IP in Pharmaceutical Industry related to TRIPS agreement and compulsory licence in the developing countries

Professor: Chen, Xiangdong

By: Paweena Kongsansatean & Abhishek Jain

Portland State
UNIVERSITY

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1. Abstract

The paper describes the effect of TRIPS agreement on the less developed nations, and the steps taken by those governments to protect the health care industry from high cost charged by the global companies. It studies the case of India and Thailand; steps taken by these nations and implications of those steps. Different legal cases and compulsory licensing grants given by these nations and the reasons behind them have been analyzed and described in the paper. It gives a glimpse of the health care system in the developing nations.

Keywords : *TRIPS Agreement, Evergreening Patent, Compulsory Licence, Developing Countries, Human Rights*

2. Introduction

The controversy of Intellectual Property (IP) protection of the pharmaceutical industry in developing countries has considerable debated between the pharmaceuticals industry and the human right organization perspective. The pharmaceutical Industry spent large amounts of money on R&D activities as well as protracted times. Before new drug approval process by Food and Drug Administration (FDA), it must be approved through preclinical trial stage with 3 phases: safety test in patients, efficacy as a treatment, and relative performance with existing treatment. The duration of drug discovery to market commercialization is 10 to 15 years and the research and development cost is extremely high approximately $430 million per a successful drug. Since the first discovery stage to the commercial stage, total budget is over than $800 million. Only one of 250 drugs in preclinical testing ever reached FDA approval, and only 30% of approved drugs reached a break event point in their R&D cost. Due to the excessive effort in research and development, the pharmaceutical companies in developed countries attempted to protect their rights from this other companies in other countries.

The Agreement of Trade-Related Aspects of Intellectual Property Rights (TRIPS) is an international agreement among members of World Trade Organization (WTO). All of WTO members must act under the agreement. A patent for pharmaceuticals is one part of the agreement, normally patent granted for 20 years from the date of filing. Due to the long period of developing drug, it can be inferred that exactly protection period remains only 5 to 7 years. Losing right protection brings about free market competition which any players are able to produce expired patents drugs in competitive price, then it comes to the red ocean market which is a nightmare for industry.

In developing countries, the critical problem to slow down development is health issue. Drugs from developed countries have powerful effects to medicate but the price of drugs are expensive, and a patent ownership company has utmost right to produce drug exclusively and tend to be a monopoly market. Therefore, people in developing countries have low ability to access drugs, which brings up to a human right perspective. In a human rights perspective insists that human rights should be over commercial benefits, and some granted patent drugs are lack of novelty but they are only changed molecular. Many organizations in developing countries such as Non-Government Organization (NGO) and patient networks has attempted to diminish the regulation for long period by protesting, urging a government to impose exemptions against TRIPS particularly in India and Thailand. Legal cases between drug manufacturers and patient networks are spurring from country to country and the consequence from opposition infects to macro vision, particularly in the economic relationship between countries.

This research identified effects from economic issue toward research and innovation issue, which affects to social; we collect cases from India and Thailand, which later became the model to other countries.

3. What is TRIPS Agreement?

The Agreement of Trade-Related Aspects of Intellectual Property Rights (TRIPS) is an international agreement among members of World Trade Organization (WTO). It was established at the end of the Uruguay Round trade negotiations when WTO was the General Agreement on Tariffs and Trade (GATT) in 1994. The objectives of TRIPS Agreement are to reduce international trade conflicts by setting minimum standards in the field of intellectual property (IP) protection. All WTO member countries have to respect and to carry out the provisions of TRIPS Agreement in their countries. The member countries have to protect intellectual property rights of its nation as well as other members nations under the principle of National Treatment (NT) which essentially means treating foreigners and locals equally, and the principle of Most Favoured Nation (MFN) means the country which is the recipient of this treatment must, nominally, receive equal trade advantages as the "most favoured nation" by the country granting such treatment.

There are 8 topics of standard concerning in TRIPS agreement

1) Copyright and Related Rights

2) Trademarks

3) Geographical Indications

4) Industrial Designs

5) Patents

6) Layout-Designs (Topographies) of Integrated Circuits

7) Protection of Undisclosed Information

8) Control of Anti-Competitive Practices in Contractual Licenses

Before the final result, there was controversy in intellectual property issue. The US. demanded to protect invention in all fields of technology, whereas the European Union required the exemption in Biotechnology, and developing countries opposed the protection in pharmaceutical patent. TRIPS Agreement requires WTO Member nations to introduce patent protection only to products "invented" after 1 January 1995. Therefore, products already in the market were exemption, only new drugs or new indications, formulations or processes invented after 1995 should be patentable in all WTO Member countries.

Nevertheless, some special trade area attempts to embed the additional regulation included in the trade area agreement, particularly in the bilateral agreement. TRIPS transforms to TRIPS Plus which emphasize on rigorous of Intellectual property protection. Either US. or EU Bilateral with other countries projects to extend patent protection period for over 20 years, it claims that extended period aims to expiate the lagged time from New Drug Approval (NDA) Process. Another interesting regulation is “data exclusivity”, typically a pharmaceutical manufacturer can produce generic drugs, which have similar drugs component comply with the original drug in case that, the expired patent of the original. A company studies bioequivalent of drugs component to proof that a generic drug has equivalent efficacy with the original drugs without doing clinical trial, therefore the patent protection period can be longed.

With this patent gap, multi-national pharmaceutical companies manage to extend their patents continually. Multinational pharmaceuticals companies manage to use the tactic by addressing new drugs by slightly modifying previous drugs formulate and claim additional therapeutic area known as

"Me-too-Drugs" or change the drug application by reducing drug dose. Overall, these drugs are lack of novelty but multi-national companies claims that products have advanced knowledge and filed them as new patents. By this tactical development, patent protection period can be extended never ending and this tactic known as *"Evergreening patent"*

4. TRIPS and Pharmaceutical industry

It was announced that the pharmaceutical industry in the entire world would be subjected to the contents of the new WTO agreement and that the prevailing practice of process patent would be replaced by product patent. The date of implementation was January 1st, 2005. The worst impact of TRIPS that the pharmaceutical industry had foreseen was the end of the reverse engineering; incidentally this was the core competence of the industry. The industry now had to emphasize and concentrate on basic research. The companies without patents for new products will be unable to offer newer drugs to customers. It was also feared that number of units in the industry may close down and only few hundreds may survive this onslaught of imposition of conditions by the TRIPS. The prescription by TRIPS for product patent implies the following for the industry:

1. The industry has to now emphasis on basic research. The days of core competence of the industry in reverse engineering are over. The units in the industry now have to offer newer drugs to the customers in order to survive.
2. The companies have to start afresh on research. They need to add the necessary wherewithal's to conduct research in their units.
3. It is now necessary to have a policy for innovation for the purpose of survival.
4. To exploit such innovations commercially over a period of time, the IPR strategy needs to be developed and implemented.
5. The novel drug delivery system (NDDS) assumes more significance. Apprehensions of the Pharmaceutical Industry The introduction of TRIPS and its compliance have posed some challenges to the pharmaceutical industry:

- The industry feels that the TRIPS in its present form, is tipped in favor of developed nations and multinational pharmaceutical firms and that there is nothing trade related about TRIPS and that the right to trade is being exploited by developed countries.
- The sovereignty and the public health policy should not be compromised at huge costs to the Indian public. It is opined that TRIPS in fact violates the human rights.
- TRIPS would strike at the industry's ability to engage in a sustainable development in self-reliant way.
- TRIPS would also hinder the preservation and in fact would become a threat to innovation and practices of indigenous medicines, especially alternative medicines like Ayurveda and Unani.
- It is feared that in this big shake up, a number of medium and small pharma companies are forced to pull down their shutters. This would mean loss of job for thousands of employees.
- Companies which do not have enough R&D competence and orientation and who want to be in the race and survive may be forced to go in for mergers, joint ventures etc.
- Companies may have to increase their R&D spending and allocations to almost double.
- Overall growth rate of the industry may slow down considerably or may be even remain stagnant for some time.
- Above all, drugs could become expensive and beyond the reach of common man.

DOHA Declaration -Concession to developing nations

However, TRIPS Agreement attempts to provide flexibility rules for social benefits for creating invention and creation for a social goal or those invention provides social and technological benefits, and TRIPS allow governments to make exceptions to patent holder right for state of emergency or anti-competitive practices. For the pharmaceutical industry, the flexibility was clearly established by the Doha Declaration on TRIPS and Public Health. The first significant achievement of the World Trade Organization's Doha ministerial Conference came on the morning of 13 November 2000 when a compromise on the 'declaration on the TRIPS Agreement and Public Health' was reached. It was as a result of staunch effort by India Brazil and about 55 other African nations. This is one of the areas where there is an assurance that the restrictive clause under the TRIPS agreement on drug patents will not over ride public health concerns. It is a positive development that in TRIPS, a public health crisis has been included as an exception for granting compulsory license (CL). What is new in the Doha Declaration is that it recognizes the fact which was implicit under Articles 7 and 8 of TRIPS, that considerations of Public Good which includes public health could be the over riding factor while offering IPR protection for medicines for specified diseases and 'epidemics', particularly for DCs and LDCs. The one hundred and forty two countries that came together at the 4th WTO Ministerial Conference at Doha clearly affirmed that governments are free to take all necessary measures to protect public health.

The declaration gave primacy to public health over intellectual property rights. It is viewed that this declaration on public health is trophy for India since WTO had accepted, unequivocally, that patents would not stand in way of Public health. This is a very important aspect for India because, now national governments can decide if a particular situation or crisis is an emergency and that whether it would warrant sidelining of patents. How far this declaration would help India would be seen in future. It is inevitable that the industry now has to face these challenges and the opportunities that the new regime would throw open. To overcome the resource crunch the industry may have to consider many options like mergers with other pharmaceutical firms, collaborations with foreign companies, joining an R&D consortia etc. The industry would learn to change its axis of expertise from re-engineering to innovation. Aggressive marketing, good branding, better products, R&D and a patent protection would be their tools of success. The past has shown that India appears to have the technological and the commercial capability to adapt to more competitive environment. It has often caught up with world technological frontiers in other sectors. It can continue to do so again in future, if the industry wants to be an important pharmaceutical development center on world map.

Finally, The WTO Ministerial Conference adopted Doha Declaration on the TRIPS Agreement and Public Health on November 14, 2001.

It clarified flexibility of TRIPS member states in patent rights for better access to essential medicines. The essential content of the Doha Declaration in Paragraph 5 is:[6]

- Each Member has the right to grant compulsory licenses and the freedom to determine the grounds upon which such licenses are granted.
- Each Member has the right to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency.

5. Compulsory Licensing

Grant of a patent provides an owner with the exclusive right to prevent others from making, using, selling, offering for sale or importing their patent. Violation of any of these actions, without permission of the patent owner, could lead to civil actions for patent infringement, resulting in monetary damages. A court may also grant injunctions in accordance with the principles of equity to prevent the violation of any rights secured by a patent, on terms the court deems reasonable.

A compulsory license is a statutorily created license that allows certain parties to use or manufacture a product encompassed by the claims of a patent without the permission of the patent owner (patentee) in exchange for a specified royalty.

- **When does an authority grant compulsory license?**

Developing countries use compulsory licensing to protect the welfare of their people against the big giant firms holding the patents, but the countries have certain criteria for allowing compulsory licensing in any patent case. If the reasonable requirements of the public with respect to the patented invention have not been satisfied; or the patented invention is not available to the public at a reasonable price; or the patented invention is not worked in that country. Each country has their own set of terms and laws if not met issue the producer with compulsory licensing to manufacture that particular drug.

Elaborating the reasons further, government has to take this step when the patentee is not ready to grant license on reasonable terms, affecting the trade or industry development in that country; or demand of the patented good is not met by the current supply by the patentee. If the patentee includes one or more clause in the license: an exclusive grant back clause for any improvements developed by the licensee on the patented product or process; when the patented good is not available at the reasonable cost in the commercial market of the country and the commercial trade of the good affects the trade industry of the country. There are several reasons when the country can grant compulsory licensing for a patented product or process and every country has their own laws and terms to grant the compulsory licensing.

- **Who can apply for compulsory licensing?**

Any individual or organization can file an application to the authority concerning the patents in the country for a compulsory licensing when the patentee violates the clauses mentioned above and can lead the country into epidemic or economic turmoil. The claims of the individual or the organization are verified thoroughly by the authority before accepting their application for the compulsory licensing of any product or process.

In case of national emergency including a public health crisis extreme urgency or in the event of public non-commercial use, compulsory licenses can be granted by the central government in the official gazette. Once these licenses are granted the Controller will grant a compulsory license to any interested person who applies for such license. The patentee either through an opposition proceeding or in court cannot challenge the granting of compulsory licenses.

In cases of export, if the other country is in public health turmoil, and not having sufficient manufacturing capacity to fight the epidemic, than the county can publish in its official gazette, with respected to pharmaceutical patented product to be imported from the certain country, then the Controller of that country will grant compulsory license to an applicant on certain terms and conditions and only for manufacture and export of the patented pharmaceutical product to the country in question. The Controller will also determine the compensation to be paid to the patentee.

- **License Revision & Termination**

Twelve months after the licensee has worked the invention on a commercial scale, the licensee of a compulsory license may make an application to revise the terms and conditions of the license on the ground that the terms and conditions settled upon have proven to be more onerous than originally expected and as a consequence thereof, the licensee is unable to work the invention except at a loss. The application must include facts and evidence to support the application as well as the remedy or relief sought by the license holder. The license holder may request a hearing. The Controller will review the application and after the hearing, will grant or deny the application. If the application is granted, the Controller will revise the terms and conditions of the compulsory license. However, such an application for revision of a compulsory license shall not be entertained more than once. Given that Bayer received a 1% increase in the royalty rate by IPAB, it will be interesting to see if after one year Natco will attempt to have the royalty rate reduced back to 6%.

A compulsory license can be terminated if the circumstances under which the license was granted no longer exist and are not likely to recur. The patentee (or another party in interest) may file an application in the Patent Office with supporting evidence requesting that the compulsory license be terminated. The compulsory license holder will be provided with a copy of the application and has a period of one month from the date of receipt of the application to object to the application. If the license holder objects to the application, he/she must notify the patentee (or other interested party) and the Controller of his/her objection. After receipt of such an objection, the Controller will hold a hearing and decide the application based on the facts and evidence submitted by the parties. If the Controller decides to terminate the compulsory license, he shall issue an order providing the terms and conditions of such termination and serve copies of the order on both the licensee and compulsory license holder. Each country has their own laws and acts for the revision and termination, but the above methodology used in India gives an idea how the compulsory licenses revision and termination works

Table 1 : Compulsory Licenses granted in different countries

Country	Drugs
Brazil	Efavirenz
Cameroon	Lamivudine, Nevirapine
Canada	Oseltamivir
Ecuador	Lopinavir/Ritonavir
Ghana	Generic HIV and AIDS medicines
Indonesia	Lamivudine, Nevirapine
Israel	Hepatitis B vaccine
Italy	Imipenem/cilastatine, Sumatripan succinate
Malaysia	Didlanosine, Zidovudine
Mozambique	Lamivudine, Stavudine, Nevirapine
Thailand	Lopinavir/Ritonavir, Clopidrogel, Erlotinib, Letrozole, Docetaxel
Zambia	Lamivudine, Stavudine, Nevirapine

6. Pharmaceutical Industry In India

- **History & Background**

TRIPs, the intellectual property component of the Uruguay round GATT treaty, gave rise to an acrimonious debate between the developed countries and less developed countries. On one side, business interests in the developed world claimed large losses from the immigration and use of their innovations in less developed countries. They also asserted that establishing strong intellectual property rights would actually benefit the developing countries by encouraging foreign investment, the transfer of technology and greater domestic research and development. On the other side, less developed countries adamantly opposed this view, worrying about the higher prices that stronger intellectual property rights would entail and about the harm that their introduction might cause to infant high tech industries. No country was more actively involved in opposing this component of the GATT agreement than India and no part of TRIPs was, and continues to be, more sensitive that the proposal to require product patents for pharmaceutical innovations. The national sentiment on this issue is well captures in an often quoted statement made by Indira Gandhi at the World Health Assembly in 1982; 'The idea of better ordered world is one in which medical discoveries will be free of patents and there will be no profiteering from life and death.'

In spite of the debate on both the sides and claims made, India agreed to this aspect of the treaty much against her will, believing it to be harmful to her interests. After a brief history, it sets out in Section III the various ways in which the introduction of product patents for pharmaceuticals may benefit or hurt the country in theory.

- **The Pharmaceutical Industry and the Indian Patent System**

In 1970, India put into place a series of policies aimed at moving the country towards self-sufficiency in medicines. At this time, the national sector was very small, estimated at less than 25% of the domestic pharmaceutical market. Of the top ten firms by retail sales. Only two were Indian firms and the rest were subsidiaries of multinationals. Much of the country's pharmaceutical consumption was met by imports.

An important part of the policy package was the passage of the Patents Act 1970 (effective April, 1972). This legislation greatly weakened intellectual property protection in India, particularly for pharmaceutical innovations. The statutory term was shortened to 5 to 7 years on pharmaceutical process patents and automatic licensing was put in place. As a result, the number of patents granted per year fell by three-quarters over the following decade, from 3923 in 1970-71 down to 1019 in 1980-81. Although all inventors were affected by the weakened patent regime, it is clear that foreigners, in particular, no longer found taking out a patent in India worthwhile.

Other aspects of the policy package set up to encourage the domestic production of pharmaceuticals included restrictions on the import of finished formulations, high tariff rates, ratio requirements and equity ceilings on foreign participation. Further, the strict price control regulation which was introduced with the 1970 Drugs Price Control Order, while making the production of pharmaceuticals less profitable for all firms selling in Indian market, made it relatively less interesting for foreign firms with market options elsewhere. Thus even the price control regime probably contributed to the shift towards a greater share of production being met by Indian firms.

Supported by this regulatory environment, by 1991, Indian firms accounted for 70% of the bulk drugs and 80% of formulations produced in the country. But after loosing against United States and

European Union in WTO dispute, the Indian government made changes to its patent act and in the legislation providing more protection to the intellectual property rights to the patents registered in India by the foreign firms.

- **Ratification of TRIPS by India**

India signed and ratified in the year 1996, the TRIPS Agreement. The component of TRIPS - Trade related Intellectual Property Rights - was included in the WTO Agreement of 1995 against the active opposition of the developing countries to include IPR in the new GATT Treaty. With the signing of this agreement the members from developing countries, Including India, had to make their IPR laws TRIPS compliant. Under this agreement, norms and standards are provided in respect of seven categories of Intellectual Property Rights, which also includes product patent in all areas of technological development. As per the agreement all member countries were expected to comply with the provisions of TRIPS from January 1, 1995. A transition period of 10 years from 1995 to 2005 for developing countries including India was provided to enact bills incorporate product patent protection. As a result of this the Copyright Act had been amended in 1999 and the Trade and Merchandise Marks Act was amended as the Trade Marks Act, 1999. The Patent (Amendment) Act, 1999 was also brought in amidst apprehensions and doubts.

- **TRIPS and Indian pharmaceutical industry**

Following are some of the new opportunities for growth the pharmaceutical industry foresees after 1 January 2005

1. It is predicated that by the time the legislation comes into force on 1 January 2005, drugs worth around US $ 30 billion would be going off the patent. This would mean a very good opportunity for the industry to sell formulations and bulk drugs through out the world. A very healthy growth is predicted to the industry even in spite of competition on the ground that most of the companies possesses strong process re-engineering skills and lower cost of development.
2. Outsourcing by MNCs in areas of bulk drugs, formulations, for patented and off-patent products. This would mean serious strategic alliances and bringing in of foreign exchange.
3. Apart from outsourcing, the infrastructure could be used by foreign manufacturers for contract manufacturing of pharmaceutical products.
4. Indian pharmaceutical could also be an important sourcing platform for many multinational in new drug research
5. The industry would use its technical and man power skills for research and innovation. However the industry would still be able to market older drugs, which is not included in the patents list.

Once a new product is developed the inventor would secure monopolistic rights of production and marketing for a period of 20 years, which is very substantial.

- **Risks faced by Indian firms**

Despite their existing competitive advantages and promising opportunities on the horizon, Indian firms have certain weaknesses and therefore face certain competitive threats, which can be summarized as follows:

1. Indian companies are relatively new to the generics business in regulated markets and there are concerns regarding their ability to manage large product portfolios, entailing numerous

regulatory filings, scaling up manufacturing, forging alliances, and legal skills to win on patent litigations.

2. The US based generic industry may be able to glean the same cost advantages as Indian firms through developing partnerships or Greenfield sites in India. US based generics companies such as Watson, Ivax, and Apotex have already secured manufacturing agreements with Indian bulk active/dosage form manufacturers and in the medium term, this may mitigate some of the cost advantages enjoyed by the fully integrated Indian companies like Dr Reddy's, Ranbaxy and Sun.
3. The research-based industry has also been increasingly interested in marketing their own generic alternatives to their patented products, spurred by the impending flurry of patent expirations and the knowledge that the majority of the profits of a generic drug are earned in the first six months post patent-expiry.
4. Pursuing the NCE strategy is risky, not least because Indian firms have a skills shortage in the area of patent writing. It has been suggested that many existing patents written by Indian professionals can be easily circumvented; so even where an Indian company has produced an innovation, it may not be protected in international settings. In addition, Indian firms are strong in chemistry, but they are relatively weak in biology and clinical research and development skills, and these are essential to compete in the innovative, NCE drug category.
5. There is a risk that the co-operative strategies employed by some firms could get in the way of the competitive strategies of these firms, especially if Indian firms do not negotiate reasonable contract terms with MNCs and/or fail to ring-fence their competitive advantages.

- **Implications for market structure and brand name multinationals :**

Changes in market structure

As a consequence of the multiple changes in the industry, pharmaceutical analysts predict that some Indian firms in this currently fragmented market (200 firms in the regulated sector, over 22,000 in the unregulated sector) are likely to experience financial pain over the next few years, culminating in market exit of the less competitive firms, and resulting in a more consolidated market structure.

Implications for large MNCs.

The impact of the evolving Indian business model is likely to have both positive and negative impacts on the major generic and branded MNCs. In the commodity based
Evolving Prospects of the Indian Pharmaceutical Industry generic business, low cost is the key success factor. United States and European generic companies are faced with several options: acquire or partner with Indian firms, establish Greenfield manufacturing sites in India, or differentiate and compete, with higher costs. Over the next few years, the effect of Indian companies on large MNCs may be more negative, as Indian companies are likely to be very competitive in the generic sector and strong patent challengers targeting branded drugs previously viewed as invulnerable because of manufacturing complexities. On the positive side, branded pharmaceutical MNCs have the potential to gain access to cheaper API and dosing formulations from Indian companies.

The research-based industry may also gain from R&D collaborations that result in new NCE or licensing opportunities. Finally, Western patent holders can gain from increased sales to the large domestic Indian market, where such sales would previously have been impeded by generic versions of on-patent products

- **Legal Litigations & Compulsory Licensing**

In past few years much legal litigation was seen in the pharmaceutical industry in India, concerning the global pharma companies. Novartis was not provided patent for its new version of famous drug Glivec, which is used to treat myeloid leukemia cancer, which will prevent Indian generic pharmaceutical manufacturers from producing drugs based on the compound. But Novartis was rejected the patent of the drug by two judges of Indian Supreme Court on the issue of ever greening of pharmaceutical patents for minor enhancements in the drug. The Supreme Court said the substance which Novartis sought to patent is known and thus not qualify the test of invention as laid down in section of the Indian Patent Act and rejected the patent application. The Indian generic pharmaceutical firms manufacture the drug Glivec at the one tenth of the cost of what Novartis does.

Another famous lawsuit was of German health care giant Bayer when the government allowed Indian generic to produce and sell cheap copies of blockbuster cancer drug Nexavar – even though the drug is patented. The court stated that Bayer had obligation in making the drug available to the people in India who needed it. The one-year treatment of Nexavar in India costs $69,000, which is 41 times the per capita income of India. Thus the drug is only available to the people who can afford it, and the rest of the patients suffer due to high cost of the drug. Further, the drug costs $80,000 in U.S. but if it would cost 41 times of the per capita income, it would cost $1.6 million. This comparison gives an idea how difficult it would be to obtain the same drug if it costs so high. The first compulsory license was granted by the high court was to the Indian pharmaceutical firm Natco-Pharma Ltd to produce the drug Nexavar, which is used to treat kidney and liver cancer, by paying royalty to Bayer.

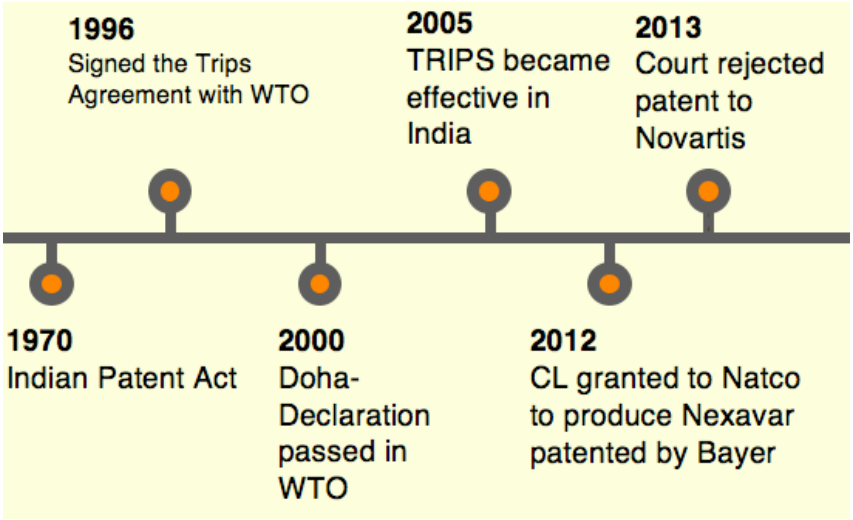

Figure 1 : Timeline of compulsory licence in India

7. Pharmaceutical Industry In Thailand

- **History & Background**

Pharmaceutical Industry in Thailand has operated by the Government Pharmaceutical Organization (GPO) and private owner companies. Since the last decade, many companies were threaten by drugs from multi-national companies, so many of them decided to disengage business and some of them was undertaken by MNCs. Moreover, private owners companies affects from the policy that the organization under government control has exclusive right to produce generic drugs without approval from Thai FDA, it seems to be the obstacle for the pharmaceutical development in Thailand hence, MNCs companies have greatly effect over Thai pharmaceuticals industry.

Thailand is in a developing country list or a less developed country (LDC) which means people in nation have average low to moderate Gross Domestic Product (GDP) per capita approximately $10,000 per year (2012). Like many developing countries, the important problem issue is health and poverty, especially AIDS crisis in the country. In 1999, there are approximately one million HIV/AIDS infected people in Thailand and only five percent of the affected population was able to access the anti-retroviral drugs and only one percent of those could afford for the drug because of high cost of treatment. Therefore, Thai government attempted to relief this obstacle by addressing the policy of universal health coverage since 2001. This policy allowed impecunious people accessed to medical treatment and drugs in the National List of Essential Medicines (NLEM) for example; HIV, Cancer. The government-subsidized cost especially for drug pricing as a result that the National Health Security Office (NHSO)'s budget had increased consecutively by year. However, this policy was not able to cover all patients in the nation, therefore some patients still had to pay for the drug by themselves.

- **The Pharmaceutical Industry and the Thai patent System**

Thailand has implemented the patent system since 1979, the drug patent principle is allowed for New Chemical Entity, New Formula, New Usage, and New Dosage Form and in 1992, the patent protection period extended from 15 years to 20 years. Companies are allowed to produce generic drugs after the expiration period of patents, therefore patent system plays an important role to Thai pharmaceutical system for studying bioequivalent of drugs for next developing stage. With the generic drugs, people in Thailand are able to access those generic drugs with affordable price.

- **Ratification of TRIPS by Thailand**

As a member of WTO, Thailand adopted TRIPS agreement automatically and the important issue was IP protection in pharmaceutical industry. Many MNCs established offices in Thailand and registered patents to protect their rights in the nation, then it brought up to the drug market monopoly and high price of drugs. Due to this situation, many organization in Thailand especially HIV/AIDS patients network rushed out to protest this unfair circumstance continuously and requested Thai government to imposed the Compulsory License (CL) over the HIV/AIDS treatment.

- **Legal Litigations & Compulsory Licensing**

The first movement of CL in Thailand started in the year 1999 by 16 private organizations, protested on Didanosine (DDI), one of the anti-retroviral drugs in HIV treatment which under the right of Bristol-Myers Squibb (BMS). In fact, two scientists working for the National Institute of Health (NIH), a U.S. public research institution, developed the DDI in the U.S. In 1989, two patents (U.S.4861759 and U.S.5616566) over DDI were issued by the USPTO to the Department of Health and Human

Services, then the patents were subsequently licensed to BMS in order to produce and market the product under the trademark “Videx” in 8 developed countries only. The licensing agreement ruled BMS to pay royalties fee of five percent of sales, contains a fair pricing clause and requires commercialization for the public benefit. However, BMS filed the DDI patent with the Department of Intellectual Property (DIP) of Thailand on July 7th 1992 by registered “improved oral dosing formulations of Dideoxy Purine Nucleosides”. It was claimed in the application that invention related to pharmaceutical components providing improved oral dosing formulations of DDI.

After approval process, BMS was granted patent in January, 1998 and the HIV/AIDS network protested aimed Thai government to abandon the patent right by imposing CL to BMS and to allow the Government Pharmaceutical Organization (GPO), Thailand to manufacture the drug autonomy. However, Thai government refused to invoke CL because it was afraid of negative trade repercussion from the U.S. Thus, GPO was asked to produce DDI powder to avoid the infringement upon BMS right, nevertheless DDI powder from GPO had some disadvantages with the ease to consume and the adverse effects. After attempts to impose CL failed, HIV/AIDS networks, NGO, and two Thai patients were plaintiff, filed a lawsuit to the Central Intellectual Property and International Trade Court (IPITC) in order to correct the invalid claim of the DDI patent No.7600 in May, 2001 by BMS and DIP were defendant.

In October 2002, IPITC adjudge that BMS need to correct the claim about limitation of dose, but BMS appealed to the Supreme Court to defer the enforcement of the instance ruling. At the same time, a second lawsuit was filed by another HIV patients and HIV foundation to the Supreme Court in order to revoke the DDI patent No.7600, the plaintiffs asserted that the grant of the patent was unlawful due yo a lack of novelty in the DDI formulation. In the meanwhile, partner organizations did movement by sending notation to Ministry of Health to provoke GPO as a plaintiff to sue BMS, with the great pressure of people and surrounding community in the world forced, GPO filed another lawsuit to prosecute BMS. Finally, in January 2003, BMS decided to reach agreement with GPO by revoke the DDI patent No.7600 from Thailand and withdraw its first appeal in the first lawsuit, while all plaintiffs had to withdraw all lawsuit, too. As a result that GPO was able to produce DDI in tablet form and market to the HIV/AIDS patients in the cheaper price so that patients were able to pay less than $30 per month instead of paying $100 per month from buying BMS’ DDI drug.

In 2003, HIV/AIDS network dissented the resolution of the patent subcommittee to amend the patent from Glaxo SmithKline (GSK), the international drug company from the U.S., which registered the anti-retroviral under the trademark “Combid”. The HIV/AIDS networks objected that Combid was lack of novelty due to drug composition between Zidovudine (AZT) and Lamivudine (3TC) which were outright for long time. This protest was supported from many international organizations such as Médecins Sans Frontières (MSF), India AIDS foundation, South Korea AIDS foundation and Malaysia AIDS foundation. From this international collaboration, GSK renounced the right on patent in August 2003, as a result that GPO and other drugs companies were able to produced the anti-retroviral drug freely. The price of drug decreased from $1.3 to $0.28 per tablet or decreased around five times.

However, Many international pharmaceutical companies had licensed drugs in Thailand under TRIPS agreement and they had exclusive owner right in the country, it could be inferred that those companies would monopolize drug market. The drugs would have high prices and hard to access in the future, moreover poor patients were not able to afford them and they would suffer from that severe disease and died finally. Therefore, Thai government raised the Compulsory Licensing (CL) to

negotiate with pharmaceutical manufacturers since the year 2006 after effort of private sector. In the first phase, 3 drugs were applied to CL scheme.

(1) Efavirenz (EFV)

EFV is the standard antiretroviral drug in the Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) class. It is in the same class as Nevirapine (NVP), which has more severe adverse reactions than EFV, such as rash symptoms that can develop into the Stevens Johnson syndrome and Hepatitis in severe cases. Merck Sharp & Dohme Co. Ltd. registered the EFV patent in Thailand under the trademark "Stockrin"

(2) Lopinavir + Ritronavir (LPV/r)

LPV/r is a Protease Inhibitor (PI), used as a second-line treatment of HIV patients who have developed resistance to the first-line treatment. Abbot Laboratory Co.,Ltd. registered the LPV/r patent in Thailand under the trademark "Kaletra"

(3) Clopidogrel

Clopidogrel is an antiplatelet drug in the Thienopyridine drug group. It is used as an alternative, or in addition to, Aspirin to increase the efficacy of treatments of coronary stenting for heart disease (Bureau of Medical Technical Treatment, 2004). It has also been found that the use of Clopidogrel with aspirin for secondary prevention in cardiovascular patients can reduce the death rate of heart disease (American Heart Association, 2008) and increase effective more than by treatment with aspirin alone (Karnon et al., 2005). Sanofi Syntec Co., Ltd. registered the Clopidogrel patent in Thailand under the trademark "Plavix"

Economic Impact from CL

After activating CL in Thailand in 2007, United States Trade Representative (USTR) announced Thailand status from Watching List (WL) elevated to Primary Watching List (PWL) in Intellectual Piracy. Moreover on July 1st, 2007, the United States counteracted Thailand in economic issue by announcing to reduce privileges under the Generalized System of Preferences (GSP) for three Thai products: gold accessories jewelry, polyethylene terephthalate, and flat screen television sets. However, some analyst argued that PWL elevation did not relate with CL.

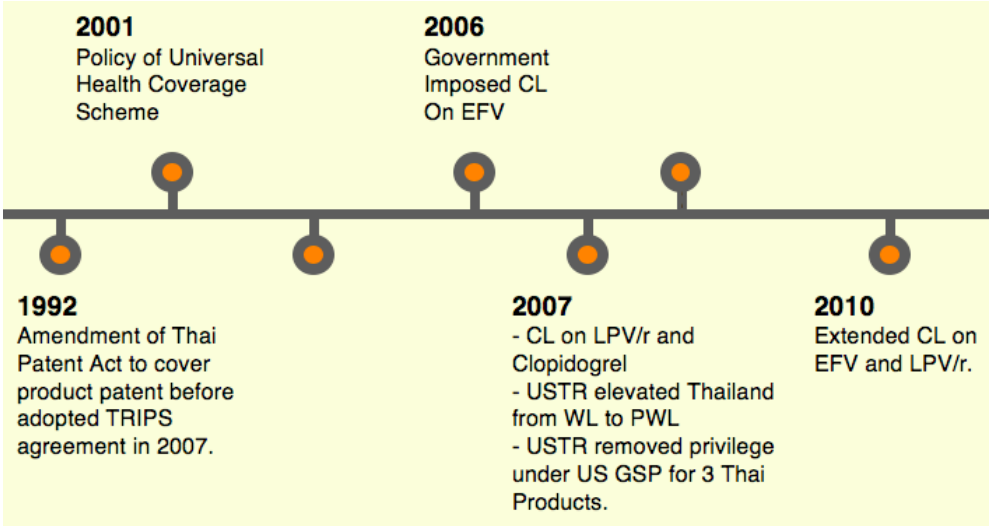

Figure 2 : Timeline of compulsory licence in Thailand

8. Conclusion

Pharmaceutical industry is of high importance for any nation to take care for providing high quality and economic health care facilities to their people. But developing new drugs for varied disesaes takes a lot of investment in the research and development. Many less developed countries are not even capable of manufacture drugs on their own, so investing in any sort of R&D is out of scope for them. In such situations, they depend mainly on other countries who can provide them the necessary medication at a reasonable cost. But after joining the WTO and accepting the TRIPS, it has led the global companies to patent their drugs and sell them at high cost. Sometimes it is way more expensive than the per capita income of the country. This has made these drugs out of reach for the people of developing countries, with only very small percentage of people getting their hands on these medicines.

The argument given by almost each of these pharmaceutical companies is the their high investment in R&D, but having a closer look on their expenses it is found these companies spend 70 percent of amount of the cost charged on marketing the product which is way higher than their R&D expenditure. Further the CSR activities of these firms are not enough to serve even 10 percent of the population of the developing nations who are in need of the medicines. So how do can developing nations improve their health care system and make it economic for people.

The paper discusses the cases of India and Thailand, and the steps taken by the government to protect the health care from high cost of patented drugs. Compulsory Licensing is one way adopted by both governments to make the drugs available to their people at economic rates. Its seen that in spite of various steps taken by the governments, they aren't successful in providing high quality medication to the people at an economic rate.

Health care is very sensitive and critical industry, and the nations need to come together to eradicate these wide spread differences in the health care center across different countries. Human life is of utmost importance, and it cannot be risked for the greed of money.

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Appendix

Table 2 : Price Comparisons After CL Scheme

Drug's Name	Trade name	Licensor	Disease	Original Price	Price after CL
Efavirenz	Stockrin	MSD	HIV/AIDS	$44/month	$22/month
LPV/r	Kaletra	Abbot	HIV/AIDS	$386/month	$67/month
Clopidogrel	Plavix	Sanofi	ACS	$2.3/tablet	$0.04/tablet

Table 3 : Current and projected increase in number of patients with access to drug in Thailand

Drug's Name	Disease	2007	2008	2009	2010	2011
Efavirenz	HIV/AIDS	2,815	6,264	10,391	14,255	17,959
LPV/r	HIV/AIDS	N/A	623	1,529	2,475	3,421
Clopidogrel	ACS	N/A	4,069	12,207	12,307	12,394

Figure 3 : Increase in number of patients accessing to Efavirenz following grant of government use license in Thailand

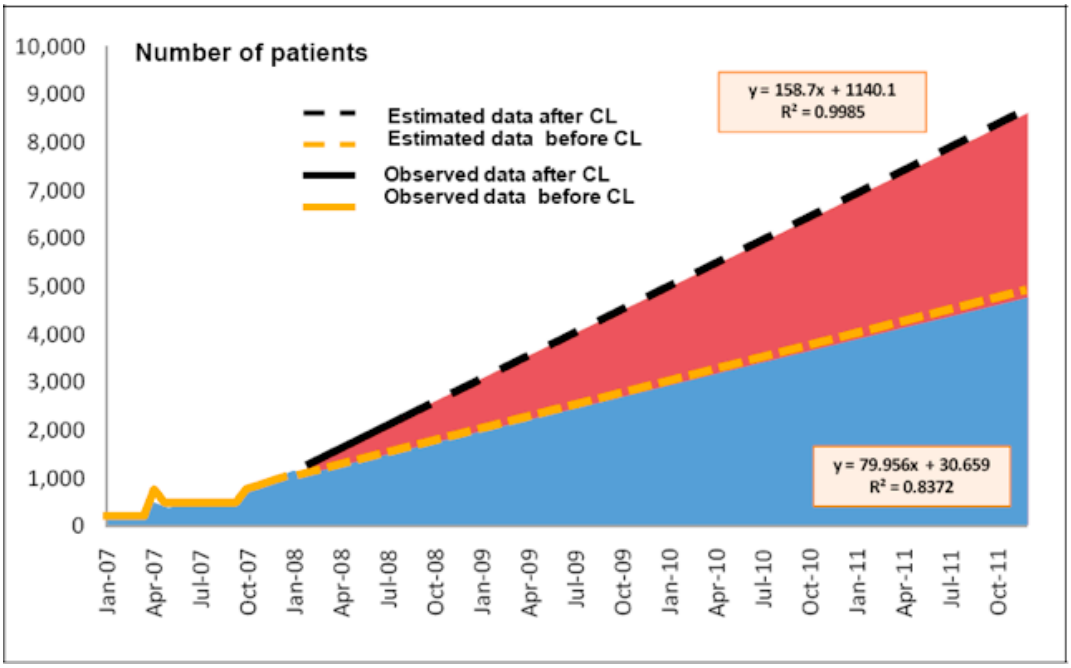

Figure 4 : Increase in number of patients accessing EFV following grant of government use license in Thailand

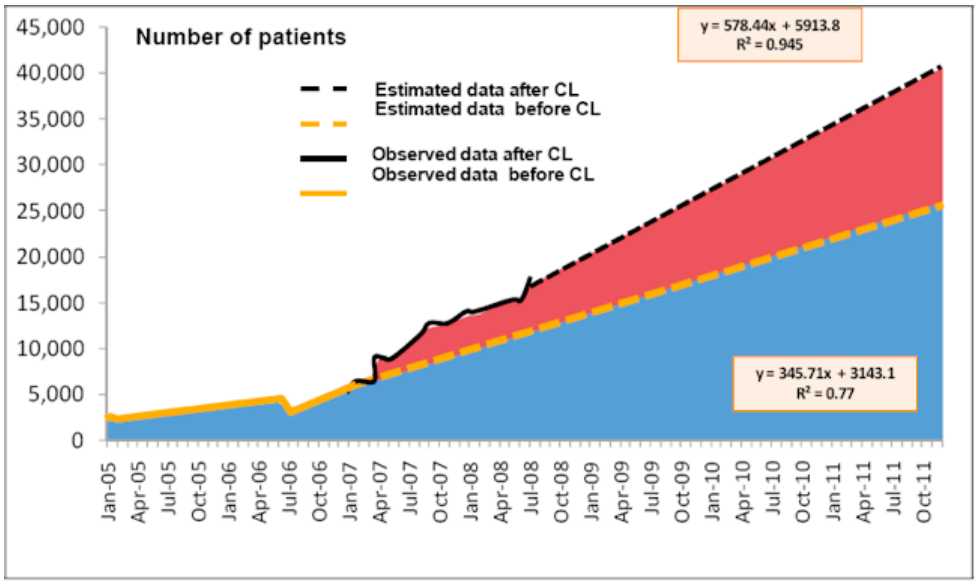

Figure 5 : Increase in number of patients accessing to LPV/r grant of government use license in Thailand