Compulsory Licensing of Medicines:
A Public Policy Intervention

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Abstract

The world continues to suffer from several communicable and infectious diseases such as tuberculosis, malaria, dengue, night-blindness, among several others. Most cures for such diseases are both antiquated and thus ineffective or not at all available. What is even more disturbing is that although such an inexcusable state of affairs has been in existence for the last several decades, we are not necessarily close to bringing out new cures. It is clear that the failure of both the state and the market are implicated in this problem that is facing humanity at large. Among the various policy level approaches to address these pressing issues, the focus of this paper is specifically on the use of Compulsory Licensing (CL) provisions within the context of India. The paper aims to provide the reasoning regarding why the use of CL is important as a strategic public policy tool for developing countries. Against the backdrop of an inability by both the state and the market to come with appropriate solutions for this predicament, brief case studies of both developed and developing countries which have employed CL are analyzed. The paper also examines and critiques the theoretical arguments in favor of CL.

Introduction

Most literature on compulsory licensing (henceforth CL) deals with cursory issues of conflict between developed and developing countries, mostly emerging during instances of specific nations invoking such licenses. It is essential to delve into more pressing matters regarding this contentious topic. This paper makes an attempt to seek answers, justifying the rationale behind nations using CL to improve their healthcare system; to identify the lacunae in current public health policies that have resulted in state as well as market failure; evaluating the fairness of impositions of TRIPS on developing nations as well as its flexibilities; and most importantly, to what extent is the rate of innovation affected in order for developed countries to raise a hue and cry about issuance of CLs by developing countries.[1]

To begin with, despite advances in science, technology and medical knowledge, there is a severe dearth in handling diseases that affect poor populations in developing and least developed nations. There is negligible drug research and development for tropical infectious diseases. In fact, the discovery and development of most of the current tropical pharmacopeia was driven by colonial requirements during the first part of the twentieth century. And with the gradual end of colonialism, western interests also shifted focus from tropical diseases to lifestyle diseases such as obesity, cardiovascular, impotency, diabetes, and the like. Tropical diseases became progressively neglected, since they did not offer sufficient financial returns for the pharmaceutical industry to engage in research and development. Currently, such a scenario has emerged wherein drug discovery and development for neglected diseases have substantially

diminished, despite an ever-increasing need for safe, effective and affordable medicines for treatment (Trouiller et al. 2002).[2]

With the emergence of a market-based world order, profits rather than global health needs, provide the necessary direction for new drug development. Being a complex, expensive and time-consuming activity subject to stringent regulations, drug development is almost exclusively confined to a consolidated and highly competitive multinational drug industry, set in developed countries. Market forces inevitable skew the direction of drug R&D towards diseases and patients (customers) that ensure the highest financial returns.[3] According to IMS Health, in 2010, US (38%), Europe (29%), and Japan (12%) accounted for nearly 79% of the world pharmaceutical market (valued at US$ 875 billion). On the other hand, developing nations with a share of nearly 85% of world population, accounted for only 21% of the global pharmaceutical market, with Asia, Australia and Africa representing nearly 15%, whereas Latin America accounting for 6% of the market.[4] Despite the global public health prevalence of infectious diseases, their predominant distribution is in developing and least developed countries. This appears to be a major disincentive for large pharmaceuticals to invest in drug discovery and development for neglected diseases, since return on investment is not adequately guaranteed.

The WHO world health report of 2008 reveals the following startling facts: About 18.5 million people died all over the world from infectious diseases, many of which were preventable or treatable such as respiratory infections (3.46 million people), diarrheal diseases (2.46 million), malaria (0.3 million[5]), tuberculosis (1.4 million[6]) and HIV/AIDS (1.8 million[7]). What is also of considerable concern is the disability caused by these diseases. In 2004, the disability adjusted life years[8] (DALYs) lost were 34 million due to tuberculosis, 58 million due to HIV/AIDS, 72 million due to diarrheal diseases, 30 million due to childhood diseases, 33 million due to malaria and 97 million due to respiratory infections.

Troullier (2002) study reports that out of the 1393 drugs marketed between 1975 and 1999 only thirteen (1 per cent) were for tropical diseases. Of these, only four were developed by commercial pharmaceutical companies. Five came from veterinary research, two were modifications of existing medicines and two were produced for the US military.[9] Global Forum for Health Research (2004) finds that only 10 per cent of global health research is devoted to conditions that account for 90 per cent of the global disease burden – an imbalance that is referred to as the 10/90 disequilibrium. According to Commission for Intellectual Property Rights (CIPR, 2002) less than 5 per cent of worldwide pharmaceutical R&D expenditure is spent on diseases which predominantly affect developing countries. UNDP Human Development Report (1999) finds that only 0.2 per cent of the R&D funds worldwide are dedicated for tropical diseases such as pneumonia, diarrheal diseases, and tuberculosis (TB), though these account for 18 per cent of the global disease burden. Even for diseases which are primarily endemic to developing countries, but are also prevalent in developed countries (for example tuberculosis), the global market for a new drug is unlikely to exceed US $200 million annually. According to Commission on Intellectual Property Rights (CIPR) what the MNCs find attractive is a market of the order of US $1 billion or more.

Chaudhuri (2005) has observed that the market failure to generate R&D for neglected diseases has not been compensated for by public funding. Public funding in developed countries has also been determined more by market considerations and, hence, is directed towards R&D for diseases of wealthy countries. Some rare initiatives have been taken by national governments

and international organizations to correct the imbalance. These include: (a) the UNICEF/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) and (b) Public-Private Partnerships (PPPs) and not-for-profit drug development initiatives – for example, the Global Alliance for TB Drug Development (TB alliance), the Medicines for Malaria Venture (MMV), among many others. But these initiatives and some recent pharmaceutical industry efforts for example, by AstraZeneca, GlaxoSmithKline and Novartis suffer from under funding.

In short, the inability to address the challenge at hand cannot be solely attributed to market failure; on their part, governments have failed too. The former (market failure) is apparently not able to provide the right R&D incentives for private firms, while the latter (government failure) is unable to attract firms despite the existence of a huge demand for such drugs. A possible question that comes to our minds: When neither the 'benevolence' of the state nor the 'interest' of the market is able to address such a yawning gap, it is quite possible that the problem lies with the very theoretical and structural formulation of the nature of such drugs? So does this imply that essential drugs (since they are the need of the hour for developing nations) are beyond ordinary consumer goods? We suggest that framing the terms of the debate in terms of a global public good can better enable us to situate the problem in its essence.

Essential Drugs and Medical Knowledge: A special case of global public goods

Global public goods are goods with benefits that extend to all countries, people, and generations (Kaul et.al. 1999b). Some goods are global naturally (e.g. climate) and others have become global by policy choice (e.g. international organizations such as UN, WHO). In more general terms, a good qualifies as being globally public when it benefits more than one group of countries and does not discriminate any population group or generation. Woodward and Smith (2003) define global public good as "a good which it is rational, from the perspective of a group of nations collectively, to produce for universal consumption, and for which it is irrational to exclude an individual nation from its consumption, irrespective of whether that nation contributes to its financing". For example, vaccination against communicable diseases is clearly both excludable and rivalrous in consumption, and its primary benefit is to the individual recipient and their respective nations. Nonetheless, if the effect on the risk of person-to-person or cross-border transmission of communicable disease is sufficient, it is not rational either to exclude an individual or nation from consumption.

Medical knowledge creates products in the form of new drugs or new delivery systems using drugs to cure a disease. Such knowledge can be considered as global public good if its benefits can reach worldwide. Once knowledge has been created in one country, the marginal cost of another country enjoying its benefit is close to negligible in the case of a pure global public good. Many pharmaceutical innovations approach this limiting case because they apply to the same diseases in all countries. Non-rivalry in consumption implies that a welfare maximizing collective regime should not exclude any country from the free use of knowledge (Pazderka and Stegemann 2005).

The critical property of a public good, non-excludability means that the provider of a public good cannot exclude poor consumers (potential non-payers) from making use of the new knowledge, such non-payers can avail themselves of the benefits for free. However as a consequence, innovators would be unable to add a premium to the price of their innovative products. They would be unable to appropriate the value of the benefits of new knowledge by

being inadequately compensated for the cost of innovating activities. Most pharmaceutical R&D consists of identifying therapeutically interesting chemical entities and testing whether they work and are safe. The relevant knowledge is embodied in the chemical composition of a successful drug. In other words, new pharmaceutical knowledge "is expensive to produce, cheap to reproduce, and difficult to profit from" in the absence of government intervention (Nordhaus 1969).

The problem that remains is the challenge of making the products of such knowledge available to all, particularly when they affect a large majority of people with life threatening diseases. The government therefore has to intervene to ensure the availability of public goods to all. Government intervention can be in the form of direct funding, subsidies or tax concessions. Government can also produce medicines by its own agencies and distribute to the needy people freely in order to protect public health.

Compulsory Licensing, TRIPS and Doha Agreement

Compulsory licensing is an authorization by the government, allowing non-patentees to produce the patented product or process without the consent of the patent owner. It is one of the flexibilities on patent protection included in the WTO's agreement on intellectual property — the TRIPS (Trade-Related Aspects of Intellectual Property Rights) Agreement. CL is a part of the agreement's overall attempt to strike a balance between promoting access to existing drugs and promoting research and development into new drugs. Compulsory licensing and government use of a patent without the authorization of its owner can only be done under a number of conditions aimed at protecting the legitimate interests of the patent holder. These include public health reasons, emergency situations, epidemics, public non-commercial use, to remedy anti-competitive practices or to protect the environment; it is entirely up to the national law to decide what the grounds to issue CL. According to Article 31b, prior to invoking a CL, the party applying for a license must have first attempted, unsuccessfully, to obtain a voluntary license from the right holder on reasonable commercial terms. If a CL is issued, adequate remuneration must still be paid to the patent holder according to Article 31h. However, for national emergencies, other circumstances of extreme urgency, or public non-commercial use (or government use), or anti-competitive practices, there is no requirement to try for a voluntary license. The purpose of such prior negotiations is to create space for outcomes short of an actual CL, including negotiated Voluntary Licenses, price reduction, donation of the branded product, or a capitulation by the member state.[10]

Some governments, particularly the African Group (all African members of the WTO), were pushing for clarity on how TRIPS flexibilities would be interpreted, and how far their right to use them would be respected. The Doha Ministerial Declaration convened on 14th November, 2001, provided the necessary clarification. In this conference, WTO members stressed that it is important to implement and interpret the TRIPS Agreement in a way that supports public health, by promoting both access to existing medicines and the creation of new medicines. The Doha Declaration provided clarity on the contentious TRIPS Article 31f, which says that products made under CL must be "predominantly for the supply of the domestic market". This article was applicable to countries manufacturing drugs, limiting the amount they can export when the drug is made under CL. More importantly, it had an impact on countries, lacking manufacturing capabilities and therefore wanting to import generic drugs. This problem was resolved in the Doha Declaration, under Paragraph 6, which provided extra flexibility, so that countries unable

to produce pharmaceuticals domestically can obtain supplies of patented drugs from other countries.

The generally accepted rationale behind CL is that if generic companies are given licenses to produce a patented drug on payment of royalty, then competition among manufacturers would drive down prices, although the royalty paid to innovators would continue to provide funds and the incentive for R&D. The literature on compulsory licensing problematizes the issue mainly in the following way: "the challenge for policy makers will be to implement patent-weakening schemes that increase access but cause minimal harm to the patent innovation incentive" (Colleen 2003).

Use of Compulsory Licensing by Developed and Developing Countries

According to Colleen (2003), there has been little consensus on how best to implement CL. And nowhere has this divergence in views been more pronounced than in the context of CL provisions in TRIPS Agreement; clear contrast in the views between developed countries with US taking the lead, and developing countries. This contrast in views is driven in part by differences in economics status. It is an observed trend in developing countries for foreigners to file most of the patents. Colleen cites an example from Brazil against which the US government and industry have initiated significant patent disputes over CL. Brazil holds less than 0.1% of the US patents issued in 1998, while US captured nearly 40% of the patents issued in Brazil that same year. This is a good example of how the patent system facilitates transfer of monopoly rents to foreigners outside the country. Also, the high price of products covered by patents can put needed technology out of reach of developing country consumers, who due to poor healthcare infrastructure, are required to pay for drugs out of pocket. According to WHO and WTO Secretariats, Report of the Workshop on Differential Pricing and Financing of Essential Drug (2001), 90% of the populations in developing countries buy medicines out-of-pocket, whereas only 20% of the population does so in high income countries. It is to compensate for such inordinate costs, that CLs are used to widen distribution of and increase access to drugs.

What is interesting is that although developed economies have often frowned upon the use of CL by developing countries, as will be exemplified in cases below, they have themselves resorted to use of CL when deemed necessary to curb anti-competitive behavior.

Case of Compulsory Licensing in United States

In 1977, the US Federal Trade Commission and its Department of Justice had issued approximately 125 decrees over thousands of patents and a wide range of technology. These were issued to address anti-competitive problems emerging out of mergers, price-fixing, or abuse of monopoly or market power. The US government thought it prudent to deliberately infringe drug patent licenses to produce drugs for public health purposes. In the 1960s and 1970s, it clearly made and used antibiotics such as tetracycline and Griseofulvin, tranquilizer meprobamate for the military, synthetic steroids, cytokine biopharmaceutical patents owned by Novartis and Chiron, and the 9-AC cancer drug patent rights assembled under the merger of Pharmacia AB with Upjohn (Scherer and Watal 2001), all without permission from patent holders.

More recently during the fall of 2001, the threat of a CL was strategically used by the US government to drive down the price of the patented drug Ciprofloxacin (Cipro) by almost 50%. This case deserves a brief elaboration. In 2001 the United States was confronted with an anticipated attack by using anthrax by certain terrorist groups. The US government did not have an adequate stockpile of Cipro to treat a large population. Cipro was patented in the United States by Bayer and priced at US $1.77 per pill. Bayer could not manufacture enough Cipro to supply the United States requirement on a timely basis. Under pressure from domestic Public Health Groups and the members of the Congress, US Secretary of Health, threatened to override Bayer patent and purchase Cipro from generic suppliers, unless Bayer lowered its prices. Bayer succumbed to the threat and lowered its price to US $0.95 per pill (Love 2005). It is important to note that, the US Government did not face any internal or external resistance when it tried to invoke 'government use' to tackle the anthrax crisis.

Case of Compulsory Licensing in Canada

In Canada, CL with respect to medicines was first introduced in 1923. From the period of 1923 to 1993, the Canadian Patent Act, allowed for CL to be granted for manufacture, use and sale of patented medicines. The law required either local manufacture to commence or local licensing on reasonable terms to occur within a two year period after the patent is issued (Reichman and Hazenzahl 2003). Although the Patent Act was in vogue, CL was not very widely used in Canada prior to 1969. This was because of the restriction that the active ingredients had to be produced in Canada. The generic producers were hesitant to undertake investments for basic manufacturing because of the relatively small size of the Canadian market.

In 1969, however, the Canadian Patent Act was amended. The grant of compulsory licenses became admissible for importation of patented medicines. Anyone could get a CL not only to produce but also to import any medicine produced with a patented process. After the 1969 revision, a large number of licenses were granted against a 4% royalty on net sale prices. The generic sector grew in number and size and the number of licenses and market competition increased. Compared to only 22 cases between 1923 and 1969, compulsory licenses were granted in 613 cases between 1969 and 1992 (Chaudhuri 2005).

The liberal provisions of the 1969 Act were reversed by a subsequent Patents Amendment Act of 1992, by abolishing the special regime of compulsory licensing for pharmaceuticals, subsequent to Canada joining NAFTA and in anticipation of TRIPS. Section 39.16 of the Patent Act provided that a compulsory license was available only for the making and not importation of the medicine. Certain exceptions did occur, for example, on October 2001, Health Canada overrode the Bayer Patents on Ciprofloxacin and authorized generic manufacture for the purpose of building a stockpile as protection against an attack of certain strains of anthrax (Love 2007). On May 2004 Canada passed Bill C-9, an act to amend the Patent Act and the Food Drugs Act, and created Canada's Access to Medicines Regime (CAMR). The purpose of the legislation was to allow Canadian manufacturers to export pre-approved 'Schedule 1' medicines under compulsory licensing to countries lacking manufacturing capacity (Love 2007).

Case of Compulsory Licensing in Thailand

Thailand is among the very few developing countries of the world where public policy has been effective in preventing the spread of HIV/AIDS on a national scale. A continuous and massive program to control HIV/AIDS by Thailand resulted in considerable decrease in new HIV infections. Though the number of new HIV infections reduced from 143,000 in 1991 to 19,000 in 2003, it was still considered rather high, as more than one-in-hundred adults in a country of 65 million people is infected with HIV, where AIDS has become a leading cause of death. There are more than 1.1 million AIDS patients in Thailand and 560,000 have died (TWN 2006).

For Thailand, a developing country, whose citizens cannot afford the high costs of new HIV drugs, the success in reducing new infections was not easy. At the heart of the government initiative was making available low priced drugs for addressing AIDS. The Thailand government had been unsuccessful in its initial attempts to obtain any Voluntary License. Merck had agreed to offer Efavirenz to Thailand at a lower rate, as voluntary reduction ["voluntary licensing"] as compared to the previous price. According to Merck, Thailand had one of the lowest prices of its product in the world. At the time the CL was announced, the price of the drug Efavirenz was 1,400 Baht/m. After the announcement, Merck offered to provide the drug at 550 Baht/m (10 Baht less than the price at which the GPO could provide). Thailand however wanted this in written form, which was not immediately forthcoming. Merck argued that the Government should have talked to the company before granting CL. The drug companies also questioned the urgency of issuing a CL as the presence of AIDS was not something new to Thailand, instead the government should have tried to obtain a Voluntary License. Although agreeing to Merck's terms, would have allowed Thailand to obtain some price relief or from having to potentially invoke a CL, there were other attendant problems such as the cost of drug would be fixed and could not be further minimized due to lack of competition as well as requiring a higher amount of royalty payment to the drug owners. Thus Thailand chose to use CL to allow greater competition and hence a potential for greater lowering of prices. The World Bank estimated that Thailand could reduce the cost of second-line therapy by 90% if it introduced CL for all the drugs it needs in second-line therapy, saving itself $3.2 billion over the next 20 years (TWN 2006).

Finally, Thailand announced a 5 year CL, from 31 December 2006 till 31 December 2011, on Efavirenz, produced by Merck, Sharp and Dohme [MSD]. The CL allowed the government to import generic versions from Ranbaxy, an Indian pharmaceutical company, as a temporary measure or if needed the government could manufacture its own generic versions. At the then current Efavirenz prices, the budget would have allowed only 17,000 people to be treated. According to published reports, Efavirenz was not patented in India, since the granting of patents under the new product patent regime only started in early 2005, when it came into full compliance with the TRIPS Agreement. The Indian government would thus not have to issue a compulsory license for the export of the drug (TWN 2006).

Case of Compulsory Licensing in Brazil

The process of developing countries invoking CLs in order to produce cheap and effective drugs for diseases such as AIDS, Cancer, or Malaria, has brought them in conflict with

developed countries. One such conflict came to surface between US and Brazil, relating to disagreements over Intellectual Property Rights (IPRs), and especially those pertaining to CL.

Article 68 of Brazil's Patent law allowed for compulsory licenses to be issued in situations where the patent holder does not locally manufacture the patented product. On January 2001, the USTR filed a complaint over Brazil' compulsory licensing law in the WTO Dispute Settlement Body, often referred to as the "Merck" case. The U.S. received a large amount of negative publicity and on June 2001, the Bush administration withdrew the complaint. However, under the agreement between the two countries, Brazil agreed to provide the U.S. with advance notice if a license would be issued under Article 68 of the Brazil Patent Act and disputes would be discussed through a bilateral 'Consultative Mechanism' (Love 2007).

In March 2001, the Brazilian Government reached a settlement with Merck for price discounts on Efavirnez in return for not issuing a CL. In May 2007 Brazil's issuing of CL for Efavirenz was a move that drew reactions among public health and industry representatives. The CL would allow Brazil to import and eventually manufacture generic versions of the drug more cheaply. Brazil proceeded with the CL after failing to reach an agreement with Merck to lower prices. With Brazil seeking a reduction from its price of US $1.57 per tablet, Merck's best offer amounted to US $1.10, a 30 per cent discount, which it said was the lowest price of any country with a comparable wealth and disease burden. However the Brazilian Minister of Health demanded a 60 per cent discount to come close to the US $0.65 that Thailand was paying. With the possibility of a CL, the generic imports from India would be available for an even lower, US $0.45 per tablet. Efavirenz is used by 75,000 of the 180,000 patients that receive free AIDS drugs from the Brazilian government. The health ministry says the CL will reduce costs by some US $240 million by 2012, when Merck's patent expires. Merck said it was profoundly disappointed by the outcome, with US-Brazil Business Council calling it a major step backward that will discourage investment in Brazil (Love 2007).

According to TRIPS, governments are not required to negotiate with patent holders prior to issuing a compulsory license in cases of national emergency, extreme urgency, government use or to remedy an anti-competitive practice. The Doha Declaration on the TRIPS Agreement and Public Health, adopted by WTO on 14 November 2001, reaffirmed the right of Members to issue compulsory licenses and "the freedom to determine the grounds upon which such licenses are granted." Despite these measures, Brazil (and Thailand before it) did attempt negotiations, in good faith, with the patent holders, Merck, before invoking a domestic legislative process to grant the compulsory license for Efavirenz (Love 2007).

Case of Compulsory Licensing in India

For the first time, India invoked the Compulsory License clause to cut the cost of the patented anti-cancer drug Nexavar (Sorafenib) produced by Bayer, for the treatment of advanced kidney and liver cancer. The drug was patented by Bayer in India in 2008, costing Rs. 2.8 lakh for a month's dosage. Natco Pharma, an India-based generics company had applied for a compulsory licence for manufacturing the drug in September 2011, after it failed to get a voluntary commercial licence from Bayer.[11]

Natco Pharma promised to sell a month's supply of the generic version of Nexavar at Rs. 8800 (£110), i.e. 97% less than the current market price of £4000. Bayer developed the drug with

US firm Onyx Pharmaceuticals with reported sales of $934 million (£590 million) in 2010. Natco will have to pay Bayer royalty pegged at 6% of net sales, every quarter.[12] As per the landmark judgment of Mr. P. H. Kurian, the then Patent Controller, Bayer had not met the reasonable requirement of the public. It had not "worked the patent" or manufactured it to a reasonable extent in India. Besides, the drug was not available at an affordable price. Bayer imported the product, and while its global sales of Nexavar were $934 million in 2010, in India it clocked sales of 16 crore in 2009. According to the judgment, Bayer demonstrated "neglectful conduct" in India. Only 2% of the 8842 patients needing the drug got the medicine, resulting in demand for drug "far exceeding" the supply of the product. India's Cipla Ltd, which has the second largest share of the local drugs market, may also benefit from the Bayer case. Cipla was fighting a Bayer suit for patent infringement after the Indian drug maker launched a generic version of Nexavar in India in April 2010.[13]

The Bayer case underscores the still fractious relationship between global pharmaceutical firms not unlike what Pfizer, GlaxoSmithKline and Novartis also face in India. This is because for the first time since Indian patent law was reformed in 2005, the pronouncement was paired with a compulsory license requirement: Given that the wording in India's Patent Act had been amended from 'reasonably priced' to 'reasonably affordable priced' which has come into play now. The new wording is seen as a lower threshold for compulsory licenses, which can be issued under world trade rules by nations that deem major life-saving drugs to be too costly. The licenses allow them to authorize the local manufacture or importation of much cheaper, generic versions. Natco has also asked for a compulsory license for Selzentry, an AIDS medication produced by US drug company Pfizer. Natco's competitor Cipla, has asked for a license for Merck's Isentress, and AIDS medication.[14]

The standoff between India and global pharma MNCs has relevance. For starters, the Nexavar decision will impact the estimated 2.5 million Indians who are HIV-positive by giving them access to a cheaper generic version of the medication. Secondly, thanks to the CL, the Indian makers of the drug are looking ahead to export possibilities. In Sub-Saharan Africa, according to Oxfam, 80% of required HIV and AIDS medication is covered by Indian generic makes. In developing countries in general, CL is increasingly being used as a means of providing cheaper antiviral products: in the past five years, Brazil, Ecuador, and Thailand have allowed for the production of various HIV drugs without seeking agreement from the inventor companies. In countries with no generics industry, such as Ghana and Eritrea, import licenses are granted for Indian products.[15]

The use of CL is not an easy solution, countries that decide to issue CL must express a clear willingness to endure lawsuits, pressure, threatening postures and threats of trade sanctions from the United States and European Union. So although the TRIPS Agreement permits Member countries to use patents without the necessary authorization of the patent holder, developing countries do not appear very eager, with few exceptions, to test the provisions under Article 31. Yet another reason is that internal administrative procedure for issuing CL may not have been established or what is established may be bureaucratically cumbersome. It is also the case that a country requires a certain level of technical and manufacturing capability for producing drugs, which is indeed possessed by very few countries. Such countries would need to depend on their ability to parallel import inexpensive generic drugs from other drug producing, mostly developing countries, which clearly creates several limitations in itself. CL therefore cannot be

seen as a panacea for providing low cost drugs. Nevertheless, evidence does suggest that a credible threat of CL may reduce drug prices faster and more efficiently than other voluntary options that have been explored.

Within the specific Indian context, it was due to the absence of patent protection in pharmaceuticals under the Indian Patents Act, 1970, that Indian generic companies could reverse engineer and produce and market in India any new drug developed abroad. The absence of any restrictions on the entry of firms resulted in a competitive market structure with relatively low prices. However with the introduction of full product patent protection in pharmaceuticals from 1 January 2005 generic companies are prevented from introducing new process patent drugs and the lack of competition may result in high prices.[16]

Impact of Compulsory License on the Licensor's Innovation Capabilities

The use of Compulsory Licensing as a health policy intervention that can potentially limit the exclusive rights conferred by patents has long been controversial. CL basically implies that a government, for reasons of public policy, can authorize itself or a third party (licensee's) to use the subject matter of a patent without the necessary authorization of the rights holder (licensor). The reasoning for such an authorization, through TRIPS, is that the public interest in terms of broader access to the invention is viewed as considerably more important than the private interest of the right holder to fully exploit their exclusive rights (Reichman and Hazenzahl 2003).[17]

There is a considerable apprehension, particularly among the developed countries research based pharmaceutical companies that widespread use of CL will reduce the incentive for innovation offered by the patent system. The argument is that insofar as patents are needed to induce innovation, the weakening of patents through CL will reduce innovation. The underlying assumption is that due to the considerable costs and risks associated with drug development, different from other inventions, compounded by the fact that the drug industry tends to rely more on patents than other industries, more is therefore at stake for this industry when measures that reduce patent protection such as CL are suggested as policy measures.[18]

How does one examine the impact of CL on the drug innovation process? The problem is particularly acute when the royalty terms of the CL are fixed, as is often the case, at below the expected market return. It is quite obvious that in such cases the drug manufacturer will not be able to earn monopoly profits. The firm's motivation for continued innovation may, in such cases, be negatively affected.[19]

There are three essential factors that largely impinge on whether and how much innovation is affected by the issuing of CL. First is the royalty rate paid to the patentee. If the rate is set essentially at what a patentee demands, then clearly there is not much reason to anticipate that innovation will be substantially harmed. However if the rate is set at a level far below the market rate, it could strip the patentee of its right to any monopoly profits.[20] There are no universally accepted precedents for administering royalty rates. To a large extent they are a function of the bargaining power of the patentee and the government issuing the CL. A government body (probably a commission set up within the Public Health Service) can designate drugs urgently needed for treatment (not for general marketing), and issue a license to any qualified firm for supplying the drug. The price would be set in the contract. The commission would also set a 'fair' royalty, which would be paid to the patent holder. The patent holder would

therefore receive a royalty without any manufacturing expense or any risk of liability, since it would not be directly responsible for providing the drug, which would be undertaken by the government or the generic company. One must keep in mind that a significant purpose of CL is to keep drug prices low by encouraging generic production.

Besides the royalty price, two other factors that play a significant role in 'motivating innovation' are the issues of: a) the "market significance" or the extent to which a licensee actually threatens the patentee's markets and b) "predictability" or the extent to which a patentee anticipates a CL. The issue of market significance relates to the degree of significance of any specifically chosen market for the licensor, in other words a CL can vary in degree with respect to the competitive threat it can pose to the licensors. If, for instance, a CL covers a known product in a licensor's target or privileged market, the licensor and the licensee will have to share the same market. The market significance of this license is thus high because the licensor's market is directly threatened. Conversely, if the license covers a market that is un-important to the licensor, or it covers a product that has yet to be proven or for which the market is immature or untested, there is a good chance that the licensee and licensor will not compete directly.

Research indicates that if CL is taken in less significant markets, their impact on innovation is marginal.[21] For global drugs such as HIV, this implies that the issuing of CL limited to developing countries and which do not impact the markets for the rich countries might not be detrimental to research efforts in the rich developed countries. So, as long as such geographical limitations in the scope of a CL stay intact, selective licensing for developing nations should have little impact on overall R&D investment.[22] Focusing exclusively on innovation concerns, one can make a case for using different approaches to CL depending on whether global or developing country specific drugs are licensed (Colleen, 2003).

The 2010 IMS Health report[23] supports such a perspective. Pharmaceutical companies make the vast bulk of their profits on secure scales in rich countries that have strong protection for intellectual property rights. These profits are substantive enough to fund future research and development. By denying access to affordable patented medicines in developing countries, they gain only marginally. Moreover certain studies conducted in the 1960s and 1970s on CL regimes in Canada or antitrust consent decrees in USA, concluded that licensing had no long-term negative impact on licensor innovation, including the pharmaceutical sector.[24]

Finally, from the point of view of innovation, it is also important to ascertain how 'predictable' a CL is. According to Colleen, it appears that where licenses are unpredictable or where they implicate insignificant markets, there will not necessarily be an adverse impact. However, licenses that are both predictable and affect significant markets, potentially are more risky, and appear to have a greater chance of being accompanied by a negative impact on innovation. One could briefly summarize saying that: "Even if licenses are predictable and affect significant markets, if the price of the license is set at market rates, the license probably will not harm innovation. The factors of predictability and significant market impact may thus be necessary but not sufficient for producing a negative impact on innovation."[25]

Colleen (2003) provides more evidence through a study conducted on the effects of CL on the innovation process to suggest that only those drug licenses that were issued predictably in significant markets were likely to harm innovation. The results of such a study are contrary to the prevalent assumption that CL necessarily harms innovation. Were the assumption true, all six

cases of the study "would reveal a drop in investment in innovation subsequent to licensing, yet no such uniform downward trend was observed."[26] In fact, if anything, the opposite is true—in all cases but one, activities of innovation continued at the same or even higher pace than before the advent of a license. These results clearly throw doubt on concerns that CL is uniformly harmful.

In a more specific context of the AIDS crisis within developing countries, at least two kinds of innovation related incentives are appropriate: 1) those that indicate research in diseases of common interest to both developed and developing countries (e.g., AIDS) and 2) those that indicate research in areas more specifically relevant to developing countries (e.g., malaria or night blindness). It would indeed be counter-productive if CL causes a negative impact on R&D for diseases specific to the developing countries, the growth of which is eagerly anticipated with the introduction of stronger TRIPS mandated patent protection. The challenge for policy makers will therefore be to put into practice patent-weakening schemes (such as CL among other choices) that increase access but cause minimal harm to the patent innovation incentive.[27]

Conclusion

It is clear that when neither the 'benevolence' of the state nor the 'interest' of the market is able to address the yawning gap of addressing research and development for treating infectious diseases, then it is quite possible, as we have argued that the problem lies with the very theoretical and structural formulation of the nature of such drugs? If drugs for infectious diseases are treated as a global public good, it is arguable that there may be more interest in eliciting R&D from diverse backgrounds. It is also the case that in the absence of such an R&D effort, the resorting to compulsory licensing, acceptable under TRIPS, creates anxieties among large pharmaceutical companies, some of which appear misplaced. The use of CL has clearly much to do with the context, both geographical and market related, where it is invoked. Clearly the use of CL has a fairly rich history in both developing and developed countries. It is finally the cure of such diseases that matters and its availability at an affordable price to millions of people all over the world.

Table 1: Distribution of New Chemical Entities (NCEs) for various therapeutic areas

Therapeutic areas (Anatomical Therapeutic Classification, ATC)	Approved NCEs 1975-99 [I]		Disease burden (DALYs and distribution) [ii]				% of world-wide sales, 1999 [iii]	NCEs by DALY	Drug sales (million $) by DALY
			World		HIC	LMIC			
	number	% of total	number (x10^6)	%	%	%			
Central nervous system	211	15.1	159.46	11.5	23.5	10.5	15.1	**1.32**	**193**
Cardiovascular	179	12.8	143.02	10.3	18.0	9.7	19.8	**1.25**	**283**
Cytostatics (neoplasms)	111	8.0	84.87	6.1	15.8	5.2	3.7	**1.31**	**90**
Respiratory (non infectious)	89	6.4	61.60	4.5	7.4	4.2	9.3	**1.44**	**307**
Anti-infectives & antiparasitics [iv]	224	16.1	409.08	29.6	4.2	31.8	10.3	**0.55**	**52**
HIV/AIDS [v]	*26*	*1.9*	*70.93*	5.1	*0.9*	*5.5*	*1.5*	*0.37*	*44*
Tuberculosis [vi]	*3*	*0.2*	*28.19*	2.0	*0.1*	*2.2*	*0.2*	*0.11*	*11*
Tropical diseases (total) [vii]	*13*	*0.9*	*130.35*	9.4	*0.3*	*10.2*	*0.2*	*0.10*	*3*
Malaria	*4*	*0.3*	*39.27*	2.8	*0.0*	*3.1*	*0.1*	*0.10*	*5*
Other therapeutic categories	579	41.6	524.54	37.94	31.08	38.59	41.9	1.10	163
Total	**1393**	100	**1382.56**	100	100	100	100	**1.01**	**148**

Table 1: Ratio of NCEs per disease-adjusted life year for NCEs developed between 1975 and 1999[1]

[i] Source: IMS Health drug monitor 1999; EMEA and FDA data; Trouiller P, Olliaro P (1999)

[ii] Global disease burden per disease category expressed in DALYs (disability-adjusted-life years) and distribution, as well as relative distribution in high income countries versus low and middle income countries; data from WHO World Health Report, 1999.

[iii] Total pharmaceutical sales for 1999 was US$ 204,700 million (IMS health). This is for private pharmacy sales for all drug classes except anti-infectives and parasitics, which also include public pharmacy sales.

[iv] Anti-infectives class includes the following sub-classes: antibiotics, antituberculosis, antivirals, vaccines and immunoglobulins.

[v] AIDS antiviral drugs (20 approved antiretrovirals and antiproteases) and drugs for opportunistic infections (6 approved drugs) are included; atovaquone is quoted in two sub-classes (malaria and opportunistic infections indication)

[vi] Approved anti-tuberculosis drugs are: pyrazinamide, rifabutin, rifapentine.

[vii] Antiparasitics drugs approved for a tropical disease indication: benznidazole, nifurtimox (Chagas disease); albendazole (helminthic infection); eflornithine (human African trypanosomiasis); artemether, atovaquone+proguanil, halofantrine, mefloquine (malaria); ivermectin (onchocerciasis); oxamniquine, praziquantel (schistosomiasis) and 2 reformulations of already approved drugs: liposomal amphotericin B (leishmaniasis) and pentamidine (African trypanosomiasis). After 1999, two new drugs were registered for malaria: arteether and artemether/lumefantrin

[1] A Needs-based Pharmaceutical R&D Agenda for Neglected Diseases; Els Torreele, Martine Usdin & Pierre Chirac (2004)

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Endnotes

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[3] *Ibid.*

[4] IMS Health Market Prognosis, March 2011

[5] World Health Organization: Global Health Observatory (GHO Report 2010): http://www.who.int/gho/malaria/en/index.html

[6] World Health Organization: Global Health Observatory (GHO Report 2010): http://www.who.int/gho/tb/en/index.html

[7] World Health Organization: Global Health Observatory (GHO Report 2010): http://www.who.int/gho/hiv/en/index.html

[8] The disability-adjusted life year (DALY) is a measure of overall disease burden. The concept of potential years of life lost due to premature death is extended to include equivalent years of 'healthy' life lost by virtue of being in states of poor health or disability. So basically, mortality and morbidity are combined into a single, common metric One DALY is equal to one year of healthy life lost.(Source: http://www.who.int/healthinfo/global_burden_disease/metrics_daly/en/)

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[10] See WIPO: Compulsory Licensing of Pharmaceuticals and TRIPS. http://www.wto.org/english/tratop_e/trips_e/public_health_faq_e.htm

[11] See: "Natco granted Compulsory License for Nexavar", at: http://www.livemint.com/2012/03/13001601/Natco-gets-India8217s-first.html

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[13] See: "Natco gets India's first Compulsory License", at: http://www.livemint.com/2012/03/13001601/Natco-gets-India8217s-first.html

[14] See: "Compulsory licensing: Patients vs. Patents", at: http://www.expresspharmaonline.com/20120415/management01.shtml

[15] See: "Drug companies battle against Indian Pharmaceutical Pirates", at: http://worldcrunch.com/drug-companies-battle-against-indian-pharmaceutical-pirates/4890

[16] See "Sparring over Sorafenib: How will Natco's move against Bayer affect Pharma licensing?", at: http://knowledge.wharton.upenn.edu/india/article.cfm?articleid=4681

[17] See Reichman & Hasenzahl, 2003, p.7.

[18] Colleen (2003), p. 20

[19] Reichman & Hasenzahl suggest that overreliance on compulsory licensing may also produce unintended negative downstream impacts on social measures other than innovation: such as discouraging domestic inventors, hindering foreign investment and technology transfer, and overshadowing regulatory or cooperative measures that might otherwise increase investment in local production facilities.

[20] p. 20 Colleen, For a deeper analysis of the ethical and economic issue of what developing countries should contribute to innovation, see William Jack & Jean O. Lanjouw, Financing Pharmaceutical Innovation: How Much Should Poor Countries Contribute? (Ctr. for Global Dev., Working Paper No. 28, 2003), *at:*http://www.cgdev.org/wp/cgd_wp028.pdf (last visited Aug. 8, 2003).See also Jean O. Lanjouw, A Patent Policy Proposal for Global Diseases (Apr. 2001), at: http://siteresources.worldbank.org/DEC/Resources/84797-1251813753820/6415739-1251814028691/lanjouw.pdf (last visited June 30, 2012). Carsten Fink, How Stronger Patent Protection in India Might Affect the Behavior of Transnational Pharmaceutical Industries World Bank Group, Policy Research Working Paper No. 2352, 2000) at: http://www-wds.worldbank.org/external/default/WDSContentServer/IW3P/IB/2000/06/27/000094946_00060905463269/Rendered/PDF/multi_page.pdf (last visited June 30, 2012).

[21] p. 43 Colleen. Another way of saying this is that an important consideration in determining whether compulsory licenses taken by developing countries will impact innovation is the type of drug licensed. Developing countries are concerned primarily about two categories of drugs, each with its own set of incentives: 1) 'global' drugs that are created for rich markets but are also useful in developing countries such as cancer drugs and AIDS therapeutics and 2) 'local' drugs specific to developing countries such as for treating malaria or tuberculosis. The latter have not been a priority of pharmaceutical companies.

[22] p. 43 Colleen. An assumption here is that the affected markets is limited to developing countries and not enlarged to include rich nations as well, for instance through parallel trade.

[23] IMS Health Market Prognosis, March 2011.

[24] p. 21 Colleen. See also Donald G. McFetridge, Intellectual Property, Technology Diffusion, and Growth in the Canadian Economy, in Competition Policy And Intellectual Property Rights In The Knowledge Based Economy 65 (Robert D. Anderson & Nancy T. Gallini Eds., 1998).

[25] Direct Quote from Colleen (2003), p. 27.

[26] Colleen (2003), p. 40.

[27] Colleen (2003), p. 20.