Chapter 6
A Practical Way to Improve Access to Essential Medicines Against Major Infectious Diseases

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Introduction

In the globalized world of the twenty-first century, diseases have spread faster than ever before, aided by high-speed air travel and the trade in goods and services between countries and continents [1]. Collaboration between, especially, developed and developing countries, to ensure the availability of technical and other resources is a crucial factor in building and strengthening public health capacity, networks, and systems that strengthen global public health security. Such collaboration could prevent the rapid spread of disease. It is estimated that 2.1 billion airline passengers traveled in 2006; a disease outbreak or epidemic in any part of the world is only a few hours away from becoming an imminent threat somewhere else [2]. Developing countries, which collectively shelter over three quarters of the world’s population, face severe public health crises from both widespread infectious diseases, such as HIV epidemics, rampant TB, malaria, and viral hepatitis as well as staggering chronic diseases, such as cardiovascular disease and malignant tumors. Approximately 15 million people die each year due to infectious diseases—predominately in developing countries [3]. The rapid progress of science and technology in the twentieth century uncovered many new forms of medicine, which greatly improved people’s health in developed countries. However, patent protection for medical drugs and patent monopoly, as stipulated by the World Trade Organization’s (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), guarantee monopolizing profits. Essentially, this guarantee causes the price of patent drugs to skyrocket, which severely hinders the accessibility of drugs that are essential to public health in developing countries.

The author acknowledges the contributions of Hong Zhu, Tao Teng, and Yinqi Wu.

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After TRIPS was signed, member countries of the WTO, especially the developing countries, were faced with increasing public health crises and have been persistently seeking a new balance between patent protection and the public health interest of providing essential medicine to their citizens. It is clear that the old WTO regulation and TRIPS agreement actually prevent developing countries from getting essential medicines and also hinder their capability to handle the frequent attacks of emerging infectious diseases. Further development and policy advancement of the WTO regulations are needed to establish a new balance between the protection of intellectual property of medicines and the interests of public health.

From TRIPS to the Doha Declaration: Building a Consensus Between Drug Patent Protection and Public Health Interest

Recent economic globalization and market growth has drawn attention to the role of intellectual property in international trade. As major exporters of these products, developed countries advocate the protection of intellectual property while developing countries worry that intellectual property rights only support the monopoly led by international companies and raise the price of the drugs and total medical costs, ultimately having a negative impact on public health emergency response capability. In 1995, the TRIPS agreement was implemented in Uruguay Round to join the protection of intellectual property rights and the cross-retaliation system of the General Agreement of Tariffs and Trade (GATT). Developing countries agreed to protect intellectual property in exchange for market access and trade preferences from developed countries. In particular, the U.S. used its economic hegemony, along with the trade preference “Carrot” and the big-stick policy of “Super 301 sanctions of penalty article” to force other countries to accept the TRIPS agreement [4], causing conflict over the protection of intellectual property and the right to obtain essential medicines.

After over 5 years of debate and negotiations with pressure from the governments of mainly in developing countries and nongovernmental organizations, a consensus was reached. The Doha Declaration on the TRIPS Agreement and Public Health (simply referred to as the “Doha Declaration”) was adopted in November of [5]. It states 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’ rights to protect public health and, in particular, to promote access to medicines for all” [6]. Therefore, the Doha Declaration reaffirms the right of WTO member states to grant compulsory licenses in a state of national emergency. Compulsory licensing refers to a government’s consent to someone other than the patent owner to produce the patented product or process without the consent of the patent owner. Specifically in the medical field, the term denotes the government allowing a third party to produce patented drugs. However, TRIPS mandates that the drugs produced under a compulsory license must be used only in the domestic market, which creates a major obstacle
for the countries with no manufacturing capacity in the pharmaceutical sector to import unregistered generic drugs [6].

In November 2003, the WTO Ministerial Conference announced the 2003 General Council’s decision on the TRIPS Agreement and Public Health (a General Council decision) and included an amendment to paragraph (f) of Article 31 of the TRIPS Agreement. The first revision of the series waived the obligations of exporting members: generic drugs produced under compulsory licenses can be exported to other developing countries lacking the manufacturing capacity instead of remaining exclusive to the domestic market within the manufacturing country. This additional stipulation to the law removed obstacles hindering developing countries’ ability to make full use of compulsory licenses. The second revision waived the remuneration to patent holders from importing countries because the exporting country already pays it. This General Council decision resolved the previous issues of paragraph 6 of the Doha Declaration. As a result, member states lacking manufacturing capacity found themselves with the means to import cheap generic drugs from countries that produced the drugs under compulsory licenses.

In December 2005, the WTO General Council adopted the Protocol Amending the TRIPS Agreement, which was the first amendment to TRIPS since 1995 [7]. Up to now, many developing and developed countries have approved the Protocol Amending the TRIPS Agreement. Developing countries should make full use of the privileges introduced by this document by granting compulsory licenses in public health related areas or use it as a tool to acquire a voluntary license in the local manufacture of drugs or in negotiation for affordable drug price. These areas should target drugs for prevention and treatment of infectious diseases and tumors, including HIV/AIDS, hepatitis B, as well as malignant tumors, to break the high price barrier of imported patent drugs and make them accessible to the respective country’s population. This direction, if taken, will significantly minimize these serious public health issues in China as well as in other developing countries.

**The Implementation of Compulsory Licenses in Developing Countries: A Case Study**

WTO treaties, including the Doha Declaration, the General Council Decision, and the Protocol Amending the TRIPS Agreement, stipulate that member countries have the right to grant compulsory licenses and provide necessary legal foundations for member countries to implement compulsory licenses. The treaties specify to what extent a compulsory license may be applied and exactly what constitutes a national emergency. Some developing countries, including Thailand, Brazil, South Africa, and a few others, have already made full use of compulsory licenses to deal with the public health crises posed by infectious diseases such as HIV/AIDS. Refer to Table 6.1 for information on the implantation of compulsory licenses in developing countries [10].
In 2005, Brazil began negotiations to issue a compulsory license for kaletra (a second-line antiretroviral drug). Eventually the threat of this compulsory license led to an agreement with the patent holder, Abbott, to reduce the price of the drug [8].

The Brazilian government has consistently sought lower prices for antiretroviral (ARV) drugs in order to support the cost of its national AIDS treatment program, which provides free access to ARV drugs for up to 180,000 Brazilians. It is estimated that 75,000 of those receiving ARV treatment in Brazil will be using efavirenz by the end of 2007. Efavirenz (in tablets of 600 mg) was sold in Brazil at $580 per patient per year, which was 136% higher than the price offered by

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**Table 6.1 The implementation of compulsory license in developing countries**

| Country     | Type                  | Type of drugs                                                                 |
|-------------|-----------------------|-------------------------------------------------------------------------------|
| India       | Compulsory license    | All drugs prior to January 1st, 2005. Drugs with a patent (about 8,296 patent drugs) submitted between 1995 and 2005, including some second-line antiretroviral drugs |
| Malaysia    | Compulsory license    | AIDS drugs                                                                    |
| Indonesia   | Compulsory license    | AIDS drugs                                                                    |
| Thailand    | Compulsory license    | AIDS drugs, anticancer drugs, cardiovascular medicine                         |
| Zambia      | Compulsory license    | AIDS drugs                                                                    |
| Mozambique  | Compulsory license    | AIDS drugs                                                                    |
| Zimbabwe    | Compulsory license    | AIDS drugs                                                                    |
| South Africa| Extended the importation, manufacture, and voluntary licensing to other African countries of antiretroviral drugs in four generic drug companies in South Africa | AIDS drugs |
| Cameroon    | Granted public procurement agencies the right to purchase antiretroviral generic drugs when the price is lower than that of the patent owners | AIDS drugs |
| Ghana       | Compulsory license    | AIDS drugs                                                                    |
| Eritrea     | Compulsory license    | AIDS drugs                                                                    |
| Guinea      | Compulsory license    | AIDS drugs                                                                    |
| Peru        | Compulsory license    | AIDS drugs                                                                    |
| Brazil      | Compulsory license    | AIDS drugs                                                                    |
| China       | Threaten to use compulsory license | Oseltamivir phosphate                                                       |
| Taiwan      | Compulsory license    | CD-R and oseltamivir phosphate                                               |
Thailand [9]. The Brazilian government attempted negotiations for a lower price with Merck beginning in November 2006. They threatened Merck with a compulsory license unless Brazil could sell efavirenz at a rate equal to or less than the rate offered to Thailand.

After 6 months of unsuccessful negotiations, the Brazilian government issued their first compulsory license on May 4, 2007. Brazil reduced the price per day from $1.56 to $0.45 by buying Indian generic products. The government expected to save $30 million in 2007 and a total of $237 million between 2007 and 2012. “From an ethical point of view the price difference is grotesque,” said Brazilian President Luiz Inacio Lula da Silva. “And from a political point of view, it represents a lack of respect, as though a sick Brazilian is inferior,” he added. “Our decision today involves this one drug, but we can take the same steps with any other that we consider necessary.”

Brazilian’s nongovernmental organizations (NGOs) are in strong support of this governmental action. The Working Group on Intellectual Property of the Brazilian Network has said that the government will no longer be a “Tiger without Teeth.” The issuance of a compulsory license was an historical decision helping to maintain the access to necessary medicines.

James Love of Knowledge Ecology International predicted “Brazil and Thailand’s large expansion of their market for generic versions of Efavirenz, will promote reduced prices, eventually reaching less than $0.24 per day” [10]. Love also added, “Brazil should set up a system of collective management of intellectual property rights and extend a compulsory license for all prescription medicines, not only for AIDS but also for other important health problems like diabetes, cancer, or heart disease.”

South Africa

The government of South Africa first issued a compulsory license in 1998 after the TRIPS agreement came into effect. HIV infected 15% of all South Africans and the HIV prevalence among its adult population was as high as 20%, among the highest in the world [11]. In response to the severe epidemic, South Africa passed the South Africa Medicines and Related Substances Act in December 1997, authorizing the government to issue a compulsory license and parallel importation. In February 1998, a South African pharmaceutical group united 40 companies who, together, filed a lawsuit on the claim that the South Africa Medicines and Related Substances Act of 1997 is unconstitutional because it gives the Minister of Public Health the power to ignore the Patent Act. Ultimately, these companies faced an ethical dilemma of protecting patents over saving human lives and finally withdrew the lawsuit and substantially reduced the price of the drugs. In response, the multinational pharmaceutical companies pressured their own governments asking them to amend the TRIPS Agreement. This action resulted in the Doha Declaration on the TRIPS Agreement and the protocol amending TRIPS [12].
On September 19, 2002, the Treatment Action Campaign and South Africa’s Competition Commission filed a lawsuit against GlaxoSmithKline and Boehringer Ingelheim. These two companies were accused of charging exorbitant prices for ritonavir, lamivudine, and nevirapine. GlaxoSmithKline and Boehringer Ingelheim were also found guilty of violating the Competition Act of 1998, abusing their high-standing positions in the ARV markets, denying competitors access to an essential facility, and engaging in an exclusionary act. The terms of the final settlement required the two pharmaceutical companies to extend the voluntary license granted to Aspen Pharmacare to the public and private sectors in October of 2001. This action granted up to three more voluntary licenses on the same terms as those given to Aspen Pharmacare, permitted the export of ARVs to sub-Saharan African countries, and charged royalties of no more than 5% of the net sales of the relevant ARV drugs. This settlement marked an historic victory in the struggle of developing countries fighting against multinational pharmaceutical enterprises using the patent to establish a profitable monopoly over the industry [13].

Thailand

Brief History

Towards the end of 2006, The government of Thailand granted compulsory licenses for two ARV drugs (efavirenz–lopinavir and kaletra) as well as plavix for cardiovascular disease at the end of 2006 and early 2007. In September 2007, the National Drugs Protection Office in Thailand announced its intention to grant compulsory licenses for four cancer drugs: glivec and femara from Novartis, tarceva from Roche, and taxotere from Sanofi–Aventis. In January 2008, the compulsory licenses were granted to femara, tarceva, and taxotere. Glivec was exempt because Novartis had promised to provide glivec free of charge to cancer patients inside the Thai National Health Insurance Program [14].

Compulsory Licenses in Thailand

Thailand has a severe HIV/AIDS epidemic. According to (UNAIDS) 2010 Global AIDS Report, there were 530,000 people living with HIV/AIDS and 12,000 new infections in 2009. The prevalence among adults is less than 1.3% [15]. The epidemic has undergone three phases: low epidemic in 1984–1990, rapid increase in 1990–1997, rapid decline from 1997 to the present. The curb of the epidemic is mainly due to the comprehensive measures of public education, prevention, and treatment adopted by Thai government [16, 17]. Despite increased funding from the government, they are still far from meeting the patients’ needs and the expensive patent drugs remain a heavy financial toll on the Thai government.
Efavirenz, which is recommended by the World Health Organization (WHO) for HIV/AIDS treatment, has been named one of the best components for first and second line therapy. The price from Merck was $468 per patient per year, which was more than double the price of Indian generics. With Merck’s original price, the Thai Ministry of Health (MOH) was only able to cover two-thirds of the population in need. After failed negotiations with Merck [18, 19], the Thai government issued a compulsory license for efavirenz on December 6, 2006, and began the local production with the government pharmaceutical organization (GPO). The price of the drug dropped about 50% from $67 to $38.5 per month [20]. This was the first time Thailand used a strategy permitted under both patent law and the Protocol Amending the TRIPS Agreement.

Lessons Learned

There are two lessons to be learned from the Thai practice of compulsory license. One is the Thai government’s planning and coordination to overcome various barriers and challenges, including a remarkably orderly implementation of the “government use” system. The Thai MOH established a government committee directing the government agency’s work on compulsory license to ensure that the drugs obtained through the compulsory license are on the national essential list for government use based on Article 51 of Thailand’s Patent Act of 1979, which stated that the government can sue the patent owner’s rights as their own under certain conditions. The committee broadened the special conditions for public use of compulsory license drugs to include the following:

- To resolve the public health issues
- To be used in emergency situations
- To prevent the infection disease outbreaks
- To save lives

Thai Ministry of Health committee also successfully used a compulsory license as an effective tool to lower the price for other ARV drugs.

From 2004 to 2006, the Thai government was actively negotiating the price of Kaletra with Abbott. In 2006, Abbott initially offered a rate of $2,976 per patient per year [21]. After being pressured by the Thai MOH and NGOs, Abbott lowered the offer to $1,000 and declared no further price reduction. Because kaletra’s cost of production was less than $400, the Thai MOH decided to issue a compulsory license. Abbott responded by arguing that the Thai government was ignoring the patent law and threatened to withdraw registration of all new drugs in Thailand. However, the WHO along with many other individual countries and NGOs affirmed that the movement of issuing compulsory licenses was consistent with International Law. In 2007, Thailand and other developing countries succeeded in reducing the price of generic kaletra to $676 per patient per year [22].
The Practice of Compulsory Licenses in Developed Countries

Developed countries such as the USA and Canada have also made full use of compulsory licenses in the field of public health to maintain the national interests and solve public crises according to the Protocol Amending TRIPS. In October 2001, there was a nationwide anthrax scare in USA resulting in rising demands for ciprofloxacin (Cipro). Anecdotally, many health professionals believe that “it is not anthrax, but the price of the drugs for anthrax that caused the panic.” The US government was faced with a dilemma during the 2001 anthrax scare. The US government consistently supported intellectual property protection for large pharmaceutical companies. Therefore, issuing a compulsory license for Cipro was a controversial act. In the end, the US government used the threat of a compulsory license to force Bayer to significantly lower its price and thus saved $276 million [23].

From 2005 to 2007, the Italian government issued a compulsory license for three drug types, including an anti-infection antibiotic, a drug for the treatment of migraine headaches, and a prostate drug. The Italian government also authorized the export of these drugs to other EU member states. These actions are countermeasures to prevent monopolies under the provisions of Article 40 in the Protocol Amending the TRIPS agreement (James 2007).

Unlike the decisions of the US and Italian governments to use a compulsory license for their own interests, Canada, the first country to amend its domestic intellectual property laws according to the 2003 General Council’s decision on the TRIPS Agreement, used the compulsory license for the purpose of helping people in developing countries to obtain urgently needed medicines. Canada’s Access to Medicines Regime (CAMR) was drafted in May 2004 and became effective in May 2005 [24]. CAMR requested the generic drug producer first negotiate voluntary licensing from the patent holder before issuing the compulsory license. After failed negotiation with GlaxoSmithKline and Boehringer Ingelheim, for a voluntary license and with petition from Rwanda to the World Trade Organization, Canada granted the Apotex company a compulsory license for TriAvir in [25] to be exported to Rwanda [26].

The Urgent Demand for Generic Drugs in Developing Countries

Generic Drug Demands for Infectious Diseases

The epidemics of AIDS, tuberculosis, malaria, and other major infectious diseases and the shortage of treatment drugs and preventive vaccines are the most serious public health problems in developing countries. Due to the lack of effective medicines and necessary medical intervention, infectious diseases in developing countries threaten global public health security. WHO officers pointed out that in many developing countries, especially in Africa, the major issue is finding a way to import drugs for infectious diseases as soon as possible.
According to Joint United Nations Programme on HIV/AIDS [15], Global AIDS Report, there were 33 million people infected with HIV in the world, with over 90% in developing countries, including 22.5 million people living in sub-Saharan Africa [15]. WHO, UNICEF, and UNAIDS reported that there were 14 million AIDS patients and HIV infected people needing ARV treatment. However, only 30% of them received the necessary medications [27]. Recently published research demonstrated that early ARV treatment in discordant couples and preexposure drug prophylaxis in MSM (men who have sex with men) can significantly reduce HIV transmission. These findings will greatly increase the demand for ARV drugs in the near future.

According to the WHO data in 2010 [28], there were 8.8 million TB cases, 1.1 million TB deaths in HIV-negative populations, and an additional 0.35 million deaths in HIV-positive populations. In 2010, there were 5.7 million notifications of new and recurrent cases of TB, equivalent to 65% of the estimated number of incident cases. India and China accounted for 40% of the world’s reported TB cases, Africa for another 24%, and the 22 countries with the highest TB rates accounted for 82%. Fewer than 5% of new and previously treated TB patients were tested for multidrug-resistant tuberculosis (MDR-TB) in most countries. The reported number of patients enrolled in MDR-TB treatment has increased, reaching 46,000. However, this was equivalent to only 16% of the 290,000 cases of MDR-TB estimated to exist among reported TB patients in 2010.

China is one of the 22 countries characterized as having a severe TB epidemic, ranking the second after India. There are 1.3 million patients diagnosed with a TB infection, comprising up to 14.3% of the global incidence and 80% of which are from rural areas, especially the northwest part of China where the economy is least developed [29]. The MDR-TB epidemic in China is very severe and accounts for 1/4–1/3 of the global incidence and is listed by WHO as one of the countries/regions requiring special attention [30]. All drugs available for MDR or XDR TB (extensively drug-resistant tuberculosis) are brand drugs manufactured by the big pharmaceutical companies in developed countries.

The 2009 WHO World Malaria Report [31] indicated that 3.3 billion people globally are threatened by malaria, exceeding half of the world’s population. Each year, there are about 250 million cases of malaria, 85% of which are in Africa with the majority being children. The most severely hit populations are in sub-Saharan Africa with an average of 3,000 children under the age of 5 dying from malaria each day. There is limited access to antimalaria treatment, especially the artemisinin-based combination cocktail medicine, in Africa. In 2007–2008, 11 of the 13 African countries with available data showed that less than 15% of population under the age of 5 with a fever received the combination cocktail medicine. In 2008, the public health facilities in some African countries could only meet half of the demand for antimalaria medicines.

Hepatitis B virus (HBV) has one of the highest morbidity rates and is sometimes referred to as the “second cancer.” There are 350 million patients with chronic HBV infection globally, 30–40% of which are chronic HBV patients. China is greatly affected by this epidemic, currently with 120 million chronic HBV infection cases and 3 million chronic HBV patients. It is estimated that the total direct and indirect
loss due to chronic Hepatitis B (including Hepatocirrhosis and Hepatocellular Carcinoma) costs 90 billion Chinese RMB each year [32]. Since all antiviral drugs for HBV and HCV are imported brand drugs, most people in developing countries, including China, cannot afford to use the antiviral drugs for their treatment.

A Case Study of the Chinese Pharmaceutical Industry

There is a high demand for medicine in developing countries. These demands are increasing each year, especially in countries such as China and India with rapid development and improving living standards. In China, Mr. Mingde Yu, President of the China Pharmaceutical Enterprises Association disclosed that because of the recent spike in demand for medical drugs and medical reform, the market share for common medicine has increased to over 160 billion RMB [33]. The annual growth of the pharmaceutical industry in China is expected to be at 30%. It is estimated that the total pharmaceutical sales in China will amount to US$46 billion in 2011 with China as the third largest pharmaceutical industry after the USA and Japan [34]. A survey conducted by CSPS Parma in the top-notch hospitals (the AAA level in the Chinese Hospital grade system) in Beijing and Shanghai showed that foreign and imported medicines comprise 97% of sales and that the top 100 drugs used in those hospitals are all imported drugs. The gross output of China’s pharmaceutical industry was 866.68 billion RMB in 2008. The total incomes of the medical and pharmaceutical industry were 778.79 billion RMB, with 449 billion RMB from chemical drugs, biological drugs, and traditional Chinese medicines. In contrast, the gross sale of joint venture and foreign enterprises was about 200 billion RMB, comprising 35–45% of China’s market [35]. Essentially, half of China’s pharmaceutical market was controlled by the foreign companies.

Statistics also showed that the market expansion for the domestic pharmaceutical industry was about 10% while it was 40% for the international pharmaceutical companies, mostly due to the patented drugs. Patented drugs usually are a dozen times more expensive than the generic drugs. Patented drugs only comprise about 5% of all drug usage in China, but make up over 20% of sales of the total drug market. To promote universal medical coverage, generic drugs are invariably a better choice for China and other developing countries.

Generic Drug Production Capacity in Developing Countries

Generic Drug Factories and their Capability in Developing Countries

China and India are among the largest global producers of generic drugs and play a major role in providing essential drugs to their people, including more than one-third of the world’s total population. China is the largest producer and exporter of
API (Active Pharmaceutical Ingredients) supplies [36] to many multinational pharmaceutical companies and takes up half of the global API market share for many antiviral drugs. According to incomplete statistics, the USA is China’s largest purchaser of API. Most of the common antibiotics API in Europe also come from China and India [37].

The four largest API manufacturers for ARV drugs in China could supply almost all of the current ARV drugs worldwide. Their annual production capacity is 7,690 tons, with 60–70% exported and with India as the largest purchaser, followed by western pharmaceutical companies. In response to the low demand of the Chinese for antiviral drugs, the four companies recently developed limited manufacturing capabilities of four to five off-patent ARV drugs. The annual production capacity of these four companies is 96 billion pills. Due to the small domestic market, the sale capacity was less than 1% of production capacity [38]. China has about 5,000 pharmaceutical companies and about 10% are on a similar scale to the above four companies. Many of them also have dual operations with majority API exported and medical drugs mainly sold in the domestic market. Chinese companies have developed many generic drugs including the popular three-ARV drug combination pill. Due to the patent issues, China’s State Food and Drug Administration (SFDA) does not accept generic drug applications for these drugs under patent protection. The small domestic market and the patent obstacles of the international market have severely restricted the ability of the Chinese pharmaceutical companies to satisfy the huge demands for essential medicines both at home and in other developing countries.

The Chinese companies hope that the government can implement compulsory licenses to improve their situation. In their opinion, if the country issues compulsory licenses, the generic ARV drugs they manufacture can be exported, which will expand the country’s production capacity and further reduce the cost of the ARV drugs. For instance, the price of lamivudine (3TC) could be reduced to one-tenth of the current price in China and nevirapine to one-tenth of its international price. Trizivir would only cost 1,000 Chinese RMB per year per person, which is two-fifths of the lowest international price. The companies promise to provide free ARV drugs for the national treatment program once they gain access to the international market [38].

**The Major Role of the Indian Pharmaceutical Industry in the Global Market**

The recent astounding rise of Indian pharmaceutical industry has made it the leading industry in the country. India ranks fourth in the global pharmaceutical market [39]. The swift rise of Indian pharmaceutical industry is greatly due to the production of generic drugs. Reddy, an Indian pharmaceutical company, started by producing API for Ibuprofen and exporting API of Methyldopa to Germany in 1986. Its API production passed SFDA (should be FDA?) certification in 1987–1990. Reddy set up distribution centers in America and France in 1992 and 1993. By 2005, 56 products...
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passed the US Food and Drug Administration (FDA) certification with a sales revenue reaching US$175 million. After 4 years of effort, Reddy’s production facility for Ranitidine (a nonpatent drug) passed the FDA certification in 1998, and the gateway for medical drugs to developed countries was opened. Currently, 35 of Reddy’s nonpatent drugs have passed the FDA certification. The company also owns many distribution sites in America (with headquarters in New Jersey) and Europe (with headquarters in England). Other Indian companies, such as Ranbaxy and Cipla, have gone through similar development paths [40].

India is arguably the largest generic product production country in the world. It houses more than 20,000 pharmaceutical companies, around 260 of which are large-scale companies. India can produce nearly all popular domestic medicines and around 350 common medicines, which meets 70% of its domestic needs. Indian medicine accounts for 8% of the global medicine sales volume. It is the fifth largest producer of APIs worldwide, with an estimated market value of $0.8 billion and is increasing at the rate of 13.4% per year [39].

Meanwhile, India is the largest exporter of nonpatent drugs; 40% of its products are exported to more than 100 countries [40]. Presently, the export revenue of most Indian pharmaceutical companies accounts for more than half of their total revenue. Indian pharmaceutical companies now account for 20% of American generic drug market share.

By 2000, the exportation value of Indian generic products had reached $1.6 billion [41]. In 2008, the confederation of the Indian pharmaceutical industry reported that medicine exportation accounted for 4.1% of all Indian exportation, and forecasted that the generic product exportation would reach US$10 billion by 2010 [42]. The International Aid Institution Oxfam reveals that more than two-thirds of Indian generic medicine is exported to other developing countries, and that the successful operation of the UN Children’s Fund, Médecins Sans Frontières, and other aid efforts rely on the low cost of Indian generic pharmaceutical products [43].

**Lessons Learned from the Indian Pharmaceutical Industry**

The success of the Indian generic drugs is greatly attributed to the Indian governmental support, its unique patent laws, and the government policy. Indian premier Rajiv Gandhi once said, “Medical inventions are not patented, and we cannot make profits between life and death.” The patent law issued in 1970 declared that food, medicine, agricultural chemicals cannot be patented; only the method of making these products can be patented. Therefore, one can make the same exact product or drug by a different methodology according to the Indian Patent Law. This regulation was vital to the rise of the Indian domestic pharmaceutical industry. For many years, the Indian government has withstood pressure from western countries and maintained efficient laws for generic production on the grounds of promoting health and equity. After its entrance into the WTO in 1995, India was pressured by western
countries to enter the TRIPS agreement but was granted a period of 10 years to adapt their patent laws to the international standards. India issued the 2004 Patent (amendment) Bill on December 26, 2004. This law mandates that India must begin accepting medicine, agricultural chemicals, and food patent applications from January 1, 2005. However, the Indian government stated that they would only recognize applications submitted from January 1, 1995 onwards and also declared that certain drugs, methods, or applications cannot be patented. At the same time, the Indian Patent Office maintains a unique flexibility in its approval process for generic drugs [44]. For example, if the US FDA has approved a drug, a generic version can be approved for use without first going through a clinical trial in India.

The Indian pharmaceutical industry is at a high level of internationalization. Facing strong foreign competitors, Indian pharmaceutical companies’ success is mainly due to their strong entrepreneurship, talented researchers and business development people, and the high quality and low price of their products. India has strategically entered foreign markets by buying up the US and European local pharmaceutical companies. Many Indians are trained in the west and thus fully understand the regulation and the western culture. Their ability to communicate in English also simplifies their international work.

Generic Drug Use in Developed Countries

It is reported in the Journal of the American Medical Association that the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR) saved an estimated $323,343,256 from 2005 to 2008 through the use of generic ARV drugs [45]. This significant cost savings contributed to PEPFAR’s ability to dramatically improve access to antiretroviral therapy in sub-Saharan Africa and other regions. In 2008, there were eight PEPFAR programs that procured at least 90% of ARV packs in generic form. Additionally, deliveries in Ethiopia, Haiti, Namibia, Rwanda, Tanzania, and Zimbabwe were more than 99% generic. The officer in PEPFAR strongly supported the use of generic drugs because saving money ultimately means saving more lives [45]. One of the biggest hurdles in the rapid scale-up of ARV therapy in developing countries is the high cost of the ARV drugs. However, developed countries in the west and large international pharmaceutical companies are strongly against the compulsory licenses. They often justify their standpoint that they believe it is against patent law to produce generic drugs and that such ability will have a negative impact on the research and development of new drugs. The use of patented drugs is acceptable in developing countries. However, given the current epidemics and public health crises in developing countries, patented drugs are simply inadequate. Generic medications provide an affordable means to provide treatment to more people suffering from HIV/AIDS. In order to solve the demand of patent drugs in developing countries, and to save more lives around the world, the best long-term solution can be provided by compulsory licensing.
Conclusion

Patent protection for medical drugs is a double-edged sword, encouraging discovery of new drugs but at the same time limiting accessibility to patented drugs. The significant polarization of the rich and the poor can be translated to accessibility and inaccessibility of medical drugs, which equates with developed countries and developing countries. Differing from other commodities, drugs are essential for saving lives. The international community has reached a consensus about the conflict between the monopolies protected by patents and public health and has chosen to protect public health and expand the accessibility of drugs. This decision is apparent in the TRIPS agreement adopted by WTO General Council in 2005. Developing countries should use the rights endowed by Protocol Amending the TRIPS agreement and issue compulsory licenses for drugs against major diseases to safeguard the health of their people and public health interests of their nations.

Some developed countries and large pharmaceutical companies had opposed the implementation of a compulsory license practice by developing countries, arguing it might hinder drug discovery research. The truth behind this claim, however, is that governments have the resources to buy the brand drugs. The large pharmaceutical companies lobbying to protect their monopolies also exert a strong influence. However, when there is a public health threat, developed countries will issue compulsory licenses without hesitation to solve the crisis. A good example is the US government forcing Bayer to reduce the price of Cipro using the compulsory licensing as a last resort after the September 11 attack in 2001. A WHO official pointed out that the global economy increases at an annual rate of 1%, much lower than the increase of average drug prices. According to the 2007 OECD report, drugs that took up 6–7% of the health budget of developed countries 10 years ago doubled or tripled their percentage in the health budget today [46]. At the present trend, developed countries may have difficulties affording the high drug prices in the next 10–20 years and may choose compulsory licensing as a tool to solve their health care.

As for developing countries, drug cost takes up a much larger percentage (20–50%) of their limited health expenditure. If strong measures are not taken, the government will be unable to provide enough drugs to its citizens, especially to the vulnerable groups. A tragic example of this occurred in the first 10 years of ARV treatment for HIV/AIDS. While the treatment was widely available in developed countries, AIDS patients in developing countries, which make up more than 90% of the AIDS patients worldwide, were still dying in large numbers. Some developing countries such as Thailand, Brazil, Malaysia, and South Africa took a bold move to provide generic drugs to their AIDS patients through the compulsory licensing. Such acts not only saved many lives, but also eased the burden of high drug costs and prevented the collapse of their national economies. Canada, a developed country and member of the G7, has initiated a compulsory license to provide ARV drugs to the HIV/AIDS patients in Africa.

Countries with large emerging economies, such as India, China, Brazil, and South Africa, are not only faced with the public health challenges of financing
essential drugs and vaccines for their huge population but also the responsibility to help other developing countries, especially the least developed countries in Africa, to solve their public health crises. China is the world’s largest producer of APIs, including more than half the global APIs used for ARV drugs and antibiotics. India is the world’s largest producer for generic drugs. Therefore, it is advantageous for all developing countries to work together for the research, production, and distribution of generic drugs.

Through the PEPFAR and other global health programs, the USA is the largest founder and the major player in the global AIDS, TB, and malaria treatment programs covering African and other developing countries. Most of the ARV drugs used in these US founded programs are actually generic drugs manufactured in developing countries, mostly in India. Additionally, the big pharmaceutical companies in the developed countries developed all of the ARV drugs and most of the anti-TB and malaria drugs. Some of the drugs were developed by developing countries, such as artemisinin, which was invented by the Chinese scientists. Without the close collaborations in the last decade between the south and the north and the private and public, the lives of several millions of HIV/AIDS patients, TB patients, and malaria patients would not have been saved. Therefore, developed countries and big pharmaceutical companies must ally with the developing countries in the war against AIDS, TB, malaria, and other infectious diseases. Due to the lack of such collaboration, the initial sparks of HIV infections in central Africa become a global AIDS pandemic killing 30 million lives in both the developing and developed world. Such tragedy can only be prevented through further strengthening collaboration between the private and public sectors in both developed and developing countries.

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