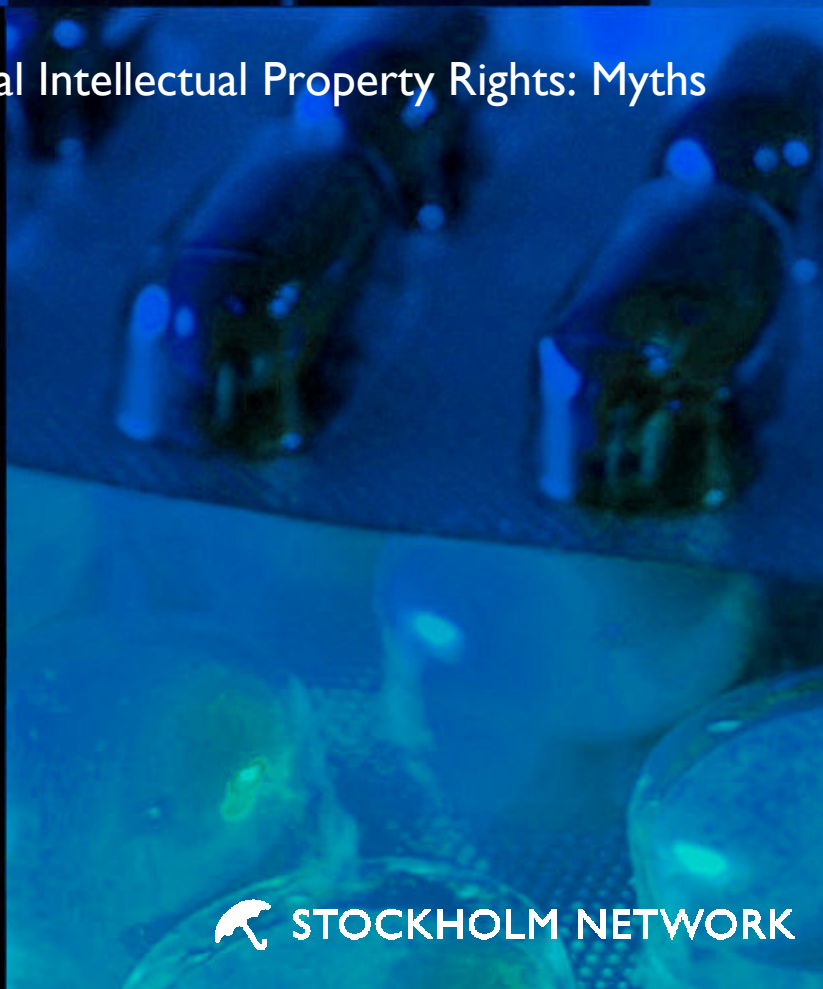
The Stockholm Network Experts' Series on Pharmaceutical Intellectual Property Rights

Developing Countries and Pharmaceutical Intellectual Property Rights: Myths and Reality



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STOCKHOLM NETWORK

Developing Countries and Pharmaceutical Intellectual Property Rights: Myths and Reality

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Contents

I. Introduction

In view of the current debates on the value of intellectual property rights (IPRs) for growth, it is worth spending time considering why developing countries should promote intellectual property (IP) protection, rather than devoting efforts to obstructing it.

While many maintain that the healthcare problems of developing countries are attributable to the IP system, in particular the global extension of IPRs to developing countries through international and bilateral agreements, one has to recall that these problems were in existence before pharmaceutical IPRs were introduced in these countries. Prior to the WTO Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) which came into effect in 1995[2], many developing countries did not grant any effective IP coverage for pharmaceutical innovations. Yet these countries still suffered from the dual problems of inadequate access to healthcare and insufficient research and development (R&D) into diseases that disproportionately affect developing countries. In fact, and as this paper will show, in the post TRIPS era the health situation in many developing countries that are now signatories to this agreement has improved rather than deteriorated. Not only has the world agenda to prioritise R&D for "neglected" diseases received a strong impetus, but world economic and social growth processes have accelerated.

As Straus[3] points out, those who vehemently complain about the international concept of IPRs neither entertain the circumstances of developing nations and industrialised countries before TRIPS, nor, even more surprisingly, do they base their theoretical deliberations on any empirical insights. Indeed, no single attempt has ever been made in this direction.

When one does look at the evidence, the post TRIPS balance - in spite of delays, incomplete and poor implementation of its minimum mandatory standards in many countries - looks positive. In healthcare terms, by 2002, the WHO recorded a world 0.1% mortality rate for "neglected" tropical diseases: trypanosomiasis and leishmaniasis and zero for other four tropical diseases, and a striking decrease in mortality from schistomiasis, which the WHO recorded at 200,000 in 1995[4]. In the social arena, the Human Development Index (HDI), created by the United Nations Development Programme, based on life expectancy, education and GDP per capita and considered a key measurements of well being has been going up for most countries.

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[2]. According to the TRIPS Agreement, developing countries were supposed to implement the agreement by 2000, while least developed countries are not required to implement the IP provisions relating to pharmaceuticals before 2015 (this is a result of the Doha Decleration on TRIPS Agreement and Public Health of 2001)

[3] Joseph Straus (Director at the Max Planck Institute for Intellectual Property, Competition and Tax Law of Law, Munich, Germany) on: "The Impact of the New World Order on Economic Development: The Role of the Intellectual Property Rights System", in The John Marshall Review of Intellectual Property Law. L.1 (2006)

[4] WHO, The World Health Report 2002. Reducing Risks, Promoting Healthy Life, Geneva, (2002)

All but three of the 102 countries for which data is available showed improvements[5]. According to Goklany, this index probably understates improvements for the majority of the world's population because it omits measurements of hunger and infant mortality, both of which have also improved[6].

In the economic area, a joint research fact finding survey (2007) by the World Intellectual Property Organisation (WIPO) and the United Nations University (UNU) measured the economic impact of IP systems in six Asian countries; China, India, Japan, Malaysia, the Republic of Korea and Vietnam. The research incorporates company data, where available, dating back over the last 20 to 30 years and was undertaken in view of the strong demand for empirical economic findings. The reports examine the impact of the IP system on areas such as R&D, foreign direct investments (FDI) and technology transfer. It finds "*a positive correlation between the strengthening of the IP system and subsequent economic growth*"[7].

Although direct correlation is hard to substantiate, many of the huge investments in technology and manufacturing activities and other advantages obtained by emerging economies, like India and China, can be linked to the laborious balance secured by the WTO Agreements, including TRIPS. In this respect, if the current round of multilateral trade negotiations (the so-called Doha Development Agenda), conclude successfully, a new impetus to development will be established[8].

II. The Real Challenges for Access to Medicines

In the past century we have seen the development of breakthrough therapeutics and the emergence of a healthy biopharmaceutical industry. Particular success has been achieved in fighting infections - such as bacterial and fungal diseases - avoiding deaths and allowing cures. Significant vaccines, crucial for prevention have also been introduced.

These enormous technological advances have allowed us to live longer and healthier lives. This looks likely to continue over the next twenty years, with the emergence of genetic profiling, pharmacogenetics, novel diagnostics, and possible gene therapy.

But, this does not mean that extraordinary global health challenges do not remain for which R&D remains the only rational way to find solutions. Among these challenges one can identify insufficient treatments for threatening diseases, such as different forms of cancer, Alzheimer's or Parkinson's disease, a lack of cures for chronic disorders such as diabetes, the availability of only palliative or symptomatic relief that does not address the underlying causes of ailments, the growing problems of bacterial resistance as well as the need

[5] UNDP, Human Development Report (2004.)
[6] Indur Goklany, Wealth, Health and the Cycle of Progress, article in Fighting the Diseases of Poverty, International Policy Press, U.K., (2007)
[7] WIPO: http://www.wipo.int/portal/en/news/2007/article_0032.html . Last visit 12 November 2007.
[8] Joseph Straus (Director at the Max Planck Institute for Intellectual Property, Competition and Tax Law of Law, Munich, Germany) on: "The Impact of the New World Order on Economic Development: The Role of the Intellectual Property Rights System", in The John Marshall Review of Intellectual Property Law. L.1 (2006)

to address adverse reactions, limitations in efficacy, doses, presentation forms and side effects.[9] Most worrying, however, is the emergence of new infectious diseases. Over 25 new infectious diseases – in addition to the existing ones - have been identified since 1973.

The WHO indicates that reducing the very high incidence of communicable diseases that disproportionately affect developing countries is an overriding priority but also recognises the importance of ensuring that the increasing prevalence of non-communicable diseases is recognised and addressed. The overall focus, however needs to be on disease conditions of significant public health importance for which adequate treatment is not available, not only because they are unaffordable or inappropriate for use in countries with poor delivery systems but also because in many cases the treatments do not exist[10]. Improving the distribution of existing medicines alone is neither the solution to the health problems of the "rich" nor for fighting the diseases of poverty as the above mentioned global health challenges clearly demonstrates. There is still a need to promote pharmaceutical innovation both for the industrialised and the developing world.

How best to achieve this goal? By undermining the IP system? The answer is a flat: No!

For a start, focusing on patents as a culprit is diverting the attention from the real health issues that need addressing.

To illustrate this point, only 20% of India's total health expenditure goes on drugs, as in most other developing countries. Of this 20%, every drug on India's essential list of 74 is already generic, meaning its patent has expired, so production is cheap. Despite this these drugs are still not accessible to all who need them[11]. Moreover, many of the patents for essential medicines are not registered or enforced in less developed countries. This is particularly true in terms of antiretroviral medicines for HIV and AIDS in Africa. Rozek reminds us that only 15 of the 306 products on the WHO's Model List of Essential Drugs - or less than 5% - are protected by patents.[12]

There are many fundamental problems in access to health services in developing countries that are unrelated to patents. These range from poor funding as a result of incorrect assignment of resources, to physical barriers, including lack of healthcare facilities, staff, equipment or distribution channels, as well as information asymmetries. In relation to the AIDS epidemic the director of the WHO's HIV division stated;

[9] David Webber, Maciej Gajewski & collaborators at IFPMA, Encouraging Pharmaceutical R&D in Developing Countries, IFPMA: International Federation of Pharmaceutical Manufacturers Associations, Geneva, Switzerland, (2003)
[10] WHO, Draft global strategy and plan of action on public health, innovation and intellectual property, 31 July 2007, Geneva.
[11] Bibek Debroy, Patents help the sick, poor globally, The China Post, 11 October 2007
[12] Richard P.Rozek, The Effects of Compulsory Licensing on Innovation and Access to Health Care, National Economic Research Associates, Washington, DC, September 2000

"*The real obstacle is the fragility of the health systems. You have health infrastructure that is dilapidated, and supply chains that do not exist."*[13]

James Killick commenting on the WHO's Commission's Report on Intellectual Property Rights, Innovation and Public Health concludes that this report often fails to address the real problems faced by developing countries. Getting access to any type of medicines and in particular to basic generic medicines that went off patent long ago is the real issue. [14].

Rozek's analysis of pricing is also revealing and indicates that government officials have been bombarded by misinformation. Rozek and Berkowitz studied prices and found that protecting IPRs does not result in an increase of real or nominal prices of existing products. They also found that strengthening IPRs had no significant impact on the prices of any drugs including those products introduced after IPRs had been strengthened in countries with price regulation[15]. It should also be remembered that the economic study made by the Latin American think-tank FIEL on Argentina - a country that did not allow patents for pharmaceutical products - revealed that the prices paid for 'generics' (medicines sold by the local firms which could be passed off as originals) were on average 60% more expensive than the original medicines marketed by the international laboratories[16].

Rozek contends that, in fact, not protecting IPRs is a likely cause of reduced access to healthcare because of the reluctance of innovators to introduce products in some countries. He provides data on six drugs. Korea - the first country in the sample to protect IPRs - received 4 of the 6 drugs studied either first or second among the nine countries studied. By comparison, there were delays in introducing the innovative products in countries with no IP protection, while two of the six products were not even introduced in three of the five countries that did not protect IPRs for pharmaceuticals[17].

III. The Role of IPRs in Pharmaceutical Research and Development

Far from being a major problem, IPRs represent a part of the solution to addressing global health needs because of the key role of IPRs in pharmaceutical innovation. This is because pharmaceutical innovation has some special characteristics which make IPRs very important.

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[13] Patricia Reaney, Interview: Creaking health systems hampering Aids battle- WHO", Reuters, News Media, 21 July 2006.
[14] James Killick, The WHO Commission's Report on Intellectual Property Rights, Innovation and Public Health: a missed opportunity, in Healthy IPRs, The Stockholm Network, UK (2007)
[15] Richard P. Rozek and Ruth Berkowitz, The effects of patent protection on the prices of pharmaceutical products. Is Intellectual Property Protection Raising the Drug Bill in Developing Countries, in the Journal of World Intellectual Property, Vol.1 N° 2, Werner Publishing Company, Geneva, Switzerland, March 1998,
[16] Fundacion de Investigaciones Economicas Latinoamericanas, FIEL, Proteccion de los Derechos de Propiedad Intelectual. El caso de la industria farmacéutica en la Argentina, Ediciones Manantial, Argentina (1990)
[17] Richard P.Rozek, The Effects of Compulsory Licensing on Innovation and Access to Health Care, National Economic Research Associates, Washington, DC, September 2000

The development of a new drug candidate is a lengthy process that can take from 10 to 14 years. The cost of bringing a drug to the global market is on average $897 million[18]. A recent analysis came up with an even higher average, but with wide variation across companies and producers (e.g., average HIV drug: 479m., average figure for rheumatoid arthritis: 936m)[19]. In addition it is estimated that very few projects complete the full cycle. The R&D process may end abruptly due to lack of efficacy of the drug candidate, toxicity or adverse reactions. Because the proportion of successful R&D pharmaceutical projects is very low risks for investors are very high.

At the same time, in the first years of the 21st century, the issue of prescription drug safety has come to the attention of the public with renewed intensity, due to highly publicised drug withdrawals and health drug risks. These are among the factors which have contributed to the deterioration of public confidence[20] and in turn much longer drug development cycles due to the need to engage in many years of clinical testing.

IPRs are essential not only when the necessary investments are made by private investors. They are also a key factor in establishing collaboration among different participants in the R&D project to cover the many phases of the process, regardless of whether they are public or private participants and investors.

Different IP categories are used in the R&D process; among others patents, trade secrets and health registration data exclusivity. IP licensing expertise is also essential.

Patents

In order to be patented, an innovation must meet the requirements of novelty, inventive step and being capable of industrial application (TRIPS Art. 27). The footnote to this Article indicates that the terms "inventive step" and "capable of industrial application" may be deemed to be synonymous with the terms "non-obvious" and "useful" respectively.

Those advocating weakening the patent system call for making use of all the "flexibilities" they consider that TRIPs allows and recommend that developing countries raise the requirements in such a manner that they would differ from the long established principles, directives and guidelines in force in the industrialised world. Under these proposals, the legal TRIPS requirement of "inventive step" would become an "inventive leap" requirement. This is not a TRIPS concept, nor does the requirement reflect the fact that in the pharmaceutical industry a great deal of innovation comes from step by step progress.

[18] Center for the Study of Drug Development, Tufts University
[19] The Economist, A survey of pharmaceuticals, 18 June 2005.
[20] Institute of Medicine of the National Academies: The Future of Drug Safety. Promoting and Protecting the Health of the Public. The National Academic Press, Washington, D.C., (2007)

Protection of Pharmaceutical Test Data

A patent only covers the invention as such, but to introduce an original medicine much more is required of the pharmaceutical industry. In order to safeguard the public, the innovator is required to invest in extensive testing and report on the efficacy, safety and quality of the proposed new medicine. The health regulatory agencies of industrialized countries demand preclinical tests in animals and clinical studies in human populations, which meet bioethical requirements and follow good clinical practices. These studies can represent up to sixty % of total R&D investments[21].

Article 39.3 of TRIPS determines that the submission of undisclosed tests or other data to the health regulatory agencies must be protected against unfair commercial use. This IP protection is known as marketing or data exclusivity. The same article excludes health officials or third unauthorised applicants to rely on or use the originator's data for the benefit of manufacturing commercially similar versions of the innovation during a certain defined period of time - 5 years in the US or 10 years in the EU. During this term, every applicant must submit a full application dossier for the evaluation of his proposed medicine. After the data exclusivity term expires, third parties are allowed to submit to the health regulatory agencies abridged information, without having to prove efficacy and safety for their versions. It is sufficient, for example, among other requirements, to furnish the results of tests of bioequivalence with the innovation first registered.

Data exclusivity was established in industrialised countries as a balanced solution to avoiding unfair competition, taking into account, on the one hand, the need to compensate the innovator for developing the clinical data, and on the other hand, allowing the generic manufacturer to avoid, after the marketing exclusivity term concludes, the efforts and investments of duplicating the full tests required of the originator.

As discussed above, data exclusivity serves the public by allowing health registration authorities to ensure that the new drug is safe for public use. Pre and post evaluation by the health authorities becomes almost impossible when several generic imitations are launched almost simultaneously or even before the original drug. This is what happens in many developing countries that deny data exclusivity based on "flexible" TRIPS interpretations under the flawed argument that manufacturing generic copies promotes local laboratories and facilitates access to medicines.

Acts or omissions of health agencies are a decisive factor in protecting the public, but also influence and effect the promotion of national R&D systems. It is undeniable that the quantity and quality of investments in pharmaceutical innovation would not be what they are if the health registration authorities of central

[21] International Federation of Pharmaceutical Manufacturers Associations, IFPMA, The pharmaceutical innovation platform, Geneva, Switzerland, October 2004

countries did not demand that the efficacy, safety and quality of medicines be proved. Therefore, TRIPs Article 39.3 on data protection offers an opportunity to improve both the efficacy and safety of medicines. It allows countries to request tests and data before and after marketing approval whilst allowing investors to be protected against *free riding*. This unfortunately does not happen when data exclusivity is not observed due to "flexible" TRIPS interpretations.

The Importance of an Adequate Exclusivity Period for the Diffusion of New Products

IP does not only cover inventive efforts, it is related to the full value chain of innovation; from research in the lab to the satisfaction of those who benefit from the new therapy. The R&D process is not completed with the approval of marketing by the health regulatory agency and the post marketing surveillance. To introduce a new medicine investments must be made to report, educate and inform on its value, its uses, actions, dosages, side effects and correct application, and improvements over existing alternatives.

Burstein[22] reminds us that the proportion of social benefit of the innovation that may be appropriable by the innovator may be small even under the most favourable property rights and circumstances. As such there is a need to guarantee a sufficient period of exclusivity to allow the market and consumers to be fully aware of the new treatment and its benefits

Success on the part of the innovator in terms of the diffusion of the benefits of a new product will attract rivals (innovators and generics) to compete in this market. When diffusion has reached its critical level, it may become highly profitable for generic companies to enter the market without much investment.

Conversely where there is a weak level of IP protection, leading to an insufficient period of exclusivity, it may well be found that educational and information investments are sub-optimal, as is the case in many developing countries. As Rozek points out, the innovator has the incentive to invest in providing good information about the proper use of its products to safeguard the reputation of the firm and the innovation which he needs to sell during at least its whole lifecycle[23]. This is not necessarily the case with imitator companies that have have no attachment to any particular research and development project and may easily change from one product to the next in any therapeutic field. Evidence on efficacy, safety, bio-availability, impurities and active substance suppliers is seldom requested by the health regulatory agencies. Thus it may be seen that claims on the benefits of the products are not based on scientific and technical evidence while risks, adverse and other side effects are silenced. Insufficient information and education, as well as sub-optimal diffusion on new drugs, are neither beneficial for patients and consumers nor for the health of the population.

[22] M.L. Burstein: Diffusion of Knowledge-based Products: Applications to Developing Economies, in Economic Inquiry, Volume XXII, Number 4 (October 1984), Simon Fraser University, Western Economic Association, California, US.
[23].Rozek (2000), OP.CIT

IV. Pharmaceutical IPRs Work for Developing Countries

Pugatch[24] maintains that the combination of IP and pharmaceuticals has become one of the most important tools in modern society. This field is complex and multidimensional and there are many debates, but, as Pugatch adds, it is essential to keep the bigger picture in mind: Pharmaceutical IP works.

I would like to add that pharmaceutical IP also works for developing countries and on three grounds: (a) the availability of original medicines that have been adequately tested; (b) the search for new medical treatments, and (c) investments in manufacturing, R&D activities and in information and education.

I have already referred to the WIPO-UNU Joint Research Project that measured the positive economic impact of IP systems on growth in six Asian countries. Another study[25], on the effects of strengthening IPRs in developing countries concluded that a stronger level of IP protection leads to increases in FDI, which accelerates industrial development. The study finds that theoretically the strengthening of IPRs will lead to an increase in the share of developing countries in global manufacturing as well as enhance the production of recently invented goods. Empirically, data measuring levels of industrial activity and initial export periods of tradable goods suggest that the expansion of multinational activity more than offsets any decline in the imitative activity of indigenous firms. Analysis of 16 countries that have improved their IP regimes confirms these predictions[26].

There are also several studies indicating that there is a positive relationship between the rate of innovation and patents in the pharmaceutical industry. The widely cited Mansfield (1986) research, as well as that carried out by Cohen and Levin (1989), Johnson, Cohen and Junker (1999) and Cohen, Nelson and Walsh (2000) confirm the importance of patents for knowledge-based sectors such as pharmaceuticals, chemicals and biotechnology. As will be discussed, new analysis in Latin America confirms the relevance of IPRs for the development of pharmaceuticals in developing countries.

Patents are especially crucial to the innovative R&D mounted by small startup biotechnology firms, which many developing countries are trying to promote. "*Indeed they are typically the only assets these firms possess that are sufficiently stable and valuable to attract the large amounts of capital they need to exploit promising research towards new drugs and diagnostics*"[27].

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[24] Meir P.Pugatch, Why Pharmaceutical IPRs?, in Health IPRs, The Stockholm Network, Great Britain (2007)
[25] Lee Branstetter, Raymond Fisman, C Fritz Foley and Kamal Saggi, Intellectual Property Rights and Foreign Direct Investment: Theory and Evidence, National Bureau of Economic Research, Massachusetts, Working Paper N° 13033, April 2007, http://www.nber.org/papers/w13033
[26] Lee Branstetter, Raymond Fisman, C Fritz Foley and Kamal Saggi (2007)
[27] Claude Barfield and John E. Calfee, Biotechnology and the Patent System, Balancing Innovation and Property Rights, page 27, American Enterprise Institute, Washington D.C., (2007)

Global Developments in R&D

The Stanford Bernstein Report[28] concludes that the industry's best hope for survival lies in innovation, its traditional strength. But, it is important to note that R&D is not as productive as it used to be. The global industry saw 24 new drugs approved by the US Food and Drug Administration in 1998 with $27 billion R&D investment. In 2006, only 13 new drugs were approved, but investments in R&D rose to $64 billion. As a result the business model of a vertically integrated approach to developing, manufacturing and selling drugs has changed in favour of outsourcing. This new model favours developing countries that are able to attract investments i.e. those with strong IP systems.

Teece [29] indicates that the increasing willingness of multinational firms to outsource appears to have gone almost unnoticed in the literature on development economics. Small science-based companies with high quality products may lose unless their IPRs are well-protected and/or if these companies are not strategically well positioned with respect to key complementary assets required to market the product. It is the complementary capacities and dynamic capabilities which must be built to transform a technological lead into a commercial success. Today, companies in the developing world can capture gains from innovation through strategies that focus less on straight imitation, as in the past, and more on developing world-class complementary assets in their countries or region to position them for relationships on attractive terms with pioneering firms located in the USA, Europe, and Japan.

Big companies are also looking for external sources of innovation. At present one-third of molecules currently in the R&D pipeline originated in biotech companies. Licensed molecules have had a higher chance of success in development in recent years because big drug companies tend to scrutinise them more closely before licensing them in at a later stage of their development. There has been significant growth in the amount of extramural or contracted out research. This includes Contract Research Organisations (CROs), Contract Research and Technology Organisations (CRTOs), and Research and Technology Organisations (RTOs), as well as a wider group of companies with some involvement in these activities, which has important implications for the development of innovation support infrastructure in local systems of innovation and their connectivity[30].

Worldwide, there are 65,000 multinational companies with 800,000 affiliates. 50% of all direct foreign investments, 50% of total investments in R&D and 10% of global sales can be attributed to these firms. 700 hundred R&D direct foreign investment centers have sprung up since 1993, mainly in China, India and Taiwan. None were reported before 1993[31].

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[28] The Economist, The Pharmaceutical Industry, Beyond the Pill, 27 October 2007.
[29] David J. Teece, Managing Intellectual Capital, Organizational, Strategic and Policy Dimensions. Oxford University Press (2000)
[30] Jeremy Howells, Outsourcing Novelty: The Externalization of Innovative Activity, in Knowledge and Innovation, pages 196-214, in the New Service Economy by Brigitte Andersen, et al. Edward Elgar Publishing Inc, US. (2000)
[31] Felix Rozanski: Intellectual Property as Part of the Free Trade Agreements, in Business Guatemala, www.amchamguate, January 2007

Post TRIPS Developments in Developing Countries

Positive post TRIPS developments in pharmaceutical R&D have been analysed in several countries. The evidence shows that economies that have made significant efforts towards implementing TRIPS, even entering into so called 'TRIPS-plus' agreements (linked to free trade agreements), have benefitted significantly from embracing IP and the knowledge economy. In particular significant benefits for the pharmaceutical and biotechnology industries can be identified.

Ryan and Shanebrook[32] conducted research into Jordan, a country that strengthened its IP system as a result of joining WTO as the 136th Member in 2000 and signing an FTA with the US in 2001. The evidence concludes that:

"*Contrary to conventional wisdom, globalization has benefited Jordan. The results include increased economic growth generally, and in particular, benefits for Jordan's pharmaceutical and bio-medical technology industries. New health sectors, including contract clinical research, have spurred a new focus on research-based innovation for Jordanian pharmaceutical companies; there is a growing multinational presence; medical tourism has taken on new importance, and the number of clinical trials has multiplied. This in turn has fueled job growth and launched Jordan as the leading knowledge economy in the Middle East".*

Similarly, Singapore is now proving an attractive destination for pharma firms thanks to efforts to create an appealing business environment, a component of which is a strong IP regime. Biopharmaceuticals are indeed driving the growth in the region's manufacturing base, with heavyweights GlaxoSmithKline, Genentech, Abbott and Lonza investing in Singapore's economy.Novartis, the Swiss pharmaceutical firm, revealed that its largest foreign direct investment in its history (US$700 million) will take place from 2008 to 2012 in the low cost, high quality biopharma hub of Singapore. Biologics currently comprise 25 per cent of the company's pre-clinical research pipeline, and according to the company they are "*increasingly a priority in research and development activities.*[33]"

India has a somewhat shakier relationship with IP in the post-TRIPS world. New restrictions on the free imitation of drugs could be said to have imposed significant costs in post-TRIPS India. It is estimated that had Indian firms been prevented from copying fluoroquinolones, for example, the Indian public would have been worse off by an estimated $255m a year[34]. However, these short term opportunity costs should be

[32] Michael P.Ryan and Jillian Shanebrook, Establishing Globally Competitive Pharmaceutical and Bio-Medical Technology Industries in Jordan, Assessment of Business Strategies and the Enabling Environment, International Intellectual Property Institute (IIPI), Washington D.C. and Achievement of Market-Friendly Initiatives and Results Programme (AMIR), Jordan, August 2004

[33] Anna Lewcock, In Pharma Technologist com 29 October 2007, http://www.in-pharmatechnologist.com/news/ng.asp?n=80948&m=1IPEO29&c=dblrcdwapdkwvkr Last visited 7 November 2007.

[34] *The Economist*, High-tech hopefuls, 10 November 2007, quoting a study of the antibiotics market made by Shubham Chaudhuri, Pinelopi Goldberg and Panle Jia.

confronted with the developments that are now taking place. India's top ten drug firms now spend US$170 million per year on R&D[35]. While China's domestic pharmaceutical industry remains largely focused on generic manufacturing of brand-name drugs and researching traditional Chinese medicine, Indian domestic manufacturers are now undertaking serious drug discovery contract research. The Indian clinical trials market is expected to reach $1 billion by 2010 and contract manufacturing currently worth $350 million is also expected to reach $1 billion by 2010. There are 85 US Food and Drug Administration (FDA) approved active pharmaceutical ingredient (API) and formulation plants located in India, the highest such number outside the US[36]. NPIL, the fourth biggest pharmaceutical firm now invests 6% of its revenue on R&D, and at least seven drugs in its pipeline count as "new chemical entities". India is now host to over 100 multinational R&D centers, some of which carry out collaborative research with western drug companies (e.g., Ranbaxy with GlaxoSmithKline, Glenmark with Forest Lab). In the past many of India's chemists ended up abroad; an estimated 15% of scientists working in the American pharmaceutical industry are of Indian origin. Evidence shows that they are slowly being lured back to India.[37]

It should be kept in mind that India's pharmaceutical firms still do not invent many drugs, but they have been active in creating new ways to deliver them and improve their efficacy, and are alert to the collaborative opportunities the post-TRIPS environment has created. However, for all its promise, India still has significant IP problems. A patent law on paper does not necessarily mean IP protection in practice and this uncertainty has limited investment.

Among the Latin American developing countries, Brazil and Argentina, also show post TRIPS positive balances in the pharmaceutical sector. Regarding Brazil, Raimundo explains that after the approval of the 1996 industrial property law N° 9.279, which ended with the exclusion of patents for pharmaceutical inventions, very important FDI and R&D activity occurred, including clinical research mainly in phases II and III. At the same time Brazilian laboratories such as Fiocruz, Biosintetica and Biolab/SanusUQ, filed patent applications, and conducted a number of technology transfer agreements. In 1996, the Ministry of Industry, Trade and Tourism predicted that investments in the pharmaceutical and chemical sector would grow by US$600 million by 1999. In April 1997 big multinational companies announced over US$1.2 billion of new investments[38] However, an ill-conceived amendment to article 299-C of the patent legislation - incorporating a revision of the health agency ANVISA of all pharmaceutical patent applications before they could be granted by the Patent Agency INPI, as well as restrictive interpretations of the scope of patents, and the

[35] *The Economist,* A survey of pharmaceuticals, June 18 2005.
[36] Heinz Redwood, Independent Consultant, UK, comments provided to the author in July 2007.
[37] *The Economist,* A survey of pharmaceuticals, June 18 2005.
[38] George K.Korenko, Intellectual Property and Industrial Growth, A Case Study, in The Journal of World Intellectual Property, Geneva, Vol.2, N°1, (1999)

severe backlog in the examination of applications - due to administrative and budgetary problems in INPI - contributed to a deterioration of the friendly investment climate that had been created by the 1996 law[39].

It is also interesting to comment on the positive developments that have occurred in the public sector. The Brazilian Federal Fundação Oswaldo Cruz - FIOCRUZ[40] FIOCRUZ has applied for 230 patents between 1989 and 2007. 105 applications are for vaccines and medicines.[41] Another good example is the University of Campinas, or UNICAMP, a Brazilian university publicly funded by the state of São Paulo, that has become a leader in technology transfer. INOVA - their technology transfer office - has signed 128 technology transfer agreements and licensed 45 technologies (41 patents and four cases of know-how) both to private companies and the government. These agreements will last for more than ten years and have already generated royalties for the Campinas University. During the same period, INOVA applied for 153 new patents, 22 trademarks, and 24 software registrations. Additionally, ten companies from UNICAMP's business incubator have become self-sustaining. They may leave the university, after which they will pay a royalty[42].

In Argentina, the Latin American think tank, Fundacion de Investigaciones Economicas Latinoamericanas FIEL[43] conducted a survey which concluded that, as a result of the introduction of pharmaceutical patents, new competitive strategies were adopted by the companies. Some multinationals that had previously closed their operations returned with investments. Foreign and domestic firms concluded agreements and alliances, for production or co-marketing. FIEL found that each company concluded an average of 5.4 agreements with other laboratories. Alliances have been made by foreign firms that offer technology developments with domestic firms that have operational flexibility and a deep penetration in the commercialization chain. There has also been cooperation in R&D activities, mainly with public/private health institutions or research laboratories. FIEL also points out that the patent legislation may give room to government arbitrariness and that one factor that has discouraged research is the lack of protection of data resulting from development tests.

At the same time, several Argentine laboratories have launched or reinforced their R&D programmemes and concluded many cooperation agreements with university research laboratories. The National Council of Science and Technology promotes the licensing of technology and their patents to the pharmaceutical sector[44]. The Secretary of Science, Technology and Productive Investments – now upgraded to the rank of Ministry by the newly elected Cristina Kirschner Government (December 2007) - has launched new

[39] Ibid.
[40] Fundação Oswaldo Cruz - FIOCRUZ, was established by Decree N° 66.624,(22 May 1970) and it is linked to the Brazilian Health Ministry to perform activities in the health sector including scientific and technological development More in www.fiocruz.br
[41] http://www.fiocruz.br/cgi/cgilua.exe/sys/start.htm?sid=186 Last visit 9 November 2000.
[42] Rosana Ceron Di Giorgio, From University to Industry: Technology Transfer at Unicamp in Brazil, in http://www.iphandbook.org/handbook/ch17/p16/http://www.iphandbook.org/handbook/ch17/p16/
[43] Monica Panadeiros, Nuevas Estrategias Competitivas en la Industria Farmacéutica Argentina y Reconocimiento de la Propiedad Intelectual, Working Paper N° 74, FIEL, Fundación de Investigaciones Latinoamericanas, October 2002.
[44] CONICET, Encuentro CONICET/INDUSTRIA FARMACEUTICA, 11 June 2007

programmemes to foster innovation. Success stories of the public/private cooperation are illustrated by the conclusions of cooperative agreements, such as "Genetic Research for Cancer and other Pathologies" concluded among; CONICET Leloir Foundation and the national private company Laboratorios Craveri; "Probiotics" signed by CONICET-CERELA and the national private company Biosidus; and "Recombinant Human Insulin" entered into by CONICET- IBYME and the private company Beta. All these efforts to spur national innovation take IP as a platform for the necessary investments to be made.

In a recent survey made on the utilization of innovation and appropriation mechanisms in the private sector in Latin American countries[45], the conclusions indicate that a small portion (not more than 10%) of the innovative firms make use of patents. This group is composed mainly of the big private firms and those in the pharmaceutical, metal mechanic and electronic sectors. The use of patents increases when qualified manpower is employed and when foreign capital participates in the firm. The study indicates that in Brazil trade secrets, rather than patents, are preferred by private firms. The authors conclusion is that although IP legal mechanisms (with the exception of trade-marks) do not seem to have a relevant role in Latin America, there are specific sectors, such as the pharmaceutical industry, where patents, and more recently data protection, are crucial for competition.

These findings indicate that in times when turning scientific discoveries into new products and smart processes means development and growth, patents are a platform to achieve this objective. Developing countries really need to attain higher levels of investment and attract private capital. In addition to foreign direct investments, national and foreign venture capital would contribute to the capital shortage. The link between venture capital and innovation is strong. "*A dollar of venture capital could be up to ten times more effective in stimulating patenting that a dollar of traditional R&D".* Policy makers should also bear in mind that surveys indicate that the amount of venture-capital money in a sector dramatically increases according to the rate at which business in that sector take out patents[46].

The Role of IPRs in Public-Private Partnerships

Today, an increasing amount of R&D, funded by public and private sources, is taking place in the developing world for prevalent infectious diseases such as malaria and HIV/Aids. Malaria, caused by a parasite carried by mosquitoes, kills more than 1 million people every year and makes 300 million seriously ill - mostly young children in Africa. Experts agree that a vaccine is the best way to fight the disease, but this has proven near impossible. The Plasmodium falciparum parasite has a complex life cycle inside mosquitoes and the human body, which helps it to evade the immune system. GlaxoSmithKline (UK) reports that its experimental vaccine had protected 65 percent of infants from infection and reduced illness by 35% after six months. Sanaria (US) is working to make a vaccine that has been shown to provide more than 90% protection, lasting

[45] Andres López y Eugenia Orlicki, CENIT, Innovación y Mecanismos de Apropiabilidad en el Sector Privado de América Latina, for WIPO/CEPAL, August 2007.
[46] Samuel Kortum and Josh Lerner, quoted by The Economist, "A Special Report on Innovation", 13 October 2007.

for at least 10 months. Sanaria has raised $45 million in grants to do this, including $9 million from the U.S. National Institutes of Health, $30 million from the Bill and Melinda Gates Foundation via the PATH Malaria Vaccine Initiative and $4 million from the U.S. Army Military Infectious Diseases Research Programme. Testing in human volunteers may begin in 2008[47].

IP is crucial to these partnership projects. The resources which the pharmaceutical company can make available arise from previous successes or private capitals that must be remunerated. Cooperative agreements need to define the corresponding appropriation and licensing provisions regarding the results of research as well as those necessary in order that the parties can make available their know-how, confidential information and expertise in drug development confident that funds can be recovered for supporting new research.

Public-private partnerships are also playing a role in the treatment of 'neglected diseases' such as chagas, visceral leishmaniasis and dengue fever. For example, The Institute for OneWorld Health, based in San Francisco, buys the rights to develop drugs for "neglected" diseases from multinationals, then carries out the laboratory work and clinical trials. OneWorld has released a serum that cures visceral leishmaniasis, a deadly disease transmitted by sandflies. Companies such as GlaxoSmithKline, AstraZeneca, Sanofi-Aventis and Novartis have instituted a no-profit, no-loss formula for work on 'neglected diseases'[48]. Another example is The Global Alliance for TB (Tuberculosis) Drug Development (TB Alliance), a not-for-profit, product development partnership. They received worldwide exclusive rights to PA-824 and its analogs for the treatment of TB in a landmark 2002 agreement with Chiron, now part of Novartis, which includes ensuring that the technology will be made available royalty-free in endemic countries[49].

Although the Western pharmaceutical industry is frequently vilified, without the initial investments in antiretroviral therapies, by leading firms such as Abbott, Bristol-Meyers-Squibb, GlaxoSmithKline, Pfizer, Roche and Merck, among others, the positive developments in the advancements in antiretroviral therapies would have not taken place. While in 1987 only AZT was available to fight HIV/AIDS, there are currently 35 medicines to treat ailments related to AIDS/HIV and 79 being developed by the innovative pharmaceutical private industry[50]. The economics which have led to the cross-subsidisation that has taken place both between drugs and between different countries, by having low-income countries pay less for the medicines than those prices obtained in high-income countries, would be threatened if IP protection was weakened[51].

[47] Maggie Fox, Malaria Vaccine Plant Takes a Gamble, Reuters, 27 October 2007.
[48] Carol Gaoar, World Transforming Partnerships, in The Star.com, http://www.thestar.com/article/274157, 7 November 2007.
[49] Global Alliance For TB Drug Development, their News Update, 8 November 2007.
[50] Dr. Jorge Raimundo, Presentation in the International Symposium, Innovation and Creativity for Development. Opportunities and Challenges for Next Decade, IDS, Sao Paulo, Brazil, 23 October 2007.
[51] John S. Gardener, IGWG: Beyond its Mandate?, A Federalist Society White Paper, November 2007

V. Global Discussions on Pharmaceutical IPRs

WIPO's Development Agenda

On September 28, 2007 WIPO member states adopted a Development Agenda consisting of a series of recommendations to enhance the development dimension of WIPO's activities[52]. This Development Agenda was first launched by Argentina and Brazil, and supported by an additional 12 developing countries (Friends of Development), at the 2004 WIPO General Assembly. The 2007 recommendations include a set of 45 agreed proposals covering six clusters of activities, including: Technical Assistance and Capacity Building; Norm-setting, Flexibilities, Public Policy and Public Knowledge; Technology Transfer, Information and Communication Technology (ICT) and Access to Knowledge; Assessments, Evaluation and Impact Studies; Institutional Matters, including Mandate and Governance. Member states agreed to establish a Committee on Development and Intellectual Property to develop a work-programme for implementation of the adopted recommendations.

The 45 measures are worded in more reasonable terms than the original proposals and much will depend on how well this programme is implemented. However, it is disappointing to observe that the WIPO Development Agenda repeatedly stresses the use of 'flexibilities" in TRIPS, but places no emphasis on the need to fully enforce TRIPS, a goal which is far from having been achieved in many developing countries. 'Flexibilities' should not mean undermining, through reinterpretations of the obligations, the balance that was achieved, after much negotiation, by TRIPS. Under the term flexibilities, there are many interpretations of rights and obligations that create confusion and tend to weaken or ignore the wording, objectives and fair trade practices aims of the Treaty. The focus needs to be shifted to compliance if the benefits of TRIPs are to be achieved.

The IGWG

The Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (IGWG) is mandated to come up with a strategy and plan of action for the May 2008 World Health Assembly meeting. There has been substantial criticism of the Draft Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (31 July 2007). Germany on behalf of the 27 EU Member States said: "*It is of utmost importance for the plan of action to stick to the WHO mandate and respect the work carried out in other international organizations, such as WIPO and WTO*[53]". The US took the stand that the IGWG should not

[52] WIPO Member States adopt a Development Agenda, PR/2007/521, publicinf@wipo.int, 1 October 2007,
[53] Consultation on "Elements of a global strategy and plan of action, Comments by the European Union, via Germany in the role of the EU presidency, 2 February 2007.

include Type I diseases[54] as well as the pragmatic position that the Group should estimate the funding needs for implementation of the plan of action.

Current discussions focus largely on weakening TRIPS, For example, paragraph 5.2.(a) of the draft action plan promotes legislation to apply flexibilities in TRIPS and Paragraph 5.2. (b) refers to the promotion of bilateral trade agreements that do not incorporate "TRIPS-Plus" protection in ways that might reduce access to medicines in developing countries. Such a proposal ignores Article of I of TRIPs, which clearly states that Members of the Treaty may implement more extensive protection than is required by the Agreement. At the same time, in view of the contradictory interpretations given to TRIPS, and the lack of correct implementation of its norms, bilateral agreements include clarifications that are considered by opponents as *TRIPs Plus*, but which should more properly be understood as facilitating TRIPS implementation.

The International Alliance of Patients' Organizations (IAPO) also expressed concerns over the draft. Although the WHO is focusing on two main barriers; lack of innovative therapies and lack of access to existing therapies, the debate has become polarised. This has the potential to create conflict, while the focus should be on access to good healthcare, including safe and effective treatments[55].

Hopefully the final version of the global strategy and action plan will build on the positive post-TRIPS developments described above, rather than attempting to turn the clock back to pre-TRIPS times.

VI. Concluding Remarks

The specific complexities of pharmaceutical innovation make IPRs essential, not only in the inventive process, but in the complete development of innovation, including the information and education process. It is related to the full value chain of innovation, from research in the lab to the satisfaction of those who may benefit from the new therapy. And this is true whether R&D efforts are carried out by the public or the private sector. It is also a key factor in establishing R&D collaboration among different participants; government, academia and the private sector to cover the many phases of the long and risky R&D process.

But this is not all; IPRs also play a critical role in the creation of a sound and sustainable positive climate, essential for investments. Developing countries, big or small, that have become aware of the opportunities that the knowledge-based economy offers to them and want to be active participants have accordingly adopted a full set of modernisation policies and made full use of IPRs to attract investments.

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[54] Type I diseases are incident in both rich and poor countries, with large numbers of vulnerable populations in each. Type I diseases increasingly prevalent in developing countries are diabetes, cardiovascular disease and cancer. Type II diseases are incident in both rich and poor countries, but with substantial proportion in poorer countries. They are: HIV/AIDS and tuberculosis. Type III diseases are those that are overwhelmingly or exclusively prevalent in developing countries. The focus is on nine neglected infectious diseases: Chagas, dengue and dengue haemorrhagic fever, leishmaniasis, leprosy, lymphatic filariasis, malaria, onchocerciasis, schistosomiasis and human African trypanosomiasis.

[55] International Alliance of Patients' Organizations (IAPO) calls on WHO to bring patient groups to the centre of discussions on public health, innovation and intellectual property, www.patientsorganizations.org .

The evidence shows that the balance achieved by the TRIPS Agreements has been beneficial for developing countries, in terms of growth, foreign direct investment, manufacturing, exports, and the decentralisation of R&D. Therefore, the international focus should be on TRIPS compliance in good faith and enforcement. Flexibilities in TRIPS should not be used to undermine the balance achieved by the Agreement. More specifically, flexibilities should not mean rewarding free-riding, political clientele, or other forms of political corruption.

Taking into account the positive balance of the post TRIPS era, it is worrying that the new multilateral negotiations in the Doha Trade-Round are stalled. Their successful conclusion could push the global development process to new heights. WIPO has a big responsibility in implementing the Development Agenda in a manner that dissipates uncertainties as to its effective value in meeting the challenge of attracting investments for growth in many developing countries. The WHO's negotiations on the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property should be closely followed in order to show that health and IPRs are mutually supportive.

Innovation is becoming more accessible and more global, opening new and challenging opportunities for both rich and poor countries alike. The hitherto neglected intellectual capital of emerging economies can be harnessed with the financial capital of industrial countries, provided their governments establish an adequate cooperative climate which includes strengthened levels of IP protection.