distinguishing features of the R&D strategies of firms interested in integrating biotechnology and the relationship between the different components of their knowledge base and their market performance. In the biopharmaceutical sector, R&D expenditure intensity is not linked to firm size, but to research orientation. Market sales are positively correlated to the knowledge base of firms, as embodied in qualified personnel outside of the R&D department, which indicates that formal R&D activity has yet to make a significant impact on firm performance. Firms doing research in biotechnology are usually young, with a high R&D expenditure intensity and with more qualified people in the R&D department. Most importantly, internal R&D expenditure is a strategic substitute for foreign collaborations or firms that go in for more foreign collaborations are those that spend less on internal R&D.

IV
Sample and Results[5]

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 interviews revealed that two types of firms are active in the biopharmaceutical and bioinformatics sectors. The first type includes firms with an established technological competence in their field, as well as industrial trusts with a strong financial base that are able to invest in the creation of a start-up. The established firms include: (i) diversified pharmaceutical firms; (ii) vaccine producers; (iii) enzyme producers; and (iv) software firms.

Their challenge is to develop a knowledge base in biotechnology and make it coherent with their present competence in synthetic chemistry or software.

The second type consists of dedicated biotechnology firms, which enter the arena with the required scientific expertise, but lack knowledge of the scaling-up process and downstream competencies like marketing. The central result that emerges from the interviews regarding the technological positioning of firms is as follows. Indian biopharmaceutical firms envisage two main areas of activity to improve their competitive position in India and abroad: (i) Creation of products for the final market: the biogenerics market and the market for off-patent diagnostics and vaccines; and creation of new pharmaceutical products. (ii) Collaborative contracts with western firms, either in biotechnology research, bioinformatics or clinical trials. The firms in the two categories are detailed in **Tables 1 and 2.**

Table 1: Companies Involved in Creation of Biopharmaceuticals for Final Market

Company Profile	Name of Company
Indian Integrated Pharmaceuticals Company (IIPC)	Wockhardt
	Cipla
	USV
	Ranbaxy
	Dr Reddy's
	Biological E
Diagnostic reagents and vaccines manufacturers	Bharat Serums and Vaccines
	Yashraj
	Artemis Biotech
	Bhat Biotech
Enzyme manufacturers	Advanced Biochemicals
	Biocon
	Bangalore Genei
Dedicated start-ups	Shanta Biotechnics
	Bharat Biotech

Table 2: Intermediate Product and Service Providers in Biopharmaceutical Sector

Company Profile	Name of Company	Name of Biotech Venture
Industrial trusts	Chaterjee Group	Chembiotec
	GVK	GVK-Bio
	Reliance	Reliance Life Science
	Dr Reddy's	Aurigene

Companies	Nicholas Piramal	Genenquest
	Dr Reddy's	Molecular Connections
	Saraca	Ocimum Biosolutions
	Gland Pharma	Questar
Information Technology Companies	Tata Consultancy Services	Advanced Technology Centre
	CDC Linux	CDC Linux
	DSQ	DSQ Biotech
	I-Labs	Ingenovis
	Kshema	Kshema Technologies
	Satyam	Satyam Biotech
	Spectramind	Spectramind
	SysArris	SysArris
	Wipro	Wipro Life Sciences
Enzyme Producers	Biocon	Syngene
Dedicated Start-Ups	Avesthagen	
	Bigtec	
	Genotypic	
	Lansky Solutions	
	Metahelix	
	Strand Genomics	

Products for the Final Market

There are two types of products being envisaged for final markets, either in India or abroad. In the first category, there are products that are going off patent, which Indian firms intend to produce as second innovators. In the second category, there are products which Indian firms envisage bringing to the market as first innovators.

Recombinant drugs, vaccines and diagnostics that are or are soon to be off patent: Biogenerics refers to therapeutic 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 per cent of the 77 biotechnology medicines approved by the Food and Drug Administration (FDA) of US were based on recombinant human proteins [Maria et al 2002]. The approved products can be categorised into blood factors, hormones, growth factors, interferon, interleukins, vaccines, and other products. The estimated worldwide sales of recombinant products were US$ 1.4 billion in 1990 and US$ 6.6 billion in 2000 [TIFAC 2002].

Over the next five years, more than $10 billion worth of products will come off patent. Many treatments for diseases like diabetes, gaucher disease, hepatitis B and C, sclerosis and growth hormone deficiency relying on biotechnology will face patent expiration between 2001 and 2005. In India, the market of approved recombinant therapeutics in 2001 was estimated to be about US$ 109 million, which represents 3.2 per cent of the total Indian pharmaceutical market, and 1.6 per cent 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 products either by local subsidiaries (i e, 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 Shanta first introduced its locally developed recombinant hepatitis B vaccine (the first recombinant therapeutic to be produced by an Indian company), it forced down SKB's local selling price of $10 per dose to 50 cents per dose. The market of recombinant hepatitis B vaccine now counts four local players: Shanta, Bharat, Panacea and Wockhardt.

This segment presently contains companies with related activities such as pharmaceutical companies and industrial enzyme producers. The former benefits from an established brand and marketing force, while the latter 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 the US, Europe and Japan may still be too costly and time-consuming for them to access. However, the domestic recombinant therapeutics sector seems to be large enough to support Indian firms, and tremendous opportunities exist in the international market for off-patent products. Therefore, we can consider this as a field where technological activity in the field of biotechnology will develop strongly in the next years in India, even in an environment characterised by stronger patent protection.

Creation of new pharmaceutical products: For new product creation, in addition to the myriad of technologies to choose from, there is the obstacle of finding resources to invest in research, run clinical trials and cross 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. Thus, in order to create a new pharmaceutical product it is necessary to have deep pockets and two types of business models are emerging in this category.

First, there are companies backed by powerful trusts that are dedicating themselves to research with long-term objectives, as in the case of Reliance Life Science, which benefits from the support of Reliance (Indian's largest industrial trust). Then there are companies, which are generating a cash flow through some means and reinvesting a part of the revenue so earned into long-term research and innovation products. For instance, Aurigene, backed by Indian pharmaceutical company Dr Reddy's, has chosen to develop a large scale platform dedicated to contract research, with the goal of developing its own research project and accessing intellectual property. Two other companies working towards becoming first innovators are Wockhardt and Ranbaxy. There are also examples of small start-ups founded by former scientists and oriented towards innovation, which generate a cash flow by offering technical services and continue to progress towards creating their own innovation.

Provision of Intermediate Products and Services

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 and allowing it to perform contract research on a service basis. Many of them hope to use the cash flow generated and the competency acquired to conduct their own research project with patenting as the primary goal.

Bioinformatics: This 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 1,00,000 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 Confederation of Indian Industries (CII) estimates that the global turnover of the bioinformatics industry was around $ 2 billion in 2001 and predicts a market of $60 billion by 2005. Identifying an objective of a 5 per cent global market share for 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 1990s [Tewari 2001]. More recently, 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 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.

Clinical research: This 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 per cent of the total cost of development of a new drug [Tufts Centre 2002]. The process of clinical testing of drugs is being normalised with the elaboration of common standards by the international conference on harmonisation. Complying with the standards so defined could allow India-based clinical research organisations (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 the convergence of Indian clinical test procedures towards international standards. After years of sluggish evolution, the government is taking proactive measures with the clear goal of making Indian standards converge towards the US-FDA standards. Some ethical norms will have to be formulated and satisfied to ensure against the exploitation of the Indian poor as 'guinea pigs' for medical research. As a first step, in order to be internationally accepted, clinical research trials have to follow strict rules (good clinical practices) that include 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 on three centres in the country and some Indian companies with activities in biotech and pharmaceuticals have launched their own divisions for contract clinical trials. Indeed, the enzyme manufacturer Biocon has set up a new subsidiary, Clinigene to conduct clinical research under contract, so have 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 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 international standards such as the Good Clinical Practices defined by ICH.

Possible Impact of TRIPS

The previous section described the strategic positioning of Indian biopharmaceutical firms. Using the results obtained, we try to argue in this section that, from today's vantage point, it does not seem that TRIPS will have much impact, either positive or negative, on the incentives for new technology creation by Indian biopharmaceutical firms. Recall that TRIPS essentially represents a broadening of the existing IPR system. This means that Indians firms now have less incentive for being second innovators and more incentive for being first innovators.

The disincentive effect of TRIPS on Indian firms as second innovators is likely to be strong as, under the new regime, they cannot produce the patented product. The only way they can get around this problem is to create a new method and, if it satisfies the criteria of being novel, non-obvious and industrially applicable, they can try to get a patent on their process. However, even if they get a patent, they cannot produce the generic without getting a licence (through the compulsory licensing route) from the original innovator, which might take a great deal of time, effort and litigation.

This leaves us with the incentive effect. Is TRIPS likely to induce Indian biopharmaceutical firms to become first innovators? Our answer is that the incentive effect of TRIPS is likely to be negligible, but before justifying our view, we note some caveats. First, it is too early to judge the impact of TRIPS. In this paper we present the scenario which, to us seems to be the most likely to occur as of today. That is also the reason that we the title of this paper is the 'possible impact of TRIPS' rather than the 'impact of TRIPS'. Second, the scenario presented is applicable for a short period of time only. The innovation creating capacity evolves with the evolution of the national system of innovation. If a major player succeeds or loses out, or a significant proportion of firms lose or win in this game, it will have an impact on all the firms in the industry. Third, innovative activity is dependent on investments in R&D expenditure. We, i e, the authors, could not build a comprehensive database on the R&D expenditures of the firms concerned over the last 10 years. Therefore, our results have the drawback of being based on the current technology focus of the firm. Having spelt out the limitations, we now continue with the justification of our proposal.

In the post-TRIPS era the biggest focus of the Indian biopharmaceutical firms is going to be on biogenerics, off-patent vaccines and off-patent diagnostics. These are totally outside the purview of TRIPS. It would have been in the interest of Indian firms anyway to focus on off-patent products. 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.

As potential first innovators, Indian firms start with a handicap, even before the start of the game, in that they do not have the deep pockets necessary to create international blockbusters. In the event that an Indian firm creates a blockbuster, it is more likely to patent it directly in the US rather than go through the Indian channel. TRIPS has no impact on Indian firms patenting in the US. Furthermore, patents not only serve to mark technological territory but also to signal technological competence. A US or European patent may be more useful if patents are used as a signal of technological competence in order to initiate international collaboration. In this case, again, patenting activity of Indian firms will be outside the range of the Indian patent system.

Even as a first innovator, it will be difficult for an Indian firm to sell a final product on its own in western markets. There is no Sony, Mitsubishi or Daewoo among the pharmaceutical leaders. Well-established, American, British or European firms, with strong brand loyalty dominate the international pharmaceutical market. Any Indian winner will make its money by dominating the Indian market and then licensing its technology to western multinationals. For such transactions, a product patent regime in India is not necessary.

The first innovator's market is a winner takes all market. Since Indian firms start with a handicap as compared to western firms in this domain, many have opted to be an intermediate product manufacturers or service providers. In this fashion, they are not competitors of western firms in the winner takes all game but rather, provide complementary services to them. This is rational behaviour if a firm does not have deep pockets and is risk averse. Indian firms are going to be cogs in the wheel that produces innovations. 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 the increasing technological competence of Indian firms and the evolution of the biotechnology sector in India. The main services offered will be contract research, bioinformatics software provision and clinical research management.

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 firms, which are investing in finding cures to diseases that mainly affect the poor, are often doing it because of a managerial vision or mission rather than the profit

motive. Even integrated pharmaceutical companies, which are trying to create blockbusters, are willing to plough some of their funds into research directly into the health problems of the most poor. The TRIPS convention does not affect the incentives for investment in finding treatment for diseases afflicting the poor, which are not money spinners.

Finally, the TRIPS convention is unlikely to increase incentives for multinational pharmaceutical firms to invest in, or to collaborate with research and production units based in developing countries. The main obstacle to north-south international collaboration is not intellectual property but other basic problems associated with developing countries, such as having access to infrastructure (especially power), getting credible information quickly and ensuring commitment to contracts undertaken.

V
Conclusion

The objective of this paper was to provide some insight into the impact of TRIPS on the innovative capacity of developing countries, by taking India to be 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 earlier 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 healthcare.

The two central results of the paper can be summarised 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 on 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 will be to force Indian firms to put their re-engineered products on the market only when they get off patent.

Let us now reconstruct the above argument in an alternative fashion. TRIPS seems to be equivalent to imposing a law that Indian pharmaceutical firms cannot re-engineer patented products anymore. Of course, it goes without saying that in the absence of TRIPS Indian firms would have happily continued with ‘re-engineering’ existing patented products. Nevertheless, TRIPS is supposed to be more than a law banning re-engineering; it is supposed to be a change in and the broadening of the IPR, which should increase the incentives for Indian firms to become first innovators. It is this latter aspect that seems to missing in the Indian case. The strategic positioning of Indian firms seems to be more a function of their current competencies in the context of the present state of the Indian national system of innovation, and the nature of innovation creation in the biopharmaceutical sector, rather than being a result of TRIPS. This is our message. We do not go further in our analysis.

In light of the above, two recommendations can be offered to increase the production and availability of biopharmaceuticals in India and 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 be provided for the transfer of technology from public laboratories and the creation of new firms by public researchers. At present, venture capital fund companies are too risk adverse and lack the technical knowledge that would enable them to identify the appropriate conditions under which to supply 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 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, as they cannot compete with them. If such collaboration is to take place, the conditions for contract enforcement and protection of intellectual property must be created within the developing countries themselves. This can be greatly helped if there is financial and organisational support from

international agencies. Cooperation between developed and developing country firms is blocked mainly due to the problems of strategic interaction, such as cheating on contracts or commitment (moral hazard) or misleading information through omission or falsification (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 even TRIPS.

Address for correspondence:
shyamar@grenoble.inra.fr
augustin.maria@ensmp.fr

Notes

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1 Modern biotechnology refers to techniques that involve an understanding, a mapping, manipulation or 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.
2 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 during 1998-1999.
3 WTO, 1994, TRIPS: Agreement on Trade-related Aspects of Intellectual Property Rights. *Annex 1C of the Marrakesh Agreement establishing the World Trade Organisation*, April 15.
4 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 the AIDS epidemic in most developing countries should be considered as a situation of emergency. This would justify the enforcement of the compulsory licensing provision. Moreover, 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 licence on recent AIDS therapies at a low cost to national pharmaceutical companies. More likely, the lack of agreement between the states and companies would allow the state to neglect the protection on the patent and allow domestic companies to produce a similar drug if they succeed in developing it.
5 This section is based on the findings of Maria et al (2002). The interviews in Maria et al covered a much larger ground. Here we use only part of the information gathered during their interviews, i e, the information pertaining to the technology focus of the firms.

References

Chaudhuri, Sudip, (2002): 'TRIPs Agreement and Amendment of Patents Act in India'. *Economic and Political Weekly*, Vol 37, No 32, pp 3354-60.
Edquist, C (2001): 'The Systems of Innovation Approach and Innovation Policy : An Account of the State of the Art', Paper presented at the DRUID conference, Aalborg, June 12-15, http://www.tema.liu.se/tema-t/sirp/chaed.htm.
Freeman, C (1995): 'The National System of Innovation in Historical Perspective', *Cambridge Journal of Economics*, 19, pp 5024.
Ganguli, P (1999): 'Towards TRIPS Compliance in India: The Patents Amendment Act 1999 and its Implications', *World Patent Information*, 21, pp 279-87.
Lalitha, N (2002): 'Indian Pharmaceutical Industry in the WTO Regime: A SWOT Analysis', *Economic and Political Weekly*, 32(48), pp 111-20.
Lall, Sanjaya (2003): 'Indicators of the Relative Importance of IPRs in Developing Countries', *Research Policy*, 32, pp 1657-80.
Lanjouw, J O and I M Cockburn (2001): 'New Pills for Poor People? Empirical Evidence after GATT', *World Development*, Vol 29, No 2, pp 265-89.
Lundvall, B A (ed) (1992): *National Innovation Systems : Towards a Theory of Innovation and Interactive Learning,* Pinter, London.
– (1998): 'Why Study National Systems and National Styles of Innovation?', *Technology Analysis and Strategic Management*, 10, 4, pp 407-21.
Maria A, J Ruet, M H Zerah and P N Giraud (2002): 'Biotechnology in India', Report prepared for the French Embassy in New Delhi, www.cerna.ensmp.fr/Documents/AM-JR-MHZ-BiotechReport.pdf
Nelson, R (ed) (1993): *National Innovation Systems: A Comparative Analysis*, Oxford University Press, Oxford.
OECD (2001): *National Innovation Systems,* OECD, Paris, p 3.
Pisano, G P (1991): 'The Governance of Innovation: Vertical Integration and Collaborative Arrangements in the Biotechnology Industry', *Research Policy*, Volume 20, pp 237-49.
Ramani, S V (2002): 'Who's Interested in Biotechnology: R and D Strategies, Knowledge Base and Market Sales of Indian Biopharmaceutical Firms, *Research Policy*, Vol 31, pp 381-98.
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 1/2, pp 95-115.
Scotchmer, S (1991): 'Standing on the Shoulders of Giants: Cumulative Research and the Patent Law', *Journal of Economic*

Perspectives, Vol 5, Issue 1 (Winter), pp 29-41.
Tewari, S (2001) 'Genomics and Bioinformatics: The Way for the Future' in *CII (ed), Business Opportunities in Biotechnology*, Confederation of Indian Industry, New-Delhi.
TIFAC (2002): 'Recombinant DNA Products', *Techno-market Survey TMS167*, Technology Information Forecasting and Assessment Council, New Delhi.
Tufts Centre (2002): 'Tufts Centre for the Study of Drug Development', *Impact Report*,Vol 4, No 5 September/October.