EMERGING CONTENTIONS AND COMPREHENSIVE LOOK INTO TRENDS IN IPR AND PHARMACEUTICAL DRUGS WITH SPECIAL REFERENCE TO ACCESSIBILITY AND INOVATION

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ABSTRACT:

While the core issue for humanities is their health protection from life threatening diseases, whereas, on the contrary, the key players, in trading the newly innovated drugs play an important role in disseminating the knowledge use with advantage of the new drugs but it is easy said than done. There are a number of compulsory economic constraints from a period commencing from manufacturing to the process of distribution to the end users (ailing people) especially affected are those inhabiting in the developing or least developed countries. At this juncture the role of TRIPS and IPR may play a quintessential role, the sooner it is understood the better it is for the people at large globally but at the same time one should not lose the sight of genuine permissible profitability to the key players which will in turn help not only the people in need but also the R&D in perpetuity in future which has inherent advantage of combating diseases and address the problems more effectively that has been practising in the past with the interest of the participating players in the entire process alive.
INTRODUCTION:

One-third of the world’s population have hardly any access to essential medicines. The proportion reaches 50 per cent in the poorest parts of Africa and Asia. In addition, pharmaceutical R&D on health problems specific to poor countries is often perceived as inadequate. Moreover, less than 10 per cent of global health research is directed towards diseases that afflict 90 per cent of the world’s population. A third of the global population where people lack access to the medicines they need rising to 50 % in parts of Africa and Asia. Up to 50 % of medicines are inappropriately prescribed, dispensed and sold, leading to wasted resources and potentially resulting in reduced treatment efficacy and potentially leading to resistance. In developing countries medicines account 60-90% of household expenditure on health and inappropriate prescription high prices low quality and improper use indicates that the poor often receive little health benefit for their spending on drugs which inturn has turned out to be a major concern. IPRs in pharmaceuticals have two principal areas of impact which affect public health. They are as follows:

First, there is the issue of access, where discussion focuses on the links between IPRs, exclusion of competitors and the availability and pricing of new medicines.

Second, there is the issue of incentivising innovation, where discussion focuses on the role of IPRs in motivating the discovery and development of new drugs, and the effect of these rights on R&D expenditure and its allocation across diseases, countries and organisations.

These two areas are at the heart of the empirical literature on the effects of IPRs on public health in developing countries. Overall, the literature suggests that strong IPRs can hamper access to medicines in developing countries and does not necessarily encourage pharmaceutical innovation that responds to developing country needs. Generic medicines are central to providing healthcare at prices affordable to developing countries. However, strong IPRs in only a select few countries that export generic medicines have far-reaching consequences for the developing world. This is because countries that rely heavily on imports of generic medicines may find themselves with a sudden shortage of suppliers.
Some have suggested that developing countries may benefit from differentiated prices, provided that strong IPRs are allowed to set high prices in the developed world and measures are taken to minimise parallel importing from developing countries where prices will be lower. However, the evidence suggests that even under such favourable IP and importing conditions, price differentiation is unlikely to be large – certainly not large enough to be of benefit to the very poor. The argument that strong IPRs will benefit developing countries through future innovation is not borne out by the evidence. Strong IPRs are important for pharmaceutical innovation, but only where there is a strong market, as is often the case for health problems prevalent in the developed world.

However, pharmaceutical industries in countries such as India, which have seen their IPR regimes strengthened, are not responding to developing country needs. Instead they too are focusing on developed country markets. So, for health issues of particular relevance to developing countries, IPRs are of value to commercial product and technology developers only if a viable market can be created (for example, through an advanced market commitment). Pharmaceuticals have brought immense health benefits to developing countries, but one third of the world’s population does not have access to existing essential drugs. (WHO, 2002b) this estimate has remained unchanged since the mid-1980s. The proportion reaches 50 per cent in the poorest parts of Africa and Asia (WHO, 2002b). Moreover, pharmaceutical research and development (R&D) on health problems specific to poor countries is woefully inadequate. The Commission on Health Research for Development (1990) showed that less than 10 per cent of global health research is directed towards diseases that afflict 90 per cent of the world’s population – the so called ‘10/90 gap’.

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1 The concept of essential drugs, as unanimously endorsed by the World Health Assembly, consists of “those that satisfy the health care needs of the majority of the population and should therefore be available at all times in adequate amounts and in appropriate dosage forms”.

It is clear, then, that IPRs in pharmaceuticals have two principal areas of impact which affect public health. Policies are required to protect the incentives for R&D in addition to reducing gross inequities of access. However, reforming IP regimes to improve access or innovation in developing countries involves making difficult assumptions, which have generated sustained debates in the context of the TRIPS Agreement.

First, weakening IPRs to allow competition (either domestic or international) in order to improve access through lower prices assumes that other (less crucial, but significant) barriers to healthcare access are being addressed. Second, strengthening IP with the aim to encourage pharmaceutical innovation assumes that there is a market over which a monopoly can be granted. For some diseases, almost all sufferers are too poor to make even a monopoly a sufficiently attractive incentive to invest in R&D. This chapter examines some empirical evidence behind these assumptions and examines how IPRs may improve access or innovation for developing countries.
THE IMPORTANCE OF PATENTS FOR PHARMACEUTICAL INNOVATION:

For more than 50 years, large empirical studies have found consistently that patents are extremely important for the pharmaceutical sector (For example Scherer, 1959\textsuperscript{3}; Cohen et al., 2002\textsuperscript{4}). It estimated that pharmaceutical R&D outlays would be reduced by 64 per cent in the absence of patent protection; while for other industries, the corresponding reduction was only 8 per cent (Grabowski, 2002\textsuperscript{5}).

The reason why patents are so critical to pharmaceutical firms in appropriating the benefits from innovation lies principally in the characteristics of the pharmaceutical R&D process. New drugs cost in the region of US$ 1 billion to discover, develop and gain regulatory approval (DiMasi et al., 2003\textsuperscript{6}). The reason why R&D is so costly in the pharmaceutical industry is that most drug candidates fail to reach the market.\textsuperscript{7} Normally, less than 1 per cent of the compounds examined in pre-clinical stages are cleared for testing on humans. Only 22 per cent of the compounds entering clinical trials endure the development process and achieve US Food and Drug Administration (FDA) approval (DiMasi, 1995\textsuperscript{8}). Moreover, the complete R&D process from synthesis to FDA approval involves undertaking successive trials of increasing size and complexity. Generally, the pre-clinical and clinical testing phases take more than a decade to complete (Kaitin and DiMasi, 2000\textsuperscript{9}).

\textsuperscript{3} Scherer, F.M. (1959) Patents and the Corporation. Boston, MA: James Galvin and Associates
\textsuperscript{7} Failure can be due to the compound’s toxicity or carcinogenicity, manufacturing difficulties, inadequate efficacy, inconvenient dosage characteristics, economic and competitive factors and various other problems
Furthermore, manufacturing plants are expensive, costing between US$50 million and US$200 million, and unique manufacturing requirements usually mean that they are suitable for only one product (Pisano, 1996\(^{10}\); Douglas, 2004\(^{11}\)). Outlays for production plants need to be committed early on, four or five years before licensing, if there is to be no gap between product licensing and market launch. Choosing to commit such large funds represents an uncertain decision with large financial risk, which patents can mitigate. These expensive R&D costs are compensated for by patent-protected profits: profitability in the pharmaceutical industry and investment in R&D was found to be strongly correlated (Scherer, 2001\(^{12}\); Giaccotto et al., 2005\(^{13}\); Vernon, 2005\(^{14}\)).\(^{15}\)

Perhaps most significantly, in the absence of patent protection, imitators can free-ride on the innovator’s regulatory approval and duplicate the compound for a small fraction of the originator’s costs. Imitation costs in the pharmaceutical industry are exceptionally low, relative to the innovator’s costs for discovering and developing a new product.\(^{16}\) Generic compounds need only demonstrate that they are bio-equivalent to the pioneering brand in order to receive market registration. This process only takes a few years and costs US$1 million to US$2 million (Reiffen\(^{17}\) and Ward, 2005). Furthermore, the prospect of success is very likely, as reflected by the fact that many generic firms typically receive FDA approval and enter the market within a short time of the patent expiration of the pioneer brand. The case of Praziquantel – which was discovered, developed and licensed by Bayer, then immediately copied, improved and sold at a lower price by a Korean pharmaceutical company – is illustrative of this (Reich and Govindaraj, 1998).\(^{18}\)


\(^{15}\) Frank (2001) adds a more dynamic dimension to Scherer’s observation that R&D outlays are affected significantly by changes in profitability, by emphasising that the link is to do more specifically with R&D investment today and expected, but uncertain, future profits.

\(^{16}\) While R&D may cost in the region of US$1 billion, imitation costs are around US$1 million. There are few other comparable industries where there is such a large disparity between the costs of innovation and imitation.


INTELLECTUAL PROPERTY RIGHTS AND ACCESS TO INNOVATIONS

In most developing countries, patent protection for pharmaceuticals is available but not used. Nevertheless, those countries remain affected, because they tend to rely on exports from countries where there is more patent protection. Firms may adopt the view that it is not worth the expense of obtaining and maintaining protection in countries that express small market demand and pose a limited threat of imitation. In a study of 53 African countries and 15 antiretroviral drugs, patenting prevalence was found to be only 21.6 per cent of the possible total (Attaran and Gillespie-White, 2001)\(^{19}\). On their own, such findings may suggest that patenting does not constrain access.

However, the picture changes when one considers that these countries import from others that may have significant market demand of their own, and do have the technological capability to imitate. Patenting in those countries is much more prevalent, such that 13 out of the 15 antiretroviral drugs are patent-protected in South Africa (WHO, 2002a)\(^{20}\).

The ability of countries such as South Africa to imitate and export to countries that cannot do so for themselves will be curtailed if strong patent rights are tightly enforced there.

Thus, even if TRIPS is enforced selectively in only a few key countries, such as South Africa and other imitation (generic) exporters, the immediate outlook is bleak for countries that appear to rely on importing generic drugs as their principal means for addressing public health challenges. They will be forced to seek other channels (discussed below) to reduce the price of accessing medicines.


ACCESSING HEALTHCARE INNOVATIONS BY LOWERING PRICES

The price of antiretroviral across 34 countries was found to be higher where there were product patents (Borrell, 2007). Introducing generic manufacturers to the market is one way to reduce the cost of accessing medicines. It follows that creating IP conditions that are favourable for generic competition will reduce price, and the empirical evidence seems to support this. In the USA, where generic competition is strong and there is little price regulation, studies have found sharp price decrease and rapid loss of market share following patent expiry on a drug (Griliches and Cockburn, 1995; Reiffen and Ward, 2005). However, it should be noted that the USA has some features of its regulatory and competitive environment that are specific. For example, the Hatch-Waxman Act of 1984 allows the tail-end of patent terms to be infringed for the purposes of testing and regulatory clearance, allowing generic products to mount the market as soon as patents expire (Grabowski and Vernon, 1992). In other countries with different specificities, where the market size may be smaller or governments exercise greater purchasing power, the generic entry effects are less pronounced (Pammolli et al., 2002).

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Another source for lowering prices is to use compulsory licensing provisions in TRIPS: this authorises a third party to make, use or sell a patented invention without the patent owner’s consent\(^{26}\). This mechanism, or simply the threat of using it, has been used by governments to try and lower prices. While a reduction is likely, the extent of reduction is difficult to gauge. Price declines can be as steep as 90 per cent in a compulsory licensing regime, but if the issuance of compulsory licences does not result in generic competition, then the price decrease is not as substantial (Watal, 2000\(^{27}\)).

Scherer and Watal argue that “the compulsory licensing opportunities opened up by TRIPS should be seized selectively and imaginatively” (2002: 939). However, pursuing this option aggressively is subject to significant power relations. For example, the US Section 301 Watch List in the Trade Act of 1974 allows it to employ measures against any country that it considers to be denying US companies or persons adequate and effective protection of their IP rights (Parliamentary Office of Science and Technology, 2001)\(^{28}\). Abbott’s (2005)\(^{29}\) legal analysis of the WTO trade rules finds that global institutions need to undertake regular checks and balances to the TRIPS framework, while ensuring that the USA does not exert its power to alter WTO rules in bilateral arrangements (i.e. TRIPS plus). It is feasible that the conditions for engaging in compulsory licensing may be made more difficult for developing countries, for example, by tightening definitions of what constitutes a national emergency (Correa, 2006)\(^{30}\).

However, when compulsory licensing is engaged, royalties to pharmaceutical companies tend to be too low to recoup R&D investments. Theoretical and empirical analyses show that the ‘adequate remuneration’ that is supposed to be afforded to the patentee under TRIPS has been much lower than would be established under the ‘foregone profits’ standard of US patent law

\(^{26}\) For example, local pharmaceutical companies may obtain compulsory licenses to produce generic versions of patented medicines, or to import generic versions of medicines from foreign manufacturers.


To avoid total free-riding on the R&D efforts of pharmaceutical companies, Scherer and Watal (2002) conclude that differential pricing strategies should be pursued aggressively, in order to ensure access for those who cannot afford to pay adequate remuneration.

DIFFERENTIAL PRICING IS LIMITED AND DEPENDS ON PARALLEL IMPORTS AND POLITICAL SUPPORT:

Some authors (Scherer and Watal, 2002; Danzon and Towse, 2003; Danzon, 2007) find that the global pricing strategy that best combines equity with coverage of R&D costs is one where prices are much lower in nations with a low ability to pay, than in wealthy countries. However, such differential pricing faces two challenges. For example, local pharmaceutical companies may obtain compulsory licenses to produce generic versions of patented medicines, or to import generic versions of medicines from foreign manufacturers.

The first issue is in parallel importing, where differential pricing is thought to be undermined by low-priced drugs and devices being exported to countries where they are higher priced. Although arbitrage between differentiated markets is overstated (Outterson, 2005), there is some evidence on the effects of arbitrage. Arbitrage lowers prices, but it does not drive down prices to levels of the lowest priced market. This is principally because intermediaries and arbitrageurs are the major beneficiaries, rather than the final importing country (Kyle, 2007).

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34 Parallel import is the import and resale of a patented product which has been put legitimately on the market of the exporting country in another country without the consent of the patent holder. This means that drugs sold at a lower price in one country can be imported into another country where same drug is sold at a higher price.
The second, perhaps more intractable, issue is one of political resistance by populations in wealthy countries who may make the observation that the same product is available for substantially lower prices in other countries. The inhibition of parallel trade may turn on the nature of media coverage and the efficacy of various advocacy and non-governmental organisations. Scherer and Watal (2002) suggest that it may be more expedient politically to adjust tax law in a way that makes more extreme differentiation in prices, or maybe even outright drug donation by pharmaceutical companies. Their quantitative analysis shows that when the marginal cost of production is low, donations actually can increase post-tax profits under US tax laws. The empirical evidence suggests not—or at the very least, that other considerations have a significant and possibly overriding effect on differential pricing (Scherer and Watal, 2002). Wong (2002) found that prices are not affected by countries’ per capita income, but rather by their income inequality, suggesting that companies are targeting well-off sub-populations in developing countries. So, price discounting occurs for public markets, but not for private markets. To the extent that public provision of healthcare meets poor people’s needs, this outcome is consistent with notions of equitable access. However, poor people often are forced to purchase their medicines in private markets. In short, relying on unregulated markets to provide differentiated prices will not be sufficient for poor people, who need prices that are lower even than marginal production costs.

**ACCESSIBILITY IS NOT DETERMINED BY PRICE ALONE**

Price—specifically the impact that IPRs have on it—is one factor among several that affect poor people’s access to healthcare. Weaknesses in country-level physical, medical, financial and political infrastructures mean that many existing products needed by people in developing countries are not being purchased by patients, healthcare facilities, governments or non-governmental organisations. Thus, for example, there is the prospect that many patients with AIDS in Africa would not benefit automatically from antiretroviral, even at dramatically lower, affordable prices. Antiretroviral require diagnosis, monitoring and long-term maintenance of demanding treatment regimens (so as to minimise drug resistance) that are difficult to sustain without parallel import is the import and resale of a patented product which has been put legitimately on the market of the exporting country in another country without the consent of the patent holder. This means that drugs sold at a lower price in one

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country can be imported into another country where same drug is sold at a higher price. Adequate infrastructure and support. In many developing countries, access is a particularly complex problem, requiring political will and commitment of new resources.

INTELLECTUAL PROPERTY RIGHTS AND INNOVATION FOR HEALTH

Some infectious disease create markets in developing countries that are not commercially viable at present

While developing countries benefit from products based on other countries’ R&D efforts, few products are tailored to the specific needs of the developing world. Indeed, very few products are now developed for diseases that primarily affect poor countries, so-called tropical or ‘neglected’ diseases. Most of the current treatments and drugs for these diseases emerged from colonial requirements (Janssens et al., 1992). As western interests drifted away from these regions, tropical diseases have become increasingly neglected. Between 1972 and 1997, 1,450 drugs were licensed worldwide. Only 13 (fewer than 1 per cent) of those were developed specifically for tropical diseases: five of which were designed for veterinary purposes, two were designed for the US military, two were simply modifications of existing drugs (same active ingredient but new formulation and/or novel use), and one was derived from Chinese medicine (Trouiller et al., 2002).

For some diseases, at least 99 per cent of cases are located in low and middle-income countries (Lanjouw and Cockburn, 2001). In 1998 alone, these diseases were estimated to have caused the loss of almost 200 million Disability Adjusted Life Years (DALYs) and more than 5 million lives, a large share of them children (Lanjouw and Cockburn, 2001).


The A-strain of the HIV virus is particularly widespread in poor countries but not in the developed world. Infectious and parasitic diseases account for one-third of the disease burden in low-income countries – nearly one-half in Africa – but only 3 per cent in high income countries (WHO, 2002a). For these diseases, there is simply no free ride. Even for diseases that affect developed countries as well as developing countries (such as cancer), the characteristics of poor countries make the products designed for developed markets unsuitable. For example, developing countries have weak infrastructure and need vaccines that can withstand breaks in refrigerated distribution chains and survive a long shelf-life. They also need products that do not require intense supervision by medical personnel. While Europe has 39 trained physicians per 10,000 people and the USA has 27, sub-Saharan Africa has only one (World Bank, 200841). The choice between vaccines and drug therapies is such an example. An HIV/AIDS vaccine would be far easier to deliver in a poor country than a combination of drug therapy cocktails, but efforts to develop a vaccine have been minimal in comparison to investment in treatment (Yaqub, 2009b)42. 15 This section concentrates mainly on infectious disease-related public health issues.

For the pharmaceutical manufacturer, the key implication of these differences between developed and developing country disease environments is a reduction in available market size. This is important because, as Acemoglu and Linn (2006)43 find, market size can be directly related to innovation: “a 1 per cent increase in the potential market size for a drug category leads to approximately a 4 per cent growth in the entry of new non-generic drugs and new molecular entities” (2006: 1084).

The Europeans, Japanese and North Americans spend more than US$317 billion a year on prescription medicines for everything from high blood pressure to dull mood – a powerful incentive for pharmaceutical companies to keep them supplied with current remedies and concoct new ones (Moynihan, 200444). In contrast, the market for pharmaceuticals in the poorest countries is tiny. The state of Connecticut in the USA spends more on health than the 38 low-income countries of sub-Saharan Africa combined (World Bank, 2008)45. In

1998, US health spending constituted US$4,000 per person, whereas sub-Saharan African nations’ spending constituted only US$8 per person, with some countries reaching as little as US$2 per person (World Bank, 2008)

**Accumulated technical knowledge is weak:**
The lack of understanding of some diseases, coupled with the complexity of the science and technology involved, makes the prospect of finding new medicines uncertain and risky. This lack of basic understanding limits the investment that it is prudent for industry to make. As noted forcefully below by Rosenberg (1974)\(^{46}\), approaches that seek to procure innovations by adjusting market incentives, such as awarding IPRs, must be implemented with an awareness of the state of accumulated scientific and technical knowledge (Yaqub, 2009a)\(^{47}\).

As Rosenberg states: The demand for higher levels of food consumption, greater life expectancy, the elimination of infectious disease and the reduction of pain and discomfort, have presumably existed indefinitely in the past, but they have been abundantly satisfied only in comparatively recent times.

It seems reasonable to suppose that the explanation is to be found in terms of supply side considerations. It is unlikely that any amount of money devoted to inventive activity in 1800 could have produced modern, wide-spectrum antibiotics, any more than vast sums of money at that time could have produced a satellite capable of orbiting the moon. The supply of certain classes of inventions is, at some times, completely inelastic – zero output at all levels of price. On the other hand, the purely demand-oriented approach virtually assumes the problem away. The interesting economic situations surely lie in that vast intermediate region of possibilities where supply elasticity’s are greater than zero but less than infinity.

To explain the investment decisions, one needs to examine the technical problems faced by companies. If these problems are perceived by the companies, whether correctly or incorrectly, to be intractable, the size of the reward becomes irrelevant. Similarly, if the perceived time to commercial revenue is far away, any rewards that may accrue are

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discounted substantially, thus relegating market characteristics and policies when considering investment. For the health problems facing developing countries, a chronic lack of scientific and technical understanding suggests a severe state of under-investment in R&D that is only just beginning to be addressed. For example, only 1 per cent of biomedical research papers make reference to tropical diseases (Lanjouw and Cockburn, 2001).\footnote{Lanjouw, J.O. and I.M. Cockburn (2001) ‘New Pills for Poor People? Empirical Evidence after GATT’. World Development 29(2): 265–89.}

**CREATING CONDITIONS FOR MORE EFFECTIVE INTELLECTUAL PROPERTY POLICY**

*Funding for R&D into neglected diseases*

Funding for neglected diseases has increased in recent years, from US$2 billion in 2004 (Morel et al., 2005)\footnote{Morel, C.M., T. Acharya, D. Broun, A. Dangi, C. Elias, N.K. Ganguly, C.A. Gardner, R.K. Gupta, J. Haycock, A.D. Heher, P.J. Hotez, H.E. Kettler, G.T. Keusch, A.F. Krattiger, F.T. Kreutz, S. Lall, K. Lee, R. Mahoney, A. Martinez-Palomo, R.A. Mashelkar, S.A. Matlin, M. Mzimba, J. Oehler, R.G. Ridley, P. Senanayake, P. Singer and M. Yun (2005) ‘Health Innovation Networks to Help Developing Countries Address Neglected Diseases’. Science 309(5733): 401–4.} to US$2.5 billion in 2007 (Moran et al., 2009)\footnote{Moran, M., J. Guzman, A.-L. Ropars, A. McDonald, N. Jameson, B. Omune, S. Ryan and L. Wu (2009) ‘Neglected Disease Research and Development: How Much Are We Really Spending?’ *PLoS Med* 6(2): 137–46.}. Attributing this increase solely to stronger IP protection is difficult, because other (possibly more significant) factors are likely to have played a role. If IP had been a leading driver, one might expect funding to have increased at both the research and product development levels. However, this is not the case – most neglected disease R&D activity has been focused on early-stage research problems (Kyle and McGahan, 2008).\footnote{Kyle, M.K. and A.M. McGahan (2008) ‘Investments in Pharmaceuticals Before and After TRIPS’. NBER Working Paper Series 13468.} Accordingly, one study found a strong increase in citations to publications on neglected diseases alongside a small increase in patenting (Morel et al., 2005).

Other factors have played a role in redressing the neglect in funding. The 10/90 gap identified in 1990 led to considerable media exposure and political momentum, particularly regarding a few high-profile diseases. This instigated renewed activity, but this was highly concentrated
on research for a few diseases. By 2004, there were 63 neglected disease projects and, while IP protection may have improved, it was thought that this rise was due primarily to increased research funding by the philanthropic sector (Moran, 2005). In 2007, only 9 per cent of neglected disease R&D funding was provided by the private sector. Neglected disease funding has increased, but these numbers suggest that these increases have been driven primarily by public and philanthropic efforts focused on a few diseases. In 2007, just over US$2.5 billion was invested in neglected disease R&D (Moran et al. 2009). The ‘Big Three’ (HIV/AIDS, tuberculosis and malaria) commanded 80 per cent of the funding, leaving many other important conditions such as pneumonia and diarrhoea still neglected (Yamey, 2002b; Molyneux et al. 2005). Moreover, 99.6 per cent of the funding was concentrated on product R&D, leaving diagnostics and delivery technologies severely neglected rather than by a strengthened IP environment which has increased funding for diseases evenly across various disease burdens.

PRIVATE SECTORS IN DEVELOPING COUNTRIES ARE NOT RESPONDING TO DOMESTIC MARKETS:

However, it would be wrong to conclude that strengthening IP protection does not have an effect on pharmaceutical industries in developing countries. For example, the Indian pharmaceutical industry has been the focus of considerable renewed discussion since India has strengthened IP protection (Chataway et al., 2007b). The problem is that the effect of stronger IP has not necessarily benefited poor people. One might expect scientists working in India to have a comparative advantage in developing drugs targeting developing country markets, and thus, that new R&D activity would be most apparent there. However, the statistical survey results show a decline in R&D expenditure directed towards products suited specifically to developing country markets, from 16 per cent in 1998 to 10 per cent in 2003 (Lanjouw and MacLeod, 2005).

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52 In 2007, just over US$2.5 billion was invested in neglected disease R&D (Moran et al. 2009). The ‘Big Three’ (HIV/AIDS, tuberculosis and malaria) commanded 80 per cent of the funding, leaving many other important conditions such as pneumonia and diarrhoea still neglected (Yamey, 2002b; Molyneux et al. 2005). Moreover, 99.6 per cent of the funding was concentrated on product R&D, leaving diagnostics and delivery technologies severely neglected.


This is despite a surge in total R&D expenditure and stock market value (Lanjouw and MacLeod, 2005; Arora et al., 2008)\(^55\). A better indication of the sector’s intentions can be found in its patenting behaviour. Pharmaceutical patenting by India-based inventors has grown rapidly as a share of all patenting in the USA – to more than 2 per cent – with a similar trend in Europe (Lanjouw and MacLeod, 2005)\(^56\). Developed countries are where their principal market interests lie. The notion that nascent pharmaceutical industries respond no differently to changes in IP protection than established pharmaceutical industries is supported by case study evidence. TRIPS is not detrimental if seen from the perspective of a growing Indian pharmaceutical industry, but it does seem to be detrimental to consumer welfare in terms of availability and access (Chaudhuri et al., 2006)\(^57\).

The Indian pharmaceutical industry provides us with the message that strengthening IP protection increases domestic R&D expenditure significantly and patenting in developed economies (Dutta and Sharma, 2008\(^58\); Liu and LaCroix, 2008)\(^59\). However, this finding needs to be qualified. It is likely that educational and broader economic development have played an important part. When these factors are controlled for, in a study across 26 countries over two decades, strengthening IP protection in the pharmaceutical sector does not seem to increase significantly domestic R&D expenditure, patenting and innovation (Qian, 2007)\(^60\). Indeed, there is a point in development at which IP regulation actually reduces innovative activities and simply serves to increase rents to established companies (Qiu and Yu, 2007)\(^61\). These results raise the prospect that low and middle-income countries have gained little in terms of domestic innovation, which could offset the new and higher flows of royalty payments to foreign firms.

One alternative to this scenario is to strengthen public sector capacities (Yamey, 2002a; Blume, 2005; Blume and Zanders, 2006). However, capacity building in the public sector is unlikely to develop the full range of competences needed to develop drugs persistently across a range of health needs. So, private sector engagement must be retained alongside these capacity-building efforts. Moreover, these efforts have been most effective when they are collaborative across developed and developing countries, or private and public sectors (Velho, 2004).

**INTELLECTUAL PROPERTY RIGHTS FACILITATE INCREASED TRADE IN KNOWLEDGE, BUT MAY STIFLE INNOVATION:**

IPRs play an important role in facilitating transactions in a market for knowledge which has come to play a much-discussed role in pharmaceutical innovation. While this sector continues to be dominated by large integrated firms that conduct much of their innovative activity in-house, recent decades have seen significant vertical restructuring of the industry, and these firms increasingly rely on externally sourced R&D (Roijakkers and Hagedoorn, 2006). Much of this industrial reorganisation has been due to underlying technological discontinuities (Orsenigo et al., 2001), but a significant factor has been the role of small firms which have been able to trade patented knowledge. In addition, other factors have included the ease with which small firms have been able to gather start-up capital and acquire ideas from universities which themselves are patented.

This is particularly important for developing countries, because small firms may be more open to risk-taking, less prone to organisational inertia, and better able to address neglected disease research problems, as evidenced by responses to the US Orphan Drug Act of 1983 (Kettler, 2000; Kettler and Marjanovic, 2004). The ability to patent their

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ideas provides a tangible point of attention which can be advertised, and perhaps traded. In drug discovery, this active entrepreneurial sector, that bridges universities and large firms, has become a very important supplier of drug candidates and tools for performing R&D (Powell et al., 1996; Owen-Smith and Powell, 2004).67 One consequence of these changes is that pharmaceutical innovation now relies heavily on a complex network of contractual agreements linking a variety of actors at various stages of the drug development process. Between 1963 and 1999, more than one-third of new drugs approved originated in industrial alliances (Danzon et al., 2005). Empirical evidence on strategic technology alliances also shows an explosion of collaborative activity in the biomedical sector since the early 1990s, with many of these alliances spanning national boundaries.

While IPRs may support markets for knowledge, often a counter-argument is made that proliferation of patents may stifle biomedical innovation by raising transaction costs (Heller and Eisenberg, 1998).68 Some studies have shown patents to affect negatively researchers’ access to knowledge, as measured by citations (Murray and Stern, 2007).69 In another counter-argument, some scholars have noted that historically, R&D departments have remained close to production and marketing departments, and that this is a fundamental reflection of innovation process (Pavitt, 1999; Nelson, 2005).70 Separating these functions across the markets is likely to have contributed to the downturn in pharmaceutical innovation and exacerbated the myth of the biotechnology revolution (Hopkins et al., 2007).

So, IPRs facilitate and govern transactions in the market for technology (Arora et al., 2001). Technology licensing, collaborative R&D and contract research are very difficult to sustain on a commercial basis without well-defined and enforceable rights over research results. Therefore, it is widely believed that strengthening IPRs will not only promote

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domestic R&D activity, but also stimulate trade in technology. However, introducing
markets between research and production is unprecedented and may harm innovation, and
issuing patents of excessive scope may be choking innovation by raising transaction costs.

NEW INSTITUTIONAL ARRANGEMENTS HAVE EMERGED; THE ROLE OF
INTELLECTUAL PROPERTY RIGHTS IS UNKNOWN
In an increasingly disaggregated and dispersed pharmaceutical industry structure, public–
private partnerships have become prevalent, particularly for the research problems affecting
developing countries. As noted in the previous sections, this partly to reconcile market
failure in addressing neglected diseases, with the reality that many R&D competences
reside in the private sector. However, the role that IPRs may have played in their emergence
is unclear. Public–private partnerships may not be effective because they suffer bad
management, political in-fighting and turf wars, as evidenced by the Children’s Vaccine
Initiative (Muraskin, 1998). However, recent detailed analyses that go beyond anecdotal
cases find no evidence that they manage their portfolios less efficiently than commercial
firms (Moran, 2005; Yaqub, 2009a). Indeed, they are likely to be more effective (Velho,
2004).

There are a variety of reasons for the success of public–private partnerships. For example,
they are being created where public institutions drive research and the private sector assumes
responsibility for production and delivery. Alternatively, private sector companies may
undertake research funded by the public sector or charitable donors. In another rationale,
partnerships between research institutions in the north and south are attempting to draw
together innovative science with local experience of how that science can be best
applied. All of these arrangements are constructed in some way on the basis that the public
and private sectors are unable on their own to resolve the deep-rooted and tragic inequalities of
innovation discussed in this section (Buse and Waxman, 200172; Towse and Kettler, 200273;
Widdus, 2003)74.

Medicines and Vaccines for Diseases of Poverty. London: Office of Health Economics
Some recent studies have focused on the emergence of one specific public–private partnership: the International AIDS Vaccine Initiative (IAVI). These studies found that IAVI may not have developed a vaccine yet, but it has boosted developing country science and technology capacity significantly (Chataway and Smith, 2006). Moreover, IAVI may be acting as an important systems integrator or knowledge broker that draws together diffuse and dispersed knowledge, to create a R&D network that it coordinates centrally (Chataway et al., 2007a). Within these two important functions that IAVI serves, IPRs may be playing a crucial underlying role in providing a tangible focus for trade and a significant advertising role. It seems that the emergence of public–private partnerships could represent a new paradigm for addressing innovation needs for public health in developing countries, at least as they relate to infectious, neglected diseases. However, in this discussion, the role of IPRs is a substantial gap in the literature. Public–private partnerships could be a way for private sectors to access public and philanthropic funding, or they could be a way of reconnecting and reorienting supply and demand. IPRs could be a contractual nexus for either of these possibilities.
CONCLUSIONS AND FURTHER RESEARCH DIRECTIONS

This paper has examined the effects of IPRs on public health from two perspectives: the role of IPRs in access, and its role in innovation.

Five main conclusions can be drawn on the role of IPRs in access.

- Patents are taken out only in selected countries, where there is threat of imitation or large market. However, countries where patents are not taken out remain affected because they rely on exports from countries where there is stronger IP protection.

- Generic competition tends to reduce price dramatically. The implies that strengthening IP protection in developing countries will reduce accessibility by harming generic competition, without necessarily improving incentives for innovation on developing country problems.

- Compulsory licensing reduces price dramatically, but only if generic competition is introduced. The issuance of a compulsory licence by a government does not necessarily result in immediate supply by a third-party company. The looming threat that a third party may begin to supply soon can reduce price, but the price reduction is not as steep if generic competition is introduced to the market immediately after the licence is issued.

- Differential pricing depends on constraining parallel imports and gathering political support, but even with these measures, differential pricing is limited. Access is not determined by price alone: broader infrastructure weaknesses can play a role. While it remains difficult to establish the relative importance of the two concerns, it is worth noting that often, people in developing countries are more exposed to the market when seeking healthcare (which makes price more important) than people in developed countries who are insulated by extensive insurance and public health institutions.
Five main conclusions can be drawn on the role of IPRs in innovation.

- IP for innovations targeted at health issues of particular relevance to developing countries is of value to commercial product and technology developers only if a viable market can be created. The degree of need (and market size) is high, but creating viable markets entails a concerted international effort, such as the one displayed in setting up an advanced purchase commitment\textsuperscript{17} for pneumococcal vaccines.

- Funding has improved, IP has been strengthened and the neglected disease landscape has changed considerably since 1990 in an effort to engage the pharmaceutical industry.

- However, pharmaceutical industries, including those in countries such as India, are responding imperfectly to developing country needs. Instead, they are often focusing on developed country markets.

- IPRs facilitate trade in knowledge but may stifle innovation by reducing researchers’ access to knowledge and increasing the costs of collaboration. For more on advanced market commitments, see Kremer and Glennerster (2004).\textsuperscript{75}

- Public–private partnerships have emerged as a prevalent new institutional arrangement for addressing neglected diseases, but it is not clear what significant roles, if any, IPRs have in their formation.

In future, IP may have a bigger role to play in dealing with the health problems common to both developed and developing countries. There is evidence that many of their problems are converging. The causes of this convergence remain unclear, but there are likely to be important implications for IP systems in both developed and developing countries. This chapter also noted a significant lack of understanding in the role of IP in public–private partnerships. Since these types of arrangements have emerged as the dominant paradigm for addressing neglected diseases, further research on this issue is needed urgently. A number of IP-related policy measures (such as government patent buy-outs, bifurcated patent systems, orphan drug legislature that extends patents and transferable IPRs) have been suggested either on entirely theoretical grounds or indirect empirical evidence. These require careful policy analysis in order to gauge their feasibility and implications with more confidence. For more detailed analysis see more in

Of the disease burden in high-income countries, 83 per cent is made up of non-communicable conditions such as cancer and cardiovascular disease (WHO, 2006). However, these diseases affect low and middle-income countries too, where cancer and cardiovascular disease are the second and third largest causes of death. In fact, nearly 50 per cent of deaths worldwide were due to cancer, cardiovascular disease, diabetes and chronic lung disease (Outterson, 2005).
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