Review article

Compulsory licensing of chronic disease pharmaceuticals in Thailand

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Abstract:

For pharmaceutical companies, obtaining patent protection for the pharmaceuticals they develop is essential. Patent protection assures that the pharmaceutical company will have a reasonable opportunity to recoup their most likely quite heavy investment in the new drug and allow the company to control the wholesale market price of the drugs. These key intellectual property rights are truly at the heart of the internationally recognized intellectual property regime.

For patent right holders in general merchandise, say an innovative paperclip or mousetrap, the absolute right of the patent holder as to the distribution and price is perfectly acceptable. Pharmaceutical patents however, with the ability to control the price present unique societal issues. A patient dying of HIV-AIDS, cardiovascular disease, or cancer must pay the full market price for the drugs, or die. It is as simple as that.

In countries where critical drugs are not available due to high prices or the refusal of the patent holder to market the drugs, the government may under a convergence of domestic and international agreements (TRIPS and Doha) issue "compulsory licenses" that enable another drug manufacturer to produce the patented drug without the fear of a patent infringement action by the patent holder. The patentee not only loses its right to control the production of the patented product in that country, but also loses the right to set the wholesale price.[1] But the citizens of that government get the needed medical treatment.

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The opinions presented in this paper are the author's own and do not necessarily represent the opinions of the Department of the Navy, Bureau of Medicine and Surgery, the Department of the Navy, the United States Department of Defense, or any other Department or Agency of the United States Government.

[1] Strictly speaking, it is not a license in that it is an involuntary transfer of rights. One could define it as "expropriated non-recourse use". Nonetheless we will continue to refer to it as a license.

Compulsory licensing of pharmaceuticals presents certain compelling social and political questions. In general, under what circumstances may a government consider that the epidemiological situation in regard to certain chronic diseases has become such a critical a public health crisis to justify the compulsory license? Do TRIPS and the Doha Agreement provide a legal basis to issue a compulsory license?[2]

The compulsory licenses the Thai government is considering at present are for chronic diseases. All prior compulsory licenses were for an infectious disease, namely AIDS, as were all earlier compulsory licenses by other governments. The compulsory licenses under consideration are for drugs used to treat coronary heart disease and several cancers. Thus, how the Thai government deals with this within the proper boundaries of international law will be a case of first impression that cannot help but influence compulsory licensing by other governments.

The issue of compulsory licenses is also allegorical. Are patent rights as the metaphorical heart of the patent system, open to change in order to help the literal heart of a living patient? Pharmaceutical companies are, after all, active participants in the worldwide healthcare system and are ethically obligated to the patients, much as much as practicing physicians are.[3] These are very intriguing questions that in addition to going to the heart of patent law, also go to the heart of the pharmaceutical and health care industry.

Keywords: Patent right; TRIPS; Doha Declaration; Compulsory licensing; Pharmaceuticals

[2] See, e.g., *Citizens United v. Federal Election Commission,* 558 U.S. 310 (2010), based on *Trustees of Dartmouth College v. Woodward*–17 U.S. 518 (1819).

[3] The grandfather physician of Lt. Commander Braslow taught him that the practice of medicine is, or ought to be, far more then a mere business proposition. Dr. Lawrence Braslow held that the practice of medicine should be viewed as a humanitarian calling analogous to the priesthood, with the primary concern the health and well being of the patient. From this viewpoint, although the pharmaceutical companies are certainly entitled to adequate compensation, consideration must be given to those who simply lack the financial means to purchase the drugs on the free market. To withhold or restrict medical aid in any form for financial reasons that will save lives or alleviate human suffering raises serious ethical concerns within the medical community and the pharmaceutical industry.

I. Introduction

On October 5, 2005, the World Health Organization (WHO) issued a Report on the global public health threat posed by chronic diseases. The Report stated that by the end of 2005, an estimated 35 million people would succumb to chronic diseases.[4] What was alarming was that over eighty percent of those deaths due to chronic diseases would occur in developing countries. As can be readily imagined, the direct cost of treating chronic diseases has already begun to strain the already burdened national health care budgets of a number of developing countries. For example, the annual cost of treating cardiovascular disease in China is currently estimated to be $40 billion, which is four percent of its gross national income (GNI).[5] India now faces the challenges of providing health care to the world's largest population of diabetes patients, a condition for which many of those affected need long-term pharmaceutical treatment.[6] The total number of diabetics in India is expected to reach 5.2 million by 2025, and this will most certainly exert tremendous stress on an already under-resourced health care system.[7]

Developing countries in general face high rates of death due from infectious diseases, including malaria and tuberculosis.[8] At the same time, many developing countries are still struggling with their own pervasive, and expensive, HIV/AIDS crisis. Compounding this situation, the WHO reports that the total number of deaths worldwide directly attributed to infectious and chronic diseases were in part exacerbated or accelerated due to AIDS. It is clear, then, that developing countries face a double burden of both infectious and chronic diseases and AIDS, a burden that threatens to quickly exhaust financial resources available for the purchase of medicines.[9]

Thailand is representative of a developing country that faces this double burden of treating infectious and chronic diseases and AIDS. At the present time the HIV/AIDS population in Thailand is about 500,000.[10] The Thai Ministry of Public Health estimates that about 300,000 patients have coronary heart disease in Thailand.[11] The prices of patented drugs for treating patients with HIV/AIDS and coronary heart diseases are very high in comparison to Thailand's GDP. The Thai government estimates that a compulsory license for Plavix, an effective treatment for coronary heart disease, would lower the price of Plavix by 90%, that is from 70 Baht to 7 Baht, making it available to patients in the National Health Care system.[12]

On January 25 2007, Thailand's post-coup Government issued three compulsory licenses: two compulsory licenses for patented HIV/AIDS drugs, and one compulsory license for a patented coronary heart disease drug. Thailand's Minister of Public Health justified the authorization of the compulsory licenses on the grounds that those three drugs were priced out of reach of the Government's universal health plan. Thailand's authorization of a compulsory license for a patented

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[4]World Health Org., "Preventing Chronic Diseases: A Vital Investment 2005" at 2, cited in Shereen Usdin, *The No-Nonsense Guide to World Health, 2007, at 109-110.*

[5]Thomas A. Gaziano, "Reducing the Growing Burden of Cardiovascular Disease in the Developing World", 26 *Health AFF., 2007, at 13 and 16.*

[6]Stefan Bjork et al., "Global Policy: Aspects of Diabetes in India", *66 Health Policy, 2003, at 61-62.*

[7]Hilary King et al., "Global Burden of Diabetes, 1995-2025: Prevalence, Numerical Estimates, and Projects", *21 DIABETES CARE, 1998 at 1414, 1417.*

[8]UNAIDS, 2006 *Report on the Global AIDS Epidemic, 2006.*

[9]Brent Savoie, "Thailand's Test: Compulsory Licensing in and Era of Epidemiologic Transition", *Virginia Journal of International Law,* Vol. 48 Number 1, at 216.

[10]The Ministry of Public Health and The National Health Security Office, *Facts and Evidences (sic) on the 10 Burning Issues Related to the Government Use of Patents on Three Patented Essential Drugs in Thailand*, February 2007 (hereafter "The 10 Burning Issues") at 14.

[11]Id. at 15.

[12]Id.

coronary disease drug was the first use of compulsory licensing to obtain access to medicines for chronic diseases.[13]

II. Economic and epidemiological basis for compulsory licenses

The official justification behind the Thai Ministry of Public Health's authorization for the use of compulsory licenses was that those three specific patented drugs were priced out of reach of the Government's universal health plan. The Thai National Health Security Act of 2002 requires the Ministry of Public Health to provide universal access to essential medicines for all Thais. Accordingly, every Thai citizen is covered under one of the three main national public health insurance programs. The three programs are as follows:[14]

(1) The Civil Servant Medical Benefit Program:

(2) Social Security and

(3) The Universal Coverage Program.

The entire Thai population of 62 million covered by one of the three above-mentioned national public health insurance programs is entitled to full access to all of the medicines on the essential drugs list, including almost 900 specific drugs, many of which are patented. Since October 2003, the Thai Government has also committed itself to the policy of universal access to antiretroviral drugs (ARVs) for AIDS patients. By putting the ARVs for AIDS patients on the national essential drugs list, the Thai Government must respond to its commitments through one of several means. One response has been to augment the public health budget, in particular the budget for access to ARVs. The Thai Government asserts that the main objective of announcing and implementing the compulsory patent license is to increase access to essential medicines among the Thai people, and not merely to save on its health care budget. Even so, this budget increased from around US$10 million in 2001, to more than US$100 million in 2007. This level of spending for access to ARVs is the highest among the lower middle income developing countries. As a consequence of the compulsory licensure, the Thai Government further asserts that many more AIDS patients will have access to the ARVs with the same budget level.

How has the Thai Government usually implemented compulsory pharmaceutical licenses? Factually, the threshold issue is the clinical effectiveness of the drug. Obviously, the drug under consideration must be more effective than alternative medications in use. Then, the cost of the drug on the open market is considered. If that cost is excessive, the patent holder might be amenable to manufacturing the pharmaceutical in country, at a cost that the government health ministry deems within budgetary reason. If this fails, the patent holder might be open to a domestic pharmaceutical manufacturer producing the drug, with the patent holder accepting a royalty that is, as before, within budgetary restraints. Only if all of these efforts are unavailing, will the government issue the compulsory license in order to get the medication available in the domestic market. A compulsory license is the grant, by state decree, of a license to a third party to produce the patented pharmaceutical.[15] Perhaps the most contentious issue from the viewpoint of the patent holder, besides assuring the efficacy and purity of the pharmaceutical, is the royalty amount.

III. Examples of compulsory licenses

We need to bear in mind that the concept of compulsory licensing has been interpreted differently in various countries.[16] In the United States, compulsory licensing has been utilized by the courts in federal antitrust litigation in circumstances where patents are used in anticompetitive ways.[17] Consequently, the great

[13]Savoie, *supra* note 9, at 242.

[14]"The 10 Burning Issues", supra note 10, at 2.

[15]August, Ray, *International Business: Text, Cases and Readings*, 2004 at 526.

[16]Sara M. Ford, "Compulsory Licensing Provisions under the TRIPS Agreement: Balancing Pills and Patients", *15 American University International Law Review,* 2000, at 941, 957.

[17]Savoie, *supra* note 9, at 233.

majority of compulsory license cases in the United States are based on what are termed "consent decrees". These consent decrees in essence are court enforced agreements (generally authored by the Antitrust Division, Department of Justice) between the purported antitrust violators and independent third parties granting the third party the right to use the purported violator's patents in their own products. The theory is that by so doing the third party is rendered capable of entering the market with a competitive product.[18] One of the landmark decisions of the United States Supreme Court on anticompetitive use of patents ordering compulsory licensing is *United States v. Glaxo Group Ltd.*[19]

In *Glaxo,* the pharmaceutical in question was a patented form of griseofulvin that was used for treating external fungal infections.[20] The Court noted that griseofulvin itself, for whatever reason, was not patented or even patentable. Glaxo held patents on the manufacturing process for the "dosage form" of the drug. A critical finding of the Supreme Court was that this particular form of griseofulvin had no substitute, thus Glaxo had a classic monopoly in violation of Section 1 of the Sherman Act. The government presented evidence that Glaxo acted in a manner that restricted the price and availability of the drug. We should note that Glaxo was not charged with price gouging or other patent abuse (as the dissent pointed out), but that their unchallenged monopoly was simply a *per se* antitrust violation. The court also noted that Galxo could at its whim cut off the entire supply of griseofulvin should it choose to do so. The Supreme Court then ordered Glaxo to grant reasonable licenses to all *bona fide* applicants in order to "pry open to competition" to the griseofulvin market.

Interestingly, the United States (and Canada as well) proposed to issue a compulsory license on the basis of a perceived potential national health crisis. After the terrorist attack on the World Trade Center in New York on September 11, 2001, the United States government was, quite properly, very concerned about a subsequent terrorist attack using anthrax as a weapon of mass destruction.[21] The drug of choice to combat anthrax was the antibiotic ciprofloxacin (Cipro), patented by Bayer. There was no question that the threat of an anthrax attack was serious and that the potential casualties, including deaths, could well be numbered in the thousands.[22] The governments of the United States and Canada took the only responsible steps that were possible, that is propose a compulsory license in order to produce the required amount of Cipro.[23] On October

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[18]Delrahim, Makan. "Forcing Firms to Share the Sandbox: Compulsory Licensing of Intellectual Property and Antitrust 2" http://www.usdoj.gov/atr/public/speechs/203627.pds, at 7,8.

[19]*Re : United State v. Glaxo Group Ltd.,* 410 U.S. 52 (1973).

[20]Note that there is a significant difference between a fungal infection than AIDS, cardiovascular disease and cancer.

[21]On September 18, 2001, anthrax spores were sent to several news organizations, two United States Senators, Tom Daschle of South Dakota and Patrick Leahy of Vermont. Five people died and 17 others were infected.

[22]One estimate was that medication for 10 million would be required.

[23]"We cannot just rely on Bayer to ensure we have a sufficient supply of Cipro," {Senator Charles Schumer, D-N.Y. stated). "First, Bayer can only produce so much Cipro, and we should not put our best response to anthrax in the hands of just one manufacturer. Second, buying Cipro only from Bayer-who charges a lot more than generic manufacturers would-means we spend a lot more and receive a lot less. Hopefully, we won't even need to use the Cipro we already have on hand, but if we make arrangements to purchase it from multiple generic drug manufacturers, we'll have it if we need it."

Ralph Nader, the well known consumer advocate stated: "We were shocked by your comments in the October 17, 2001 Washington Post, indicating that you do not have the legal authority to authorize generic production of ciprofloxacin ... This, of course, is not true. As your own staff is well aware, you may use 28 USC 1498 to issue compulsory licenses for patents, and you could immediately authorize the five companies who have already satisfied US FDA requirements for the quality of their products to speed the manufacturer of ciprofloxacin, and indeed this could and should be done for any other medicine needed to confront the current crisis. By failing to act, you are putting Americans at risk. By acting to authorize generic competitors to manufacture ciprofloxacin, you would reduce public anxiety over the supply of the drug, and take steps to introduce competition which would ensure redundant capacity and a more favorable procurement environment." http://www.salon.com/2001/10/18/cipro_patent/.

October 18, 2001, Letter from Ralph Nader and James Love to DHHS Secretary Tommy Thompson, cited in http://www.cptech.org/ip/health/cl/cipro/ciproquotes.html.

24, 2001 in lieu of the compulsory license, the United States and Bayer agreed to lower the market price of $1.77 per dose to $0.95 each, with a second order for $0.85, and additional quantities, if needed, for $0.75.[24] Implicitly then, the United States recognizes that when the citizenry are under a significant health threat, compulsory licensure is appropriate.

IV. Thailand's legal basis for compulsory licensure

In contrast to the usual United States compulsory licensing, the Thai Ministry of Public Health relies on Section 51 of the Patent Act of B.E. 2522 (1929) (hereinafter "Section 51"), to issue compulsory licenses in the form of a "Notification of the Department of Disease Control, Ministry of Public Health." (See Addendum I) Section 51 of the Patent Act provides in pertinent part as follows:

> In order to carry out any service for public consumption or which is of vital importance to the defense of the country, or for the preservation or realization of natural resources or the environment, or to prevent or relieve a severe shortage of food, drugs, or other consumption items, or for any other public service, any ministry, bureau, or department of the Government may, by themselves or through others, exercise any right under Section 36 by paying a royalty to the patentee or his exclusive licensee under paragraph 2 of Section 48 and shall notify the patentee in writing without delay, notwithstanding the provisions of Section 46, 47, and 47 bis. In the circumstances under the above paragraph, the ministry, bureau, or department shall submit its offer setting forth the amount of remuneration and conditions for the exploitation to the Director-General. The royalty rate shall be agreed upon by the ministry, bureau, or department and the patentee or his licensee, and the provisions of Section 50 shall apply *mutatis mutandis.* (Emphasis added.)

1. AIDS compulsory licenses

The Thai Government has issued three Notifications pursuant to Section 51 between November 2006, and January 2007. The first Notification, that for HIV/AIDS medication Efavirenz on November 29, 2006, has been fully executed, and will be described below. However, there has been no enforcement action taken in respect to either the Notification on January 25, 2007, for a combination of Lopinavir and Ritonavir known as Kaletra, a "second line" HIV drug, or in the Notification for Clopidogrel (known in the United States as Plavix), an antiplatelet drug to reduce the incidents of coronary artery disease and peripheral vascular disease. Hence, they are only mentioned here and are not discussed in full.

It is important, if not critical, for the legal community to try and understand the nature of the "double burden" of AIDS and cardiovascular and cancer developing countries and governments are struggling under. It is the lot of legal professionals to abstract and strip to the essentials real-life situations so that the structured rules of law can be applied in an impartial and antiseptic manner. Here, the raw numbers of patients and medical costs are important, of course, but the result is sterile and lifeless. The issue before us is a matter of life and death, in the thousands and tens of thousands. Practicing physicians can understand in part, but the numbers alone tend to dull the full impact of the problem. For the legal community, the task is far harder.

Instead of focusing exclusively on the numbers, except noting them in passing where appropriate, the authors have determined on a different approach. We will present short medical stories on the specific drugs that are under consideration for compulsory licenses. These stories will tell the international legal community in an abbreviated manner how the targeted disease functions, and how the drug works. To begin to have a general understanding of the interaction of the

[24] http://www.cptech.org/ip/health/cl/cipro/dhhs10242001.html.

medicine and the disease will put a humanitarian, but still scientific focus on the problems that the developing nations must deal with.

A. Efavirenz[25] notification date November 29, 2006.[26]

One somewhat effective AIDS treatment is to decrease the amount of the HIV virus in the blood stream. This regimen is not a cure, of course, but decreasing the quantity of the HIV virus acts to decrease the incidents of AIDS itself, as well as other AIDS related cancers. Thailand produces Nevirapine which is in a class of pharmaceuticals termed "non-nucleoside reverse transcriptase inhibitors" that reduces the amount of the virus in the blood by combining with the virus and inhibiting the virus's reproduction. In order to be effective, however, the patient must continue to use Nevirapine indefinitely. In one aspect, Nevirapine is a useful "first line" drug for use in Thailand in that it is produced at a reasonable cost under the usual licensure from the patent holder, Boehringer Ingelheim Pharmaceuticals, Inc.[27]

The use of Nevirapine, however, can have some extremely serious adverse side effects. As in all AIDS related treatments, there is the danger of hepatotoxicity. Nevirapine can adversely affect the levels of ALT (alanine aminotransferase) and AST (aspartate aminotransferase) in the blood, evidencing severe liver damage within weeks of ingestion.[28] There are dermatological issues, as well as nausea, fatigue, headache, vomiting, diarrhea, abdominal pain, and muscle pain, some of which are secondary to the hepatotoxicity issue. Statistically, the incidence of the latter more minor side effects range from 16% to 18% of those using Nevirapine, whereas the incidents of liver damage manifesting as jaundice and leading to hepatic necrosis and failure are up to 4%, and mortality in 1% of users.[29] Bearing in mind these are just the effects of using Nevirapine, and not considering the mortality of the underlying HIV/AIDS, these added risk factors of using Nevirapine are not desirable.

The Thai government then considered the use of Efavirenz as a replacement to Nevirapine whenever possible. Efavirenz reduces the amount of HIV virus in the bloodstream in a manner somewhat similar to Nevirapine. Essentially, in pharmacological terms Efavirenz is also a non-nucleoside reverse transcriptase inhibitor like Nevirapine that enters the viral RNA structure and modifies it in a manner that interferes with the ability of the virus to reproduce. As with Nevirapine, Efavirenz is "virustatic" and will not act to eliminate the HIV virus from the blood. As with all non-nucleoside transcriptase inhibitor drugs, Efavirenz has the inherent risk of clinically significant side effects on the liver.[30]

However, the toxicity with Efavirenz is significantly lower than Nevirapine, which makes it clinically more desirable. The incidence of notable side-effects with Efavirenz is approximately 8% for the generalized dermatological issues, as well as nausea, fatigue, headache, vomiting, diarrhea, abdominal pain, and muscle pain. The most important, however, is that the incidence of acute hepatotoxicity is far lower, approximately at 1%.[31]

In developed countries, Efavirenz-based triple ARVs is preferred as the first line treatment. However, Efavirenz is quite costly. As of 2012, the annualized cost of Efavirenz per standard bottle is 1,400 baht, which the imports under the compulsory license reduced to 645 baht.[32]

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[25]The 10 Burning Issues, *supra note* 10, at 13-14. Efavirenz is marketed as Atripla in the United States, patented by Bristol Meyers Squibb.

[26]See Annex 1.

[27]GPO-VIR is the first line ARVs produced by the Thai Government's Government Pharmaceuticals Organization (GPO).

[28]Describe this stuff.

[29]Physician's Desk Reference (hereinafter cited as PDR), 2011, 3470.

[30]PDR, 2011, page 3471. "Lactic acidosis and severe hepatomegly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate, a component of ATRIPLA."

[31]PDR, 2011, 3482, 3584.

[32]The 10 Burning Issues, *supra* note 10, at 147.

Due to the high price of Efavirenz in Thailand, all new cases of AIDS patients will have to be put on the more toxic Nevirapine base triple ARVs as their first line treatment. That approximately 20% will develop adverse reactions to Nevirapine is regrettable, but simply unavoidable. Only when they develop severe adverse drug reactions will they be switched to the more costly Efavirenz.

B. Kaletra (Lopinavir and Ritonavir)

Kaletra is simply combination of Lopinavir and Ritonavir. Its mechanism is, likewise, a non-nucleoside reverse transcriptase inhibitor that penetrates the viral RNA structure and interferes with the ability of the virus to reproduce. At first, these multiple medications, Efavirenz and Nevirapine and Kaletra for AIDS treatment seem redundant, but they are not. Due to the nature of the HIV virus, it has an unfortunate ability to quickly adapt to attempts to eradicate it by mutating into resistant viral strains. Thus, the virus presents a moving target, necessitating the use of newer medications. Although the Thai government has determined that Kaletra would be a viable treatment regime for those AIDS patents that have developed resistance to both Efavirenz and Nevirapine.

In this sense, then, the use of Kaletra is just as vital for the Thai healthcare system as is Efavirenz. The use of Efavirenz is critical to avoid the toxicity and attending subsequent medical issues as described above. Although Kaletra certainly has its own toxicity issues, most importantly liver damage and pancreatic issues, in regard to patients that have developed resistance to Efavirenz and Nevirapine, those issues are purely of secondary concern.

Nonetheless, the Thai government has not to date acted on implementing the Kaletra compulsory license, despite a price reduction of approximately 80%.[33] The reason is quite simple: there has been what appears to be considerable international political pushback from the patent holder, Abbott Laboratories. In particular, soon after the Kaletra license was issued, Abbott decided to withdraw seven drugs from the Thai market, including Aluvia. Aluvia is simply a re-naming of Kaletra, nothing more. Although Abbott did eventually market Aluvia in Thailand, (which accounts in part for the non-action on the Kaletra compulsory license) it resisted marketing the other six pharmaceuticals. However, it appears that part of the rationale for marketing Aluvia was for distribution in the developing countries, in particular Africa.[34] It is odd, then, that Abbott withdrew marketing Aluvia in Thailand when it seems that it was launched for the very purpose of assisting countries in Thailand's particular predicament.

2. Cardiovascular and cancer licenses

It has been stated that Thailand is suffering from a "double burden" of HIV-AIDS and other chronic diseases. The epistemological basis for this is that AIDS in and of itself does not cause the death of the patient. As is well known, AIDS so degrades the immune system that the patient is unable to fend off other opportunistic diseases. Of particular concern to this paper, is that with a compromised immune system the incidence of cancer rises, in some cases dramatically. It has been reported that with AIDS, Kaposi's sarcoma can be up to 800 times more likely, Non-Hodgkin's lymphoma some seven times more likely, with sharply elevated instances of cervical, liver and lung cancer.[35]

The successful AIDS compulsory license was based on the AIDS patient population in Thailand of approximately 500,000.[36] In terms of simple numbers, the number of cardiovascular patients is about 300,000.[37] The number of over all cancer patients is difficult to

[33]Id.

[34]In It's website dated 2008, Abbot states with pride that Aluvia is available in numerous African nations, that is Angola, Botswana, Cameron, Camoros, Central African Republic, Congo Brazzaville, Cote'd Ivoire, Djibouti, DN Congo, Ethiopia, Gabon, Guinea, Conorkey, Kenya, Lesotho, Libya, Malawi, Mauritius, Mauritania, South Africa, Togo, Uganda, and Zambia.

[35]Cancer Sourcebook, 6th ed. K. Bellenir, ed., at 96, (2011).

[36]The 10 Burning Issues, *supra* note 10 at 14.

[37]Id.

ascertain with any real degree of accuracy. However, based on statistics published by the Ministry of Health, in 2007 alone the recorded instances of new cancers was a total of about 100,000, with fatalities of about 30,000 per year.[38] When the instances of leukemia are considered, the total number of patients that are in need of the compulsory licenses to obtain access to the drugs under consideration for approval, is well in excess 400,000, approaching the 500,000 AIDS patients that justified the AIDS compulsory license. In the Thai Society of Clinical Oncology, 2007, there is the rather uncompromising statement that cancer is "No less serious than AIDS", as cancer is the number one killer disease in Thailand.[39]

Consequently, the Thai Ministry of Health has determined that dealing with HIV-AIDS alone simply cannot meet the healthcare obligations of the nation, and that the Ministry must consider issuing compulsory licenses of certain targeted anti-cancer drugs. As with the AIDS drugs, the Ministry must balance the efficacy of the drug, the necessity for that particular drug, and the cost on the open market. The following pharmaceuticals, along with a brief explanation as to how they function, and thus their importance to the Thai healthcare system, are under active consideration for compulsory licensing.

Clopidogrel bisulfate (Plavix)

Plavix, clopidogrel bisulfate, is a preferred treatment for acute coronary syndrome (ACS) that is myocardial infarctions or heart attacks. This is caused by the narrowing of the coronary arteries when structures called "platelets" adhere to the coronary artery walls. Platelets can be thought of as blood cell fragments that have the ability to stick to breaks in the blood vessel wall, and to other platelets, in order to stop bleeding. The wall of the blood vessel is coated with specialized cells called endothelium to which the platelet normally will not attach.[40] If there is break in the endothelium, however, the platelets will adhere to the underlying tissue and other platelets, forming a physical barrier (i.e. a blood clot) to stop the bleeding.

With a build up of a hard substance like plaque, formed essentially from cholesterol and fatty acids (lipids), in the coronary artery, it can form what is termed a "vulnerable atherosclerotic plaque" that can rupture. It is at this point that the natural function of the platelets attaching to the blood vessel wall occurs, and this can initiate a "thrombotic occlusion (blockage in the blood vessel)", which will in turn cause the myocardial ischemia (the sudden decrease or total lack of oxygenated blood to cardiac cells) and resulting in possible infarction. The "infarction" is when the resulting sharp decrease or stoppage of the blood supply to the heart causes the heart tissue serviced by the affected artery to die. This causes the heart to be unable to function efficiently, leading to abnormal heart rhythm, or death. When the cerebral arteries experience a thrombotic occlusion and subsequent ischemia, the blockage of the blood flow to the brain tissue can result in a debilitating stroke, or death.[41]

Clopidogrel functions to decrease the ability of the platelets to adhere to each other or to other structures on the blood vessel. Common aspirin has this same ability, although aspirin is not nearly as effective.[42] Consequently, Clopidogrel has become a favored treatment for those patients with recent myocardial infarctions, atherosclerosis, prior strokes and peripheral arterial disease.[43] The government estimates that a

[38]The 10 Burning Questions Regarding the Government Use of Patens on the Four Anti-cancer Drugs in Thailand, Ministry of health and the National Security Office, 2008.

[39]Thai Society of Clinical Oncology, 2007, page 17.

[40]The actual physiologic process of blood clotting is far more complex than this over-simplified explanation, but in essence this is correct and serves the purpose of this paper.

[41]ACS and MI are more complex than this simplification, but as in the clotting process outlined above it will suffice for this paper.

[42]Because of aspirin's ability to do so, when appropriate it is routine procedure in hospital emergency rooms to administer aspirin to patents presenting angina or any other symptoms that could indicate a myocardial infarction.

[43]Due to the side effects of Clopidogrel, namely a marked reduction in the ability to stop bleeding, it is not prescribed until evidence of incipient myocardial infarction or stroke.

compulsory license will reduce the cost by some 90%, from 70 baht to 7 baht, putting it within the reach of the national health care system. The alternative is that the patients will be compelled to take acetylsalicylic acid: aspirin.

3. Cancer pharmaceuticals licenses under consideration

A. Erlotinib (Tarceva)[44]

As non-small cell lung cancer is the leading cause of cancer related deaths in the world, and it is reported that the usual chemotherapy, radiotherapy and surgery have "reached a plateau", the importance of Erlotinib and other cancer pharmaceuticals is obvious.[45] The incidence of lung cancer in Thailand is such that over 300 new cases are diagnosed every year.[46]

Under consideration for compulsory licensure is Erlotinib, marketed by Genentec Inc. (part of the Roche Group in California) as Tarceva.[47] Erlotinib is considered a first line maintenance treatment for advanced stage non-small cell lung cancer that has not grown or spread to other organs after chemotherapy, and as a second or third line treatment when the cancer has metastasized or grown despite at least one regime of chemotherapy. It is also used to treat advanced state non-small cell pancreatic cancer that has grown or metastasized, that has not undergone any chemotherapy.

It is believed that the cancer is caused by a molecular aberration in the genetic structure of the lung or pancreas or other affected tissue, such as in the gastrointestinal tract. This abnormality apparently causes an abnormal "tyrosine kinase" receptor in the cell. One way of understanding this is to consider the tyrosine kinase as a kind of chemical mechanism that enables a cell undergoing mitosis, that is in the process of reproducing itself, to regulate and control the mitosis process. When the tyrosine kinase malfunctions due to a chemical abnormality, the cell cannot divide and reproduce itself appropriately resulting in rapid and uncontrolled growth, that is a cancer or tumor. Erlotinib is classified as a tyrosine kinase receptor inhibitor. In other words, Erlotinib functions to directly impact on the molecular abnormality, inhibiting or blocking the reproduction of the cancer cells.[48]

B. Imatinib (Gleevec)[49]

Imatinib, marketed as Gleevec by Novartis Pharmaceuticals Corporation in New Jersey, is a tyrosine kinase inhibitor as is Erlotinib. However, Imatinib is a unique pharmaceutical, in that it is specifically intended to treat Philadelphia chromosome positive chronic myeloid leukemia of the white blood cells.[50] In this cancer, there is a defect in the "Philadelphia" chromosome in the bone marrow structure, specifically in abnormal tyrosine kinase in the chromosome, giving rise to the unregulated increase of cancerous white blood cells in the blood. If allowed to progress, the increase in the abnormal white blood cells will, in effect strangle the production of red blood cells normal white blood cells and platelets. Death at that point is imminent.

Gleevec was introduced into the market in 2001. It functions by entering into the cell structure, inhibiting the reproduction of the abnormal white blood cell. This approach was quite innovative in that it was the first to deal with the underlying molecular abnormality. Prior to this treatment, the only viable alternatives were toxic chemotherapy and bone marrow transplants. The use of Gleevec has led to outstanding results, with survival rates of up to 95%.[51]

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[44]The market price of 27,000 baht would be reduced to approximately 735 baht.

[245]Schiller JH, Harrington D, Belani CP, et al. Comparison of four chemotherapy regimens for advanced non-small cell lung cancer. *N Engl J Med* 2002;36:92-98, cited in The Oncologist, July 2007 vol. 12 no. 7.

[46]Cancer Registry (2006 to 2011) National Cancer Institute, Department of Medical Services, Ministry of Public Health.

[47]As of 2011, Genentec and Roche have not participated in the Physician's Desk Reference.

[48]http://www.res-medical.com/oncology/9171.

[49]The market price of 917 baht would be reduced to 50 to 70 baht.

[50]As a tyrosine kinase inhibitor it is also effective in the treatment of gastrointestinal stromal tumors.

[51]PDR, 2549.

C. Letrozole (Femara), Novartis[52]

Letrozole is prescribed for post-menopausal breast cancer. Data suggests that for the years 2007 to 2011, there were nearly 800 new cases diagnosed.[53] Studies indicate that the incidence of breast cancer is directly tied to estrogen, the cancer being either stimulated or maintained by the presence of estrogen, most of which is produced by the ovaries. Thus, controlling the estrogen level is viewed as an effective treatment regimen.[54] Generally, estrogen levels in pre-menopausal women presenting with breast cancer can be controlled by surgery (generally the surgical removal of the ovaries or adrenal glands) or medical treatment to inhibit the effects. However, for post menopausal women with breast cancer, as the ovaries have ceased actively producing estrogen the removal of the ovaries is not indicated.

After menopause, estrogen is still produced by a chemical reaction of an "aromastase enzyme" that converts androgen produced in the adrenal glands, as well as in the cancerous tissues, into estrone (an estrogenic hormone) and estradiol (another estrogenic hormone that is significantly more potent than estrone). Letrozole targets the chemical conversion of the androgen in to estrone and estradiol, inhibiting the chemical conversion process. This treatment results in a 75% to 95% decrease in the level of estrone and estradiol, which is as effective as surgical removal of the ovaries.[55]

D. Docetaxel (Taxotere)[56]

Docetaxel is a relatively wide spectrum drug used for several cancers: advanced or metastatic breast, advanced or metastatic lung, prostate, gastric (stomach) cancer, and squamous cancers in the head and neck. In treating breast and lung cancer, Docetaxel is useful as both a first and second line therapy in conjunction with other drugs after the failure of conventional chemotherapy. There is some indication that it might be effective in treating esophageal, gastric and ovarian cancers as well.[57]

Docetaxel functions as an "antineoplastic" agent, which is a chemical compound that prevents the proliferation and spread of cancer cells. In this case, Docetaxel disrupts the microtubular network within the cancerous cell that enables the cell to function during both mitosis (dividing and reproducing state) and in interphase, when the cell is simply quiescent. Within the cell are protein compounds in filament or string-like forms that are called "tubulins" that function to organize the formation of the dividing cell during mitosis, and as such are vital to the cell division and reproducing process. Docetaxel chemically bonds to the free tubulins during the mitosis stage when tubulin "strings" are disassembled, so as to speak, thus rendering it incapable of reconstituting itself in a new cell. In this manner, the spread of the cancer is halted, at least until the patient develops resistance to the drug.

V. Implementation of the Efavirenz license

As we noted above, the only compulsory license that the government has fully implemented is that for second line HIV treatment, Efavirenz. Specifically, on January 5th, 2007, the Government Pharmaceutical Organization (GPO), which is authorized by the Department of Disease Control (by virtue of the Notification dated November 29, 2006) to exercise the implementation of the license, entered into a contract with an Indian drug manufacturing firm, Ranbaxy, to import 66,000 bottles of Efavirenz.[58] The terms of the compulsory license were in fact quite restrictive and

[52]The market price of 230 baht would be reduced to 6 to 7 baht.

[53]Cancer Registry, *supra* note 45.

[54]Oddly, estrogen in and of itself is thought to be carcinogenic, due to the effect of estrogen metabolites, and other factors. www.ncbi.nlm.gov/pmc/articles/PMC2001216.

[55]Http://rxlist.com/femara-drug/clinical-pharmacology.htm.

[56]The market price of 25,000 baht would be reduced to 4,000 baht.

[57]PDR, 3051,; http://drugs.com/ppa/docetal.html.

[58]The 10 Burning Issues, *Supr*a note 10, at 8.

designed to accomplish only the mission of making Efavirenz accessible through the state sponsored healthcare system, and no more.

The Efavirenz license, despite its importance for AIDS patients, is strictly subject to the following conditions.[59]

(1) the right shall be exercised from now on through until December 31st, B.E. 2554 (2011);

(2) the exercise of the right is limited to an annual provision of the drug having the aforesaid generic name to no more than 200,000 patients who are entitled persons under the National Health Security System Act, B.E. 2545 (2002), insured National Health Security System Act, B.E. 2533 (1990), and persons entitled to medical benefits for civil servants and government employees scheme;

(3) a royal fee of 0.5 per cent of the total sale value of drug having the aforesaid generic name by the Government Pharmaceutical Organization shall be paid to the patent holder.

The practical impact of the Efavirenz license can be readily seen. The first batch of the generic Efavirenz drugs arrived in Thailand in January 2007. This Indian-manufactured Efavirenz has reduced the price by more than half, from around 1,400 Baht (about US$39) to 650 Baht (about US$18). This enabled the Ministry of Public Health to provide Efavirenz to an additional 20,000 AIDS patients at the same cost.[60] If price competition between the branded drug and generic drug is allowed to continue under the Thai Governments Use of Patent, it is expected that the price may go down further. If the price goes down to 20 percent of the original price, then the Ministry of Public Health will be able to support up to 100,000 patients with the same budget. This will allow all new patients to be treated with Efavirenz based triple ARVs in the next five years.[61] If the compulsory licensing for the second-line HIV/AIDS drug, Lopinvir and Ritonavir, is enforced in the future, the drug price will go down about 80%.[62] In the case of Clopidogrel, the patented drug for cardiovascular disease, the price will reduce dramatically and accessibility will increase 6 to 12 times.[63]

According to technology expert James Love, if one looks at the effect of compulsory licenses from an economic perspective, Thailand is seeking to create a policy that will strengthen competition among generic suppliers and enhance its own capacity to manufacture AIDS medicines.[64] The benefits of this policy will be more pronounced over time, as competition, economies of scale, and learning by doing lead to more efficient production by generic producers.[65] This policy is extremely critical to Thailand because of its domestic economic situation. Assuming that the ability to pay is linear in terms of income, a second line AIDS drug that is sold for $1,000 in Thailand would be equivalent to a product selling for $70,000 in the United States.[66] With inexorably increasing health care costs worldwide, in large part driven by the cost of patented pharmaceuticals, the adverse long term economic impact is even worse for lower income countries than the developed nations.[67] We would note that even the economies of the developed nations are being severely stressed by these ever mounting healthcare costs.

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[59]Notification of the Department of Disease Control, Ministry of Public Health, Re: Exercising of Right under Drugs and Pharmaceuticals Products Patent, dated the 29th of November, B.E. 2549 (2006) (in Thai), at 2.

[60]Id.

[61]Incidents of Liver Injury After Beginning Antiretroviral Therapy with Efavirenz and Nevirapine, Luz Martín-Carbonero[1], Marina Núñez[1], Juan González-Lahoz[1], Vincent Soriano[1], HIV Clinical Trials, Volume 4, Number 2/March-April 2003.

[62]The 10 Burning Issues, *supra* note 10, at 147.

[63]Notification dated January 25, 2007, at 2.

[64]Loves, James, Director. Consumer Project on Technology, in his letter to Ambassador Susan C. Schwab, United States Trade Representative, dated December, 2006 reprinted in the 10 Burning Issues, *supra* note 10, at annex 30, at 70.

[65]Id.

[66]Id.

[67]Id.

It is also important to consider one of the economic justifications argued by the Thai Government for issuing the compulsory licenses is that the total sale of the patented drugs will remain the same or even increase. The drugs produced under the license will be distributed only to those patients who are covered by the several national healthcare plans only. Those who are well off and can afford to pay out of their pocket, including around two million foreign patients, will have to pay the market price of patented products.[68] These well-off people, and the foreign patients, are currently the only market for the patented products. Without the compulsory license, the majority of Thais whose medicine costs are paid by the Government would not be in the market. Thus, the patent holder derives no benefit whatever from this vastly larger market that will result form the compulsory license.[69] The Governments Use of Patents has opened this new market for those who cannot afford these patented drugs.[70]

VI. Public policy choices for the Thai Government to bring down the prices of patented drugs

The National Health Security Act of 2002 requires the Ministry of Public Health and the National Health Security Office to provide universal access to essential medicine for all Thais. Accordingly, the 62 million Thais who are covered by one of the three above-mentioned national public health insurance schemes (The Civil Servant Medical Benefit Scheme, The Social Security Scheme, or the Universal Coverage Scheme) are entitled by law to full access to the medicines on the essential drug list. This list is comprised of some 900 drugs, many of them patented.[71] The Government has responded to this national entitlement in a number ways. One response was to raise the public health budget. The public health budget has increased from around 4 percent of the overall budget in the 1980s to 7 percent in the 1990s to more than 10 percent at present.[72] The budget for ARVs increased from around US$10 million in 2001 to more than US$100 million in 2007, representing a tenfold increase in only six years.

This level of spending of national public resources for access to ARVs is the highest among the lower middle income developing countries.[73] To date, the Ministry of Public Health and the National Health Security Office have not been able to fully achieve the goal of ensuring the right of access to all the medicines on the essential drugs list due to the high drug prices and a limited budget. Given the reality that to increase to the level that would enable the state to have access to patented drugs at the market level is simply impossible without beggaring the national fisc, the Thai Government has three public policy choices to choose from in order to bring down the drugs prices.

1. Applicable international and domestic law

In the case of Thailand, several domestic statutes and international treaties are potentially available. First is Thailand's Trade Competition Act (1999), dealing with the possibility of using the general provisions of anti-trust law. Second, is Thailand's Act Relating to Prices of Merchandise and Services (1999) which make authorizes the government to address prices under certain closely defined circumstances. As for international treaties, the primary authority is the Agreement on Trade Related Aspects of Intellectual Property Rights, better known as TRIPS, and in conjunction with TRIPS the 2001 Doha Declaration.

As will see, using TRIPS and Doha are the only realistic way in which the government can fulfill it's obligation to it's citizens, and yet comply with it's international obligations. This is so for the following reasons. First, the pharmaceutical manufacturers are "international citizens" in that not only are they domiciled

[68]The 10 Burning Issues (English version), *supra* note 10, at 6.
[69]Id.
[70]Id., at 7.
[71]Id., at 2.
[72]Id.
[73]Id.

generally in the United States and Europe, but they are in the international market. Consequently, the nations in which they are domiciled have a legitimate interest in the companies. Second, compliance with TRIPS in issuing compulsory licenses is directly linked to domestic law, thus Thailand, and all other signatories to TRIPS, must have appropriate domestic law. In other words, there must be a convergence of the TRIPS provisions and domestic law in order for any signatory to issue a legally effective license. Consequently, we must address the Thai domestic law that can serve in that function.

A. The Trade Competition Act of 1999, Section 25 (1)

Thailand adopted the present Trade Competition Act of B.E. 2542 in 1999, which deals with the unreasonable restraint of trade.[74] Section 25 (1) of this statute provides that the Thai Competition Committee may act and deal with products that are set at an "unreasonable selling price" by a dominant player in the market.[75] As this law has been in effect only a short time, Thailand simply does not have much experience in enforcing antitrust law. To date, Thailand has not taken any official action under this statute although this is expressly provided for by the TRIPS Agreement.[76] In addition, there is the legal question of whether the enforcement agency under the statute, the Thai Trade Competition Committee, has any authority to apply the provisions of the Trade Competition Act to the exercise of patents by multinational pharmaceutical companies.

Assuming, *arguendo,* the Thai Competition Committee does have authority to regulate the exercise of patents by multinational pharmaceutical companies, there are two formidable obstacles. First, simply pricing the patented drugs at a level that happens to be out of reach of patients, is not a violation of antitrust law. Second, assuming the retail price of a patented drug is too high, that alone is not a violation of antitrust law unless there is resale price maintenance by the patent owner. Where the patent owner dictates the retail price after it already sold its patented drug to the wholesaler or distributor. The enforcement agency would have to establish that there were agreements fixing the retail price between the patent owner and drug retailers before any action could be taken. That task is very difficult for even experienced enforcement agencies.

A well-known case in India demonstrates how the "unreasonable selling price" approach may work to reduce drug prices.

In ***Re: Hazel Tau et al. v. Glaxo Smith Kline and Boehringer Ingelheim.*** The South African AIDS Law Project lodged a complaint in September 2002 with the South African Competition Commission against Glaxo Smith Kline (GSK) and Boehringer Ingelheim (BI) on behalf of four people living with HIV/AIDS, four health care workers, the Treatment Action Campaign (TAC), and two trade unions. The complaint alleged that the two multinational pharmaceutical companies, holding patents on important ARVs medicines in South Africa, were charging excessive prices to the detriment of consumers in violation of Section 8(a) of the Competition Act.[77] On October 16th, 2003, the South African Competition Commission announced that it found three

[74]This approach is expressly approved in TRIPS Article 8.2, "Appropriate measures, provided that they are consistent with the provisions of this Agreement, may be needed to prevent *the abuse of intellectual property rights* by right holders or the resort to *practices which unreasonably restrain trade* or adversely affect the international transfer of technology." (Emphasis added)

[75]Section 25 of the Thai Competition Act reads:

"A business operator having market domination shall not act in any of the following manners:

(1) unreasonably fixing or maintaining purchasing or selling prices of goods or fees for services."

[76]TRIPS Article 31 (k) provides, "Members are not obliged to apply the conditions set forth in subparagraphs (b) and (f) where such use is permitted to remedy a practice determined after judicial or administrative process to be anti-competitive. The need to correct anti-competitive practices may be taken into account in determining the amount of remuneration in such cases. Competent authorities shall have the authority to refuse termination of authorization if and when the conditions which led to such authorization are likely to recur."

[77]Section 8(a) of the Competition Act (RCA) prohibits dominant firms from charging

"an excessive price to the detriment of consumers". An excessive price is defined as "a price for a good or service which–(aa) bears no reasonable relation to the economic value of that good or service; and (bb) is higher than the value referred to in subparagraph (aa0)."

violations of the Act. In addition to violating of the excessive pricing prohibition, the Commission found the companies violated Section 8(b) of South Africa's Competition Act. The case settled on December 10, 2003, without being referred to the Competition Tribunal.

The Indian experience, however, may not be easily replicated in Thailand. Although Section 18(5) of the Competition Act allows anyone to lodge a complaint alleging a violation of Section 25 (1) with the Office of the Thai Competition Committee no AIDS or any other activist organization has done so. As a matter or record, about three months after the three notifications of compulsory licensing were issued, Abbott Laboratories withdrew its applications for one HIV/AIDS drug and seven chronic diseases drugs for marketing approval from the Thai Food and Drug Administration. Abbott Laboratories withdrawing the applications was interpreted by AIDS activist organizations and consumer protection activists in Thailand as retaliation against the Thai Government's issuance of compulsory licensing for Plavix.

In response, on April 26, 2007, three AIDS activist organizations and one consumer protection organization lodged a complaint with the Office of the Thai Competition Committee against Abbott Laboratories. The complaint alleged that Abbott Laboratories by withholding the applications for approval of those drugs by the Thai Food and Drug Administration, Abbott violated Section 25(3) of the Thai Competition Act that prohibit a dominant firm from suspending, reducing distribution or importation without justifiable reasons. The conduct of Abbott Laboratories was seen as an illegal protest against the Thai Government action by withdrawing its pending-for-market-approval drugs from the Thai market and suspending importation of those drugs into the Thai market. On December 27, 2007, the Thai Trade Competition Committee held that Abbott Laboratories did not have a market dominant position in the market for those drugs, on the reasoning that those drugs were not in the Thai market.[78]

Because of the substantive provisions of the Thai Trade Competition Act, and limited enforcement experience of the Thai Trade Competition Committee, it would be rather difficult for Thailand to bring down the prices of patented drugs by relying upon the use of competition or antitrust law. Moreover, even if competition or antitrust law was applied, the results may fall short of goal of assuring reasonable access to the dugs.

B. Price control laws to bring down prices

The other public policy choice available is to use price control law to bring down the price of patented drugs. The Thai Government has used a number of price-control laws to maintain prices of essential commodities for many decades. Under the present 1999 *"Act Relating to Price of Merchandise and Service,"* a Government committee headed by the Minister of Commerce has the authority to "Prescribe the purchase price or distribution price of merchandise or service...", "prescribe maximum profit per unit..." and set the terms and conditions-including maximum permissible volumes-of any goods and service in the kingdom.[79]

The Thai Government retains authority to set de facto price ceilings for 33 goods and two services, including, staple agricultural products, liquefied petroleum gas, and medicines, among other sundry items.[80] Price control review mechanisms are, however, non-transparent and thus open to criticism, which poses significant problems as to the fairness of the process and determination of the prices.[81] Moreover, at times price control determinations are sometimes based on outdated assumptions and may, in spite of repeated petitions made for review by affected parties, drag out for long periods without any review or oversight.[82]

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[78]Prachathai Newspaper, dated the 7th of January, 2008 reprinted in http://www.ftawatch.org/news/vies.php?id=12621(visted on January 9th, 2008.)

[79]Office of the United States Trade Representative, 2007 *National Trade Estimate Report on Foreign Trade Barriers, April 2007,* at 588.

[80]Id., at 587.

[81]Id., at 588.

[82]Id.

The Canadian approach to using price controls gives us some idea as to how this process might function. Canada represents an OECD country which is regarded by many as an example of a country that has succeeded in controlling prices of prescription drugs. In Canada, the mechanism employed to reduce prescription-drug spending consists of the federal quasi-judicial Patented Medicine Price Review Board (PMPRB) charged with controlling factory-gate prices.[83] The PMPRB, established in 1987, does not set drug prices, but determines whether they are "excessive."[84] For existing patented drugs, the Board restricts price increases to less than the price in the consumer price index (CPI).[85] The prices of most new (though not "breakthrough") patented drugs are limited to the range of prices of existing drugs in the same therapeutic class.[86] The price of a breakthrough drug must not exceed the median of its prices in seven designated countries, namely France, Germany, Italy, Sweden, Switzerland, the United Kingdom, and the United States.[87]

In Thailand and other developing nations, price-control laws will not bring down the price of patented drugs for at least two reasons. First, most developing nations, including Thailand, do not have independent committees similar to the Canadian PMPRB, which are indispensable for effective and rational enforcement of the aforementioned Act. Second, members of the independent committee must be qualified experts in the domestic and international pharmaceutical industry in order to identify "excessive" price in a fair and equitable manner. For example, to a certain extent research and development costs must be reasonably quantified by the independent committee, as it is believed that drug companies spend a lot more on administration, advertising, marketing, and on research and development than on the chemical composition of the pharmaceutical itself.[88] This is quite unlike sugar, for example, were there is almost no research and development involved at all. Without any proper means and mechanisms to determine if the market price of the drug is "excessive", the final determination of the price would be arbitrary. It would be absurd, of course, if both a breakthrough patented drug and sugar were to be put under the review of the same general price-control committee.

C. The use of the TRIPS and Doha to bring down the prices

1. TRIPS Provisions

Complementing the language in the Paris Convention, the TRIPS Agreement never mentions the phrase "compulsory license" within the text.[89] Yet, Article 31 describes an allowable exception to patent enforcement in language implying compulsory licensing.[90] Article 31 of the TRIPS Agreement states the following:

Other Use Without Authorization of the Right Holder

Where the law of a Member allows for other use of the subject matter of a patent without the authorization of the right holder, including use by the government or third parties authorized by the government, the following provisions shall be respected:

(a) Authorization of such use shall be considered on its individual merits;

(b) Such use may only be permitted if prior to such use, the proposed user has made efforts to obtain authorization from the right holder on reasonable commercial terms and conditions and that such efforts have not been successful within a reasonable period of time. This requirement may be waived by a Member in the case of national emergency or other circumstances

[83]Stegemann, Klaus and Bohumir Pazderka, "The TRIPS Agreements as an Alliance for Knowledge Production: The Funding of Pharmaceutical Innovation", *The Journal of World Intellectual Property,* Vol. 6 No. 4, July 2003, at 550.

[84]Id.

[85]Id.

[86]Id.

[87]Id.

[88]Usdin, *supra* note 4, at 55.

[89]Ford, *supra* note 16 at 958.

[90]Id.

of extreme urgency or in cases of public non-commercial use. In situations of national emergency or other circumstances of extreme urgency, the right holder shall, nevertheless, be notified as soon as reasonably practicable. In the case of public non-commercial use, where the government or contractor, without making a patent search, knows or has demonstrable grounds to know that a valid patent is or will be used by or for the government, the right holder shall be informed promptly. (Emphasis added.)

Thus, Article 31 sets forth a series of conditions WTO Members must respect prior to implementing compulsory licenses. In the introductory note (Chapeau) of Article 31, there is an important requirement prior to issuing a compulsory licensing: the national law of that WTO Member must provide for compulsory licensing. Thailand asserts that Section 51 (Government Use of Patent) of the Thai Patent Act of 1979 fulfills this critical requirement.[91]

2. The Doha Declaration

Under closer examination, those conditions concerning compulsory licensing left a number of important questions unanswered-particularly for developing countries. In response to the concerns of developing countries over the TRIPS Agreement's impact on public health, the WTO began the Doha Fourth Ministerial Conference on November 9th, 2001, in which the WTO aimed to clarify the TRIPS Agreement's flexibility regarding public health. The debate proved predictably contentious, as government and industry representatives from developed countries argued that the TRIPS Agreement already provided developing countries with sufficient public health flexibility.[92] Developing countries contended that the aggressive protection of pharmaceutical patents in the face of serious public health crises demonstrated the inadequacy of the TRIPS Agreement's public health assurances.[93] Separate drafts reflecting the divergent interests of developing and developed countries were circulated before the ratification of the final declaration.[94]

The final Doha Declaration on the TRIPS Agreement and Public Health was ratified on November 14th, 2001 and represented a carefully negotiated compromise between protecting intellectual property rights and public health. Developing countries achieved several of their primary objectives in clarifying the TRIPS Agreement flexibilities for public health in the Doha Declaration.[95] The overall objective achieved by developing countries, as one prominent commentator pointed out is that the Doha Declaration is implicitly a human rights instrument, as well as a trade instrument.[96] The Doha Declaration was adopted in part to clarify that the right to health plays an essential role in interpretation of the TRIPS Agreement. This is reflected in paragraph 4 of the Doha Declaration.[97] Other concrete objectives achieved by developing countries are as follows.

First, it is important to note the express language of the pertinent part of the Doha Declaration, paragraph 5 (c):

Each member has the right to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health

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[91]The 10 Burning Issues, *supra* note 10, at 3.

[92]Id.

[93]Id.

[94]Id.

[95]Id.

[96]M. Abott, Frederick. "The 'Rule of Reason' and the Right to Health: Integrating Human Rights and Competition Principles in the Context of TRIPS", in Thomas Cotttier and Joost Pauwelyn (eds.), HUMAN RIGHTS AND INTERNTIONAL TRADE, 2005, at 283.

[97]Paragraph 4 of the Doha Declaration states:

"We agree that the TRIPS Agreement does not and should not prevent members from taking measures to protect public health. Accordingly, while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all."

crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency.

This apparently open-ended ability for countries to declare national public health emergencies stood as a major victory for developing countries.[98] Second, developing countries also succeeded in securing the WTO's recognition that members with limited or no pharmaceutical manufacturing capacity could face difficulties in making effective use of compulsory licensing.[99] The Doha Declaration instructed the Council for TRIPS to find a solution to this problem before the end of 2002.

Finally, the Doha Declaration emphasized that the TRIPS Agreement recognized the right of each member to establish its own regime for the exhaustion of intellectual property rights.[100] Therefore, a developing country can adopt a system of national exhaustion which gives patent holders absolute control the distribution of their product on an international scale.[101] A developing country can benefit from adopting this system if a multinational pharmaceutical company charges different prices for the same patented drug in different markets. Under this system, in which parallel imports are prohibited, "both the firms and the consumers in the poor country would be better off, and consumers in the rich country would not be worse off." If the firm charges the same price for the same patented drug, then the poor country will be worse off.[102] Thus, it will depend on the pricing policy of multinational pharmaceutical firms. On the other hand, a developing country can adopt a system of international exhaustion which allows parallel imports.[103] This system is based upon the economic theory of comparative advantage which promotes free trade because specialization and free trade will benefit all trading partners.[104]

While the Doha Declaration was a significant victory for developing countries and health advocacy NGOs, the core intellectual property protections enshrined in the TRIPS Agreement remained intact. The Doha Declaration did not materially alter any of the text of the TRIPS Agreement and only offered a way to balance existing protection for intellectual property rights within an interpretative framework more amenable to public health.[105] For years, compulsory licensing's only practical use appeared to be as a negotiation tool.[106] Only after the Doha Declaration in 2002, almost ten years after the signing of TRIPS, did the first large-scale use of compulsory licensing to address a public health concerns occur among numerous developing countries.

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[98]Savoie, *supra* note 9, at 235.

[99]Paragraph 6 states:

"We recognize that WTO members with insufficient or no manufacturing capacities in the pharmaceutical sector could face difficulties in making effective use of compulsory licensing under the TRIPS Agreement. We instruct the Council for TRIPS to find an expeditious solution to this problem and to report to the General Council before the end of 2002"

[100]Paragraph 5 (d) states:

"The effect of the provisions in the TRIPS Agreement that are relevant to the exhaustion of intellectual property rights is to leave each member free to establish its own regime for such exhaustion without challenge, subject to the MFN and national treatment provision of Article 3 and 4".

[101]B. Conley, Christopher. Comment, "Parallel Imports: The Tired Debate of the Exhaustion of Intellectual Property Rights and Why the WTO should Harmonize the haphazard Laws of the International Community", *16 Tul. J Int'l & Comp. L.* 189, Winter 2007, at 5.

[102]Id., at 6.

[103]Id., at 7. Essentially, once drugs produced by the patent holder or under a legally effective license (including a compulsory license) the patent holder has no right to control any subsequent resale or distribution of the drugs.

[104]Id.

[105]Savoie, *supra* note 9, at 236.

[106]Id., at 238.

VII. Are the proposed compulsory licenses for chronic disease drugs consistent with TRIPS?

As discussed above, after the Doha Declaration in 2002, many developing countries successfully used compulsory licensing to address their public health concerns over infectious diseases, primarily, HIV/AIDS. However, special challenges exist in the authorization of compulsory licenses for medications targeting chronic diseases. The international political will that has supported prior attempts to authorize compulsory licensing is closely tied to larger advocacy efforts related to ensuring access to medications for infectious diseases. Given the lack of international public attention to chronic diseases, developing countries may also face significant challenge in mobilizing public support for issuing compulsory licenses for chronic diseases.

The pressure placed on developing countries to refrain from authorizing licenses for chronic diseases medications is also likely to exceed the actions exerted in the context of compulsory licensing for HIV/AIDS. Medications for chronic diseases play a much larger role in pharmaceutical portfolios than medications for infectious diseases, such as, HIV/AIDS.[107] The expansion of the TRIPS Agreement compulsory licensing provisions to include chronic diseases thus poses a serious threat to pharmaceutical companies that is not likely to be ignored.[108] Pharmaceutical companies also have a more advantageous public relations position than they did when opposing compulsory licensing for HIV/AIDS medication.[109] Not only can many chronic diseases be addressed through non-pharmaceutical interventions, but most can be treated using off-patent pharmaceutical therapy. While newer, patented pharmaceutical interventions for chronic diseases may offer significant improvement in patient outcomes, opponents of compulsory licensing for chronic diseases medications can argue that access to these medications is not necessary.[110]

In addition to the political challenges as mentioned above, there are the legal challenges, the most important of which is whether chronic drugs are included in the Doha Declaration. The Doha Declaration, which is the authoritative guide to interpret the TRIPS Agreement's compulsory licensing as they apply to public health, is at first blush couched in the language of contagious disease.[111] While the Doha Declaration recognizes the gravity of public health problems afflicting many developing and least-developed countries, it mentions particular diseases of concern, such as HIV/AIDS, malaria, tuberculosis, and other epidemics.[112] Although it could be argued that Doha is limited to infectious diseases, thus excluding chronic diseases, this is not as a matter of law tenable.[113]

Under the most fundamental rules of statutory construction, the mention of certain specific diseases in the text is clearly illustrative only. Section 5 (c) in pertinent part states "... including those ... and other ...". is on its face determinative. There is no hint that the list is exclusive, nor any implication that the Declaration applies to only a certain type of class of disease. Professor Corlos Correa, a prominent scholar who has closely observed the whole negotiation process of the Doha Declaration and the Decision of the General Council of August 30, 2003, concurs. He wrote that the Doha Declaration requested the Council for TRIPS "to find an expeditious solution to this problem and to report to the General Council before the end of 2002."[114]

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[107]Savoie, *supra* note 9, at 241.

[108]Id.

[109]Id.

[110]Roger Bate, "Thai-ing Pharma Down", *Wall St. J ASIA,* Feb. 9 2007 available at <http://aei.org/publications/filter.economic,pubID585/pub_detail.asp>

[111]Savoie, *supra* note 9 at 239.

[112]See paragraph 5 (c) of the Doha Declaration.

[113]Savoie, *supra* note 10, at 239.

[114]M. Correa, Carlos, "TRIPS Agreement and Access to Drugs in Developing Countries", *SUR-International Journal on Human Rights,* Number 3, Year 2, 2005 at 28.

An Agreement was reached on August 30, 2003, only after a diplomatic battle, when the United States finally accepted a text covering all diseases as mandated by the text of the Declaration.[115] At the behest of the pharmaceutical companies, the initial position of the United States was aimed at limiting the possible solution to HIV/AIDS, malaria, and tuberculosis.[116] The U.S. Government argued that solution is based on a compromise developed by the Chair of the TRIPS Council and on a "Statement by the Chair" proposed by the United States, as a condition to accept the deal and, incidentally, to satisfy the American Pharmaceutical industry.[117] Thai scholar Jakkrit Kwonpot argues, correctly we believe, that there is nothing in the Doha Declaration that limits the kind of diseases for which a WTO Member can authorize a Compulsory License.[118]

VIII. TRIPS and the future public health crisis: Thailand and the world's test

Thailand is the first country to expand the scope of compulsory licensing beyond HIV/AIDS to include medications for chronic diseases. To date, most developing countries have not felt the full burden of their chronic diseases epidemics and may not judge the benefits of authorizing compulsory licenses for chronic diseases medications as out weighing the substantial risk of political and economic isolation by developed countries and the pharmaceutical industry.[119] Ensuring continued access to new medication for chronic diseases in the developing world should be a priority for all countries, including the World's wealthier countries.[120] In the long run, chronic diseases threaten to pose an even greater economic threat to developing countries than HIV/AIDS and may generate even more hostility towards the intellectual property system.

This trend cannot help but destabilize the economic systems of the developing nations, contributing to regional if not global economic instability. Consequently, this issue should be just as much a priority for developed economies, as well. Industry and government officials should be mindful of the powerful and growing economic rationales that will guide the decisions of developing countries to pursue TRIPS flexibilities. The WHO estimates that 80 per cent of the 35 million annual deaths due to non-communicable diseases in 2005 occurred in low-and middle-income countries.[121] In addition, the WHO estimates that China alone will lose over US$55 billion annually due to chronic diseases.[122] At the very least, industry and government officials should expect developing countries to act as economically rational actors and should take proactive steps to prevent the cost of adhering to TRIPS from outweighing the benefits of WTO membership. If patents stand as a barrier to substantial reductions in the direct and indirect costs of chronic disease drugs, developing countries are likely to start using compulsory licensing more aggressively.[123] If TRIPS and the Doha Declaration are interpreted in a way that excludes the compulsory licensing of new medications for chronic diseases, especially "blockbuster" medications, they may be begin to question the fundamental negotiation strategy of the WTO-the Single Undertaking.[124]

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[115]Id.

[116]Id., at footnote 8.

[117]Id., at 28. According to Opensecrets.org, as a group the pharmaceutical lobby may have spent upwards of $125,000,000.00 in lobbying efforts.

[118]Kwonpot, Jakkrit. "Compulsory Licensing and Access to Medicines Legal and International Law consideration", at 29 available at http://www.ftawatch.orgat CL Information (in Thai).

[119]Savoie, *supra* note 9, at 246.

[120]Id., at 247.

[121]Usdin, *supra* note 4, at 110.

[122]Savoie, *supra* note 9, at 247.

[123]Id.

[124]Id.

While Thailand's compulsory license for Plavix, a cardiovascular heart disease medication, is the first attempt to use compulsory licensing to address the growing burden of chronic diseases, it is unlikely to be the last. Indeed, Thailand's Minister of Health Monkol Na Songkla recently indicated that he is considering issuing compulsory licenses for cancer drugs as outlined above.[125] The use of compulsory licensing by developing countries to address the growing economic burden of chronic diseases will test the ability of TRIPS, the pharmaceutical industry, and the international community as a whole to adapt to the rapid epidemiological transition occurring in developing countries.

Annex

Notification of the Department of Diseases Control Certified Translation

Notification of the Department of Diseases Control, Ministry of Public Health.

Re: Exercising the Right under the Drugs and Pharmaceuticals Products Patent.

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By virtue of section 51 of the Patent Act, B.E. 2522 (1979), as amended by the Patent Act (No. 2), B.E. 2535 (1992), and the Patent Act (No. 3), B.E. 2542 (1999), the Ministry, Sub-Ministry, and the Department are empowered to exercise the right under any patent without authorization of the patent holder. The objective of this provision is explicitly expressed that all service providers with non-commercial purpose, particularly the service providers of the State which provide such public service as public health, may lawfully exercise such right.

It is generally accepted that the HIV (AIDS) epidemic is one of the most grievous public health problems. Approximately, more than one million Thai people have been afflicted with HIV. More than five hundred thousand of those afflicted are still alive and will eventually need long term use of HIV antiretroviral drugs to maintain productive lives. The budget allocated for health services for the people who have been infected with HIV, as well as AIDS patients, under the national health security system for the fiscal year B.E. 2549 (2006) is limited to 2,796.2 million Baht for the target group of 82,000 patients.

Even now there are many effective HIV antiretroviral drugs which are capable of extending the life span of HIV infected persons. The Royal Thai Government has launched, since 1st October B.E. 2546 (2003), a policy to promote access to HIV antiretroviral drugs for all HIV infected persons and has also allocated a budget for this purpose. However, accessibility to some kinds of HIV antiretroviral drugs, which are both effective and have a low level of side-effects, is difficult to achieve for most HIV infected persons. This is due to fact that all of those HIV antiretroviral drugs are under patent protection in accordance with the law on patent which enable the patent holders to dominate the market without any competition. The price of those HIV antiretroviral drugs are, as a result, very high and are therefore a hindrance to the State to acquire the drugs for distribution to all HIV infected person.

Efavirenz has already been proved so far to be one of the most effective and safe HIV antiretroviral drugs with very low side-effects. It has also been placed in the National System for Secured Accessibility to HIV Antiretroviral Drugs. This HIV antiretroviral drug, however, is subjected to patent protection which deters the Government Pharmaceutical Organization or other manufacturers from manufacturing and importing this specific drug for sale in the market. The price of Efavirenz in Thailand is twice the price of a generic drug in India. The budget allocated by the government is therefore sufficient to provide only some patients with Efavirenz, while the rest have to use non-patie drugs with a higher

[125]The Information and Public Relations office, Ministry of Public Health, Minister of Public Health will not give up on using compulsory Licenses of 4 cancer drugs (in Thai), available at http://www.moph.go.th/ops/iprg/iprg-new/include/admin_hotnew/show_hotnew.php?idHot (visited on February 8, 2008).

level of side-effects than Efavirenz because of their lower prices.

According to the Doha Declaration on TRIPS Agreement and Public Health, each member country has the right to protect public health, in particular, to promote access to medicines for all in case of emergency and for public benefit, especially accessibility to those relating to HIV/AIDS, tuberculosis, malaria, and other epidemics. In this regard, the Thai law on patent empowers the Ministry, Sub-Ministry, and the Department to exercise the right under any patent without prior authorization of the patent holders so as to provide public service as mentioned above.

Therefore, the Department of Disease Control, the Ministry of Public Health, hereby notifies, by virtue of section 51 of the Patent Act B.E. 2522 (1979), as amended by the Patent Act (No. 2), B.E. 2535 (1992), and the Patent Act (No. 3), B.E. 2542 (1999), that it is now exercising the right under drug patent of the drug under trade name "Stocrin®" (generic name: Efavirenz). In this regard, the Department of Disease Control entrusts the Government Pharmaceutical Organization to exercise the right in its name in accordance with section 36 paragraph one of the Patent Act B.E. 2522 (1979), as amended by the Patent Act (No. 2), B.E. 2535 (1992), and the Patent Act (No. 3), B.E. 2542 (1999) subject to the following conditions:

(1) the right shall be exercised from now on through to 31st December B.E. 2554 (2011);

(2) the exercise of the right is limited to an annual provision of the drug, having the aforesaid generic name, to no more than 200,000 patients who are entitled persons under the National Health Security System Act, B.E. 2545 (2002), insured persons under the Social Security Act, B.E. 2533 (1990), and persons entitled to medical benefits for civil servants and government employees scheme;

(3) a royalty fee of 0.5 per cent of the total sale value of the drug having the aforesaid generic name, by the Government Pharmaceutical Organization shall be paid to the patent holder.

The Department of Disease Control, Ministry of Public Health, shall notify the patent holder and the Department of Intellectual Property for information without delay.

It is hereby announced:

Given on the 29th Day of November B.E. 2549 (2006).

(Signed) Thawat Suntrajarn
(Mr. Thawat Suntrajarn)
Director-General
Department of Disease Control

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