Globalization of Biotech-based Drug Markets and its Implication for the IP System

Takuma Takahashi*

Abstract: Examining the development of the patent system which addresses to the birth of biotechnology in the past three decades, we argue that the patent system set by the United States have finally come to function as the “one size fit for all” system for the global markets. This may illustrate that good laws and rules contribute to the economic development advocated by Romer, in the sense that they have contributed to transforming the industry which used to be separated between normal and pirate market into a more integrated condition. Interactions between interest groups and some other factors such as NPO have augmented the “one size fit for all” system.

Key Words: Patent, public goods, pirate, biotech-based drug, boundaries of community,

1 Introduction

In the biotech drug markets the concept of translational research has worked as the key word that embraces science, patent, and drug. Translational research is defined by Pisano (2006) as the research bridging between the early stage of basic research and human clinical testing1. Business models in biotechnology have long been taking the shape of the so-called molecule-to-market companies, which have found a particular molecule presumably applicable for drug and developed it to the marketable level.

The boundaries of public goods, scientific results and patentable items have, however, become blurred, as the research in biotechnology and biotech-based drug markets have globalized and as the world economies themselves deepened. This has led to the frequent disputes over the boundaries.

Let us look at the people’s attitudes towards the patent or science in facing the risk of air flu through two examples.

The first example is that Cipla, an Indian company, won in a 2008 court case in India permitting it to manufacture a cheaper generic version of oseltamivir, marketed by Hoffman La Roche under the trade name Tamiflu. The Indian justice is that what are badly needed for the poor should be delivered at reasonable prices. While the basic U.S. patent term for the medicines is 20 years, as much of the time is spent in research

*Meijigakuin University. The author thanks to Tadatoshi Higashizono, Hiroshi Kohno, Yoshihiro Ohtaki, and Teruo Susumu, for their comments on the earlier draft.

1 Translational research is, in a broad sense, a way of thinking about and conducting scientific research to make the results of research applicable to the popular and practical areas in the natural and biological, behavioral, and social sciences.
and development. Thus the effective patent life for medicines is much shorter. According to Grabowski and Kyle (2007), the average time on the market for medicines with annual sales of more than $100 million (which accounts for 90 percent of the sales of medicines exposed to generic competition) before generic competition that started in 2005 was 11.5 years. This is a real challenge to the patent system which is designed to prevent the relevant invention from free-riding. In other words, there is no single industrial community in the world: what prevails is the confrontation between the developed nations and the developing nations2. We can say that the world drug industry had two different markets: the normal one and the so-called pirates one, until India adopted the product patent system in 2005, paving the way to its joining of the WTO.

As the second example, we witnessed the dispute between the academic community and the security community, when the US government intervened to stop the publication of scientific discoveries. The National Science Advisory Board for Biosecurity (NSABB) argued that the work by Yoshihiro Kawaoka’s group (accepted by Nature) and an independent study (accepted by Science) led by Ron Fouchier of the Erasmus Medical Center in Rotterdam, the Netherlands contains very serious points because H5N1 viruses have the potential of spreading among mammals. While scientists argue that they should pursue transmission studies of the highly pathogenic avian influenza viruses to urgently cope with the potential future pandemic, the US biosecurity chiefs deeply concern that the research papers may be applied to the bio-hazard weapons just as the international terrorists used the anthrax bacteria in the past. Kawaoka, a University of Tokyo professor, has conducted his research in Canada and the United States because University of Tokyo doesn’t have any P4 level facility. At the same time he has long been stressing the need to discuss the way of appropriate disclosure of this kind of articles. After a two day emergent meeting of expert on bird flu and securities, the WHO declared that these studies should be published as soon as the international regulations and guidelines for the flu virology laboratory operations are set forth3.

We have witnessed in rather e extreme cases. While the Indians seem to have claimed what is needed in a certain community within the deepening and expanding global economy should be public goods, the U. S. government seems to limit the boundary of the public goods from the security point of view. As air flu episodes suggest,

---

2 This situation is similar what Takahashi (2005a) described as the rivalry between the United States and Japan in the 1980s and that between Japan and Korea in the early 2000s in case of electronics industry, but the degree of confrontation is severe in this case.

3 Keiji Fukuda, an assistant general secretary at the WHO, told the steering committee would set the international guidelines within few month.
there are many interest groups that ascertain their desires and their own justices. Indeed, the rules depend to a very large extent on individual norms about right or wrong. A variety of participants will interpret differently what they believe to be the best path to pursue (Simon, 1982).

Merges (2011) argues that IP rights are based on a solid ethical foundation, and when subject to fair limits, these rights are an indispensable part of a well functioning society. Many reports revealed that unlicensed use of patented inventions is common in the context of research (Walsh, Arora, and Cohen, 2003; Cohen and Walsh, 2008). Supporting such practices, Cohen and Walsh (2008) and Strandburg (2010) argue that ignoring patent rights in the academic community is permissible, or even relevant as a “working solution,” as its norms are different from those in the industrial community.

How should we cope with these situations? Romer (2010) argues that an analysis of the interaction between rules and technologies may help explain important puzzles such as why private firms have successfully diffused some technologies (mobile telephony) but not others (safe municipal water.) He has tried to explain developing nations’ strategies for growth through better rules and institutions in a broader picture, i.e. the explanation of the great divergence\(^4\). As he takes up the patent system as an example for better rules and institutions, we would like to take up the biotech-based drug industry which used to be in some conditions like safe municipal water, and to explain that a set of global patent laws, such as the “one size fit for all” system, contribute to transforming the industry to assume a more integrated condition.

It’s often said that the government should maintain patent incentives at home and support them abroad to assure a greater certainty that encourages continued medical innovation for the patients. If we assume all of the people in the world were living in the same community, it might be natural for many scholars to advocate the clarification of the law and tough actions on infringements (Besen and Meurer, 2008; Lemley, 2008). Lamenting that high information costs and transactions costs provide shelter for infringing behavior that might otherwise lead to either licensing or liability, Eisenberg (2008) might rightly argue the clarification of certain area could preserve the patent laws as ‘one size fits all.’

However, these kinds of arguments are not relevant for the real world which is consisted with quite different communities. It is difficult to find a single set of norms in different communities. In other words, the wisdom on patent described above could not be applicable in the 1980s. A new norm in the age of biotech-base drug age was created

in the United States when the Supreme Court upheld the patentability of a genetically modified bacterium in 1980, quoting the Congressional report. Since then, the US government has asked other nations to adopt the same system in order to produce the business environment suitable for the US firms. With fast progress in biotechnology, the developed nations have adopted the same patent system rather quickly. But the process of adopting the same patent system by the developing nations was very slow despite the emergence of integrated and enlarged global economy. Even when almost all of the nations have adopted the same system like that of the United States, the system would become loose and altered by the interests of various participants and those of different communities as seen in the free use of Tamiflu in India.

Despite these facts, however, many pharmaceutical companies have come to target BRICs markets as they form critical masses and grow faster than the developed nations such as the United States. As the so-called the sense of the global community has emerged and expands its scope, the interests in the pandemics and tropical diseases have also aroused. The interactions between the different communities seem, in turn, to have gathered a momentum for forming a global community for the patent laws. But we need some different augments such as free-libre biotechnology to support a set of global patent laws as “one size fit for all.” Advocating the free-libre biotechnology within the researchers community, Pénin and Wack (2008) wonder how the patent system would look like if localized communities which have different norms and rules try to adopt their own free-libre biotechnology.

To explain the development of the patent system which addresses to the birth of biotechnology in the past three decades, we will first present the anatomy of intellectual property rights in the next section. Then, in Section 3, we will discuss on globalization which has occurred as a two-step phenomenon: first as the triad economy and second as the so-called globalization, in line with the upsurge of such countries as China and India. We will also touch upon the role of the international organizations such as the WIPO and the WTO.

In Section 4 on the consequences of two track approaches, we take up the problem of the IP system integration between the communities with different interests. The first track is seen between the science community and the business community, while the second is found in India’s strategy as a caching-up economy to make a leap to a full membership of the WTO. Using such techniques for bargaining and leveraging, we note that things have gone better. In Section 5, which asks if the global community has emerged, we will first point out that some big pharmaceutical companies come to regard the emerging markets as their strategic target, whereas others seem to have stayed as
they were. We will take up the role of the NPOs to ask to take an affirmative action for the business side through its financing, and to coordinate research agenda, eventually augmenting the shortfalls of the patent system. Thus we would help integrate efforts in various communities in the global economy by applying a set of global patent laws as the “one size fit for all” system. Final section will present a short conclusion from these qualitative observations.

2. Anatomy of Intellectual Property Rights

Romer (2002) asserts that economic analysis of property rights proceeds in two steps. The first distinguishes rival from nonrival goods. Whereas rival goods like cake will disappear when they are consumed, nonrival goods like music are not consumed when they are used. Presenting Table 1, he explains the two types of goods have different degrees of appropriability or excludability (Romer, 1998). Nonrival goods imply that the marginal production costs are zero. Few goods are completely nonrival as rivalry can emerge at certain levels. We had better, as Romer himself asserts, to view

<table>
<thead>
<tr>
<th>Degree of Appropriability</th>
<th>Rival Goods</th>
<th>Nonrival Goods</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td><em>Private Goods</em></td>
<td><em>Scrambled satellite broadcasting</em></td>
</tr>
<tr>
<td></td>
<td><em>Underdeveloped land</em></td>
<td><em>CD music</em></td>
</tr>
<tr>
<td></td>
<td><em>Automobile</em></td>
<td><em>Design of MPU</em></td>
</tr>
<tr>
<td></td>
<td><em>Works of laborer</em></td>
<td><em>Computer code</em></td>
</tr>
<tr>
<td></td>
<td><em>Fish in open sea</em></td>
<td><em>Operation manual of Wal-Mart</em></td>
</tr>
<tr>
<td></td>
<td><em>Clear air</em></td>
<td><em>Theory of chemical engineering</em></td>
</tr>
<tr>
<td></td>
<td><em>Sterilized insect to prevent pest</em></td>
<td><em>Windows-based GUI</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Do loop in computer programming</em></td>
</tr>
<tr>
<td>0%</td>
<td></td>
<td><em>Public Goods</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Basic Research in Physics</em></td>
</tr>
</tbody>
</table>
rivalry as a continuum rather than in binary category, where many goods are someplace between the two extremes of completely rival and completely nonrival. Although public goods can be defined as both nonrival and zero approriability goods, rival goods such as clean air are generally accepted as public goods.

The second step contrasts the welfare effects of property rights for these two types of goods. As to the rival goods, strong property rights lead to efficient outcomes. As North and Thomas (1990) pointed out, land ownership was an important trigger for European economic development in the Middle Ages. For non-rival goods, property rights involve the tradeoff formalized by Nordhaus (1969). Weak property rights lead to under-provision. Strong property rights create monopoly distortions. The patent system is to address the intellectual property rights, which are nonrival or possibly public goods.

While Price and Bass (1968) define knowledge as the stock of information, Romer (2010) tries to explain that the massive accumulation of knowledge has been instrumental to the development of the economies. Indeed, we can produce information after studying and becoming inspired by the existing stock of information, including the works of predecessors in the origination of knowledge, as Scotchmer (1991) stated. Late comers tend to assert that all stock of information, including newly originated knowledge, should be utilized as public goods. Inventors, on the other hand, argue that the rights to new information should be protected. While these views conflict with each other, the anti-monopoly policy will take the balance between these interests. This relationship is just that between the developing nations and the advanced nations as we will see in the moment.

As to information called Arrow (1962)’s paradox is known: Purchasers of information would not buy the information if they don’t know its usefulness, but if they possess the information, they need not to buy it any longer.

It is, therefore, grounded in order to promote the progress of science and useful arts, by endorsing only for limited times, to authors and inventors the monopolistic powers to their respective writings and discoveries. To be patentable, an invention must consist of a process, machine, manufacture, or a composition of useful, novel and non-obvious matter. The requirement of usefulness or utility, is satisfied if the invention is operable and provides a tangible benefit.

Thus the patentable area can be explained by the notion using interpreted information and originated in formation (See the plain diagram of Figure 1). The zone for patents is denoted by triangle ABC, while the zone for copy rights is ABD. The
granting of a patent depends on inventiveness or obviousness of novelty, and thus, the area of patents granted is limited to the shadowed area of triangle ABC.

As the economies developed, more nonrival goods have been produced and rival goods have been equipped with more rival goods. In other words, society becomes more geared toward the origination of knowledge through the use of information technology. In the past, steel-making technology, which contained tacit knowledge, was not easily copied. By contrast the semiconductor chips, which are expressed by explicit knowledge or digital information, can easily be copied. However, the birth of the US biotechnology was more dependent on human and tacit knowledge (Zucker, Darby, and Brewer, 1998). To comply with this situation, the modern society has needed the expansion of the intellectual property rights by introducing the Semiconductor chip Law, under which designs come to be protected and copy rights expanded. The patent and copy rights used to be different because of the different features of usefulness and expression, but today’s intellectual property rights are integrated, and the boundaries between the patent and copy rights become blurred as shown in the stereographic diagram of Figure 1.

Considering Arrow’s paradox, the patent system is constructed by combining the elements of exclusivity and revealing the patent information so that it may prevent free-riding of the invention and save the information cost of accessing the invention value. With this configuration, the patent system has contributed to disseminate

Figure 1  Anatomies of Intellectual Rights: From Plain to Stereographic View
knowledge within a certain community, help create a market for technologies (Arora and Fosfuri, 2000; Gans and Stern, 2003) and ease inter-firm negotiations and collaborations (Pénin and Wolff, 2008).

3. The Deepening of the Globalized Economy

A patent application filed under the PCT of 1970 is called an international application, or PCT application. A PCT application itself does not ensure the grant of a patent, but these will be the announcement or something, in which patent protection is pending under a single patent application filed with the patent office of a contracting state of the PCT. In other words, a PCT application, which establishes a filing date in all contracting states, must be followed up in step with entering into national or regional phases in order to proceed towards grant of one or more patents. While it is the hope that the PCT procedure essentially leads to a single standard international patent application, the PCT application today suggests the existence of a number of important patentable items.

The patent system that the United States set in the 1980s and thereafter is not industry specific as described in Figure 1. The Patent Law Treaty (PLT) of 2000 will bind 60 states and European Patent Organization to harmonize the patent systems of the participating member states, excluding such important states as China and India. In term of the number of PCT patent application, China’s ranked 4th in 2011. But the country’s total applications for patents including the domestic filings which, not by the same standards as those of the developed nations, exceeded those of the United State in 2011. As a result, the troubles have also increased in conjunction with China’s patents, and now to negotiate to include China in the PLT scheme has become an immediate agendum. With the Corsica Meeting in June as a kickoff, a meeting of the patent office chiefs will start negotiations to harmonize their systems in 40 items.

In this section, we will also examine the past developments of interactive spreads of the US patent system, focusing on the area of biotechnology: first over Japan, one of the developed nations and then India, one of the developing nations.

The Triad Economy and the Age of Information and Knowledge-Origination

We have argued that the age of information and knowledge-origination began around 1985, changing from the age of industrialization. According to DataStream, corporate
expenditures on R&D exceeded investment in plant and equipment in 1985, and since then the gap between the R&D and physical investment has been expanding. The same trend has been observable in Japan, though it is feeble due to the so-called “lost decade” that ensued the burst of a bubble economy in 1990.

In the information and knowledge-origination society, corporations can make profits only when they can make the difference by producing new knowledge. But as new knowledge goes obsolete quickly because of digitalization of knowledge, corporations have to produce new knowledge again and again. This situation is similar to the relationship between the developed and the developing nations. Arrow (1962) believed that a failure in the production of new information stemmed from the failure to separate the risk that is inherent in the production of information from the negligence which occurs in decision-making regarding the production of originating information. The developing nations decide not to produce originating information and to learn from the predecessors. Thus, the game between the developing and the developed nations is, as Gerschenekron (1962) pointed out, usually in favor of the former.

As we have discussed before, choosing right policy and rules is crucial for the development of the economies. While the property rights in the age of agriculture age centered on land ownership, while corporate ownership was of paramount importance in the long history of capitalist development in the age of industry. With an advent of the information and knowledge-origination the intellectual property rights have come to the fore.

It was the United States that addressed to the changes in the economic elements by opening the door to the registration of computer software through revising its copyright law in 1980. In 1980 Supreme Court upheld the patentability of a genetically modified bacterium by quoting the Congressional report which referred to the 1952 Act that "anything made by man under the sun" should be patentable. Thus, copyrights protect microbes (they must be deposited), new species of plants made by asexual reproduction, and even mathematical solutions. In order to swing the balance between the IP rights and the anti-monopoly, the U.S. created the Court of Appeals for the Federal Circuit (CAFC) in 1982. By utilizing the CAFC, there arouse the litigations over the IP rights and resultanty strengthened the IP rights, applying the doctrine of equivalents.

The doctrine of equivalent empowered the U. S. court to claim the infringement of a certain invention, even when the infringing device or process does not fall within the

---

5 We can see further evidence from a different side. Prices for natural resources hit a peak in 1985, causing severe economic damage to such resource-producing countries as Australia, New Zealand, and Malaysia.
literal scope of a patent claim, but nevertheless is equivalent to the claimed invention. This doctrine gives favor for the so-called breakthrough innovation, when it is an achievement of an inventor who produces C different from A with b as a catalyst as seen in Figure 2. On the other hand, an incremental or follow-on innovation is A', something similar to A. Breakthrough innovation should have more originated information in addition to the interpreted information, in comparison with an incremental or follow-on innovation. Under the doctrine of equivalent, the invention is broadly defined to the extent to ban analogy and metaphor in advance. Thus, this doctrine hinders late comers in trying to pursue the follow-on innovation.

Figure 2 Breakthrough Innovation and Incremental Innovation

![Diagram of Breakthrough and Incremental Innovation]

Previously, the assumption was that the patent royalty fee would be 2-5% of sales. This was used to calculate damages, but the CAFC sharply increased the amount, which sometimes reached as high as 30%. When the CAFC found the cases of willful infringement of a patent, it frequently imposed multiple damages, which amounted to double or triple the amount, invoking Article 284 of the Patent Law. Thus, the creation of the Federal Circuit Court of Appeals has, if nothing else, led to a more coherent body of law than existed previously (Takahashi, 1995).

After modifying its patent system from ‘process patenting’ regime to ‘product patenting’ regime, the US government asked other countries to adopt the same system. In 1985, Japan and European countries followed the example of the United States and revised their copy right laws to protect computer software. Furthermore, Japan passed the Conductor Circuit Law in 1985, extended copyright protection to databases in 1987. In anticipation of an advent of a new biotechnology paradigm, Japan needed new registration and introduced Microbe and Plant Protection Act in 1990 as it was not under the precedent judicial system as in the United States.

Amgen’s victory in the case of Chugai-Genetic Institute has been well documented (Takahashi, 1993). But the Toyobo’s loss in the tPA (tissue plasminogen activator) case to Genentech in the US-Japan dispute of the doctrine of equivalents has not been popular even among experts on biotechnology. Toyobo, a Japanese textile company, tied
with a U.S. firm, Integrated Genetics, and by the end of the 1980s it developed tPA, a protease that converts plasminogen to plasmin and dissolves blood clots up to the clinical Phase III.

On April 15, 1987 the Japanese Patent Agency published the substance of tPA and Genentech manufacturing patent application. tPA is a new biotechnology derived substance which is reportedly very effective for thrombosis and other blood-clotting related diseases. In the U.S. context this should have an effect on all the Japanese counterparts including Toyobo which had tried to manufacture tPA by using the biotechnological methods. Japanese firms plan to file a protest against the agency's decision because European authorities seemed to define the discovery not so broad. For example, the July 1987 decision by the UK court found that Welcome's products did not violate any of Genentech's patents. On the other hand, Genentech in June received approval from the government of France to start the manufacture and sale of the tPA in France. Genentech's patent was judged ineffective in Germany on August 30, 1991, in part because of erroneous listing of amino acids. Toyobo counter-sued Genentech to suspend shipment of tPA to Japan on the principle that Genentech's patent was found ineffective in Germany and Britain, both of which have the same "first-applied, first-patented" system as Japan.

Indeed, Courts in Britain and Germany had judged the accurate sequence announcement that appeared in Nature, and therefore rejected Genentech's patent claim. Japan's Patent Office, which was examining the case simultaneously, granted the patent in 1991 after instructing Genentech to correct the description of amino acid sequences, applying a doctrine of equivalent under the heavy pressure by the U.S. government. In October 1996 the Osaka District Court rejected Toyobo's countersuit, enabling Genentech to become the biotech champion as Amgen.

It is true that the U.S. government was pressuring Japan to harmonize its system with that of the United States. Indeed, Japan responded by a two-stage reform. First, in 1994 Japan adopted product patents and revised its disclosure rules to increase secrecy. Second, the revised Patent Law of 1998 allowed broader patent claims. These revisions were necessary. As Japan became a frontrunner in science and technologies, its patent policy should establish the rights to scientific discoveries.

These harmonization efforts themselves, however, cause another problem: while the U.S. judicial system is flexible enough to chart new directions through an accumulation of cases, Japanese one doesn't have such flexibility. The United States has been expanding the scope and value of intellectual property rights since 1982.

But the 1996 Supreme Court decision in the Marksman case seems to have reined
in over-inflation of IP rights, recognizing the adverse consequences of defining patent rights too broadly. Thus, the court’s focus shifted to try to ensure that the protection given by any one patent was not overly broad compared to the significance of the invention that had been made. Pisano (2006) regrets that the U. S. biotech industry has not produced big integrated biotech-based drug company other than Amgen, but it is difficult for the biotech startups to have materials which have large scope of patents with large scope equivalent to those given to Amgen. As the biotech industry has matured, the scale of discoveries has shrank too.

The Japanese judicial system has not this flexible and case law cannot shift quickly enough to reflect new developments because Japan’s system depends very much on the clauses stipulated in the law. But the system and operations have changed gradually. Thus, the scope of patents in these days has been narrower than before.

To cope with this trend, many biotech companies have tried to expand its business scope of a certain biotech-based material or technique. The patent strategy of Merck & Co. applied for ivermectin may tell the way of broadening the patent, since the family of patents, whose story we will discuss soon, allowed the companies to develop a variety of drugs for animals and for human beings. Since ivermectin is a kind of antibiotics, or very old generation of biotechnology, this doesn’t directly show the patent strategy for the new biotech drugs though the almost same strategies are adopted in case of the new biotech industry. But it is visible for outsiders how a family of patents is chosen, because we can tell that the researchers predict certain outcomes in line with the evolitional progress of a certain targeted material⁶. This kind of patent strategy leads to the practice of “evergreening” of pharmaceutical patents.

Shinya Yamanaka’s iPSC (induced pluripotent stem cell) patent is believed to command exceptionally broad scope of protection in the sense of these days. IPS technology was pioneered in 2006 by Yamanaka of Kyoto University by using a mouse. By early 2008, Kazuhiro Sakurada, who had also been working on iPS technologies at the Kobe-based drug company Bayer Yakuhin, succeeded in making iPSC by using human cell and applied for the patent. Sakurada left Japan to head research at iZumi Bio — a biotech firm which focused on commercializing iPSC technology. iZumi Bio, now iPierian, was founded by Gladstone Institute where Yamanaka has been invited as a visiting professor, and Kleiner Parkins. iZumi Bio bought the human iPSC patent from

---

⁶ Another clear example is also seen in old biotechnology, not in the case of drugs. Novozymes, a Danish biotech company, discovered state-of-the-art enzyme solutions, Cellic, for converting biomass, which has more complex structure than traditional starch substrates, into cellulose ethanol by identifying the gene that codes for the desired enzyme and transferring it to a production organism known to be a good enzyme producer. The company is clever enough to have patented a family of Cellic, by prospecting the evolutional progress in enzyme to block the followers of this magical solution.
Bayer. Therefore, a potential conflict over the exploitation of patents for iPSC technology would be put to rest if Sakurada tried to claim human-based patent rights. But the US venture and Kyoto University announced in 2009 their collaboration to develop methods for using iPS technologies for drug discovery and therapy. This is probably due to the tacit agreement between the two parties that the discovery was done in Japan. By the same token, the patent scope of small interfering RNA (siRNA) is believed to be broad because it was tacitly judged as an invention of the United States. The patent rights of iPSC should not remain broad, if it takes a lot of time to apply for therapy or new technology which is superior to iPSC were appeared in the future. In other world, it seems to depend on the perception. But one thing that has confused the patent rights was the U. S. first-invent basis system. The current U.S. first-to-invent rule has given the protection to the trade secrets and resultantly the extension of patent protection period, because inventors are allowed to delay in the disclosure of discoveries until they file or challenge in the court (Friedman et al., 1991). Therefore, there arouse many priority dispute cases including the so-called patent troll under the current system, which would be resolved via costly ‘interference’ proceedings conducted at the USPTO. The U.S. government has been aware of this problem for a long time. But the Congress had failed to adopt the first-file basis because of domestic political circumstances up until recently when the U.S. passed the American Invent Act of 2011.

Adopting the first-to-file system, inventors are able to avoid the lengthy interference proceedings in an attempt to prove dates of inventive activity that occurred many years previously. Addressing to the shortfall of the first-to-file system, Japan also revised its patent law in 2011 to identify the true inventor in the case of stealing the invention by third party or others. Thus, the patent systems in the triad economies now have largely become harmonized, and the harmonized patent systems in turn would create efficiencies for inventors to seek patent protection in the U.S. and other markets.

Poor Integration of the Developing Nations into WIPO and TRIPs

The global economy has been integrated to foster the newly industrized countries and given the birth of BRICS, which in turn are leading the world economy. For example, China appeared as the second largest economy and the largest exporter in the world. No one denies that international organizations under the United Nations such as the WTO

---

7 We once pointed out that it is difficult to judge the nature high-tech products apart from its palace in the path of technological development(Takahashi and Namiki, 2003). The same thing is true in biotechnology.
and IMF have facilitated these developments. The globalization has, on the other hand, shown its adverse effects such as frequent financial crises and epidemics, including the AIDS.

The UN sets up the WIPO in order to promote innovation and creativity for the economic, social and cultural development of all countries, through a balanced and effective international intellectual property system. But developing nations have only limited knowledge as Bardhan (1995) pointed out. Therefore, it may be natural for them to have boycotted the WIPO by saying that the WIPO is only to promote the monopoly of the developed nations in the area of intellectual property.

In 1994, a new trend emerged, at least in part as a result of renewed attempts at globalization of the patent system, which had been grafted on to the Uruguay round of amendments to the General Agreement on Tariffs and Trade. This agreement, commonly known as TRIPS (Trade Related aspects of Intellectual Property rights) imposed certain minimum standards in patent protection on all member countries. It becomes important for the developed nations to include the developing nations as ideas and knowledge are an increasingly important part of trade. Many products that used to be traded as low-technology goods or commodities now contain a higher proportion of invention and design in their value, e.g. brand-named clothing or new varieties of plants.

As we discussed earlier, it is almost impossible to balance between the interest of developing nations (late comers) and that of the developed nations (inventors) without a true global institution. It is very conceivable that the extent of protection and enforcement of the IP rights is varied widely around the world. These differences became, therefore, a source of tension in international economic relations, as intellectual property has become more important in trade. China adopted about the same IP rights as prevailed in the developed nations in 2002, but the very poor execution level of these laws has been the source of complains from the developed nations. Having adopted the process patent up until 2005, India had been the leader of the so-called pirates drug markets, which cover many developing nations including Brazil and South Africa. This kind of activities is, by all means, against the interest of the global research-based drug companies.

On the other hand, the developing nations demand fair share of the benefits arising from the utilization of genetic resources, by appropriate access to genetic resources and by appropriate transfer of relevant technologies. This kind of demand stemmed from the Convention on Biological Diversity (CBD) born at the 1992 UN Conference on Environment and Development (the Earth Summit). The Nagoya
Protocol at the 10th COP takes into account all rights over those resources. The developing nations also demand the WIPO for paying fair fees on the knowledge of the traditional natural drugs such as quinine. Pandemics such as AIDS and bird influenza have put the relationship between the global drug companies and the developing nations in more complex situations. However, these parties have tried to find some solutions assuming they share the target of conquering the pandemic.

4. Consequences of the Two-Track Approaches

Patentable items are all originated information which have, as Schacht and Thomas (2011) point out, a nature of public goods. Intellectual property rights as one of non-rival goods, however, inevitably involve the tradeoff as formalized by Nordhaus. We will first take up the struggle between the scientific sphere and commercial sphere in the genome reading race and then discuss Indian efforts to comply with the product patent system, a standard prevailing in the developed nations.

A Genome Reading Race in Scientific Sphere and Commercial Sphere

Scientific activities are clearly conducted within boundary of public goods according to the definition of science by Paul Romer as shown in Table 1. Strong patents such as the PCR method, however, impose heavy burdens on the scientific activities. And more researchers have claimed their rights on their discoveries. Therefore, Heller and Eisenberg (1998) argue that the proliferation of intellectual property rights in biomedical research as an “anticommons” in which people underuse scarce resources because too many owners can block each other. This is the opposite to the case of the “tragedy of the commons” in which people overuse shared resources, but both are equally tragedies. This concern has been shared by many scholars (Walsh, Arora and Cohen, 2003; Nelson, 2004).

If we follow their advice, patent holders should make their patent portfolio available for licensing through ‘public license offers’ that offer needed technology to everyone on reasonable terms, while retaining the defensive benefits of patents. Otherwise, more intellectual property rights may lead paradoxically to fewer useful products for improving human health. While many empirical studies identified that unlicensed use of patent inventions is common in the context of research, as we have already discussed, some have advocated the creation of the biomedical commons (Benkler, 2006, David, 2006; Pénin and Wack, 2008).
Heller and Eisenberg assert that the privatization of biomedical research must more carefully be deployed to sustain both upstream research and downstream product development. We witnessed, however, the challenge to their advice, that is to say, the genome reading race between the scientific sphere and the commercial sphere (Takahashi, 2000). While the academic community infringed the patent rights of research tools, it was the investment community that invaded into the sphere of the academic in this case. The Human Genome Project started in 1990 as such an attempt, with a primary goal of determining the sequence of chemical base pairs which make up DNA, and of identifying and mapping the approximately 20,000-25,000 genes of the human genome. As a business model of selling access rights to its platform which provides proprietary genomic database, Incyte Pharmaceuticals was established in 1994 by venture capitalists.

When James Watson and Harry C. Crick presented the helix structure of DNA in 1953 and opened the door to generic engineering, the sequencing of genomes was very slow, because they were obtained only as the result of new discoveries of new genes or proteins. Since the early efforts to decipher DNA sequences were frustrated, no one had challenged them.

The first person that advocated the automated genome sequencing was a Japanese professor, Akiyoshi Wada at the University of Tokyo, who contributed to Nature in 1982. Hitachi provided the best DNA sequencer at that time. However, Wada’s idea was never supported by academia nor by the private sector in Japan. Instead the idea was accepted by American counterparts, and led to the Human Genome Project. Under the strong leadership of Jim Watson the HUGO was established as a framework of international cooperation in 1988. When he visited Japan in 1989, he insisted that Japan should contribute at least 30% of the project for human genome sequencing. However, the Japanese government rejected his idea and failed to provide enough budget to his counterparts in Japan for their pursuing of a proper proportion of the project.

As an alternative approaches, Ken-ichi Matsubara, another strong advocator of genome analysis, tried in vein to tap private money by organizing a consortium of genome project for profit. However, he felt that he and his colleagues in Japan stood on or in front of the frontlines of genome analysis, when he gathered topnotch genome enthusiasts such as Sydney Brenner and David Gallus, sponsoring in 1992 a genome workshop, “cDNA Research Today” in Osaka. J. Crag Venter of NIH, who was then regarded as one of obscure participants, got hint on his future attempt to start TIGR (The Institute for Genomic Research) on this occasion. Although it was not until 1998
that Venter started Celera Genomics with PE Corporation, now Applera Corporation, many biotech ventures such as Incyte Genomics were mashrooming. These ventures including TIGR and Incyte used the automated sequencers made by PE Corporation which got a license for its technology from Hitachi and improved it substantially.

The Human Genome Project and Celera Genomics in 2000 jointly announced their completion of reading human genome sequences. Since the Human Genome Project, whose research activities have been in the public domain, provided a complete and accurate database for human genome sequences, the economic value of genome sequence data provided by Celera Genomics or Incyte Pharmaceutical has become almost nil or modest. Reflecting this, the stock price of Incyte, which soared to $103 on March 3, 2000, declined sharply upon the announcement of completion, and was staying at a low of $4.56 as of December 31, 2002. In other words, the information on genome sequence has become common knowledge. Millennium Pharmaceuticals claimed that it used the database for hunting the drug targets. That was a different strategy from those adopted by Incyte Genomics and Celera Genomics. Indeed, its stock prices had behaved differently between them (see Figure 3). Having hunted for targets, Millennium Pharmaceuticals has remained as a vital biotech company, which was bought at $8.8 billion by Takeda Pharmaceutical in 2008.

When the human genome project was completed, Japan’s contribution was 6% against 67% by the U.S. and 23% by the U.K.. And the efforts in the private sector were almost completely absorbed by the scientific results achieved by the Human Genome
Figure 3 A Difference in Stock Price Behaviors between Incyte and Millenium

Project. When Koichi Tanaka, an employee at Shimadzu Corporation, was awarded the Nobel Chemical Prize as one of three scientists who invented the methods to inquire the structure and function of protein in 2002, Japanese hailed his achievement with fever, but at the same time reflected, with complex psychology, on the speed with which genomes of a living organism had been sequenced. It took only five years since the first full genome of a living organ was sequenced in 1995 to the completion of human genome sequencing in 2000. Without the two-track approach led by the Human Genome Project and the U.S. biotech ventures, the progress in the genome sequencer should not have been speedy and the competition between Hitachi and Applera Corporation might have yielded a different result.

Leveraging on the Dual World Pharmaceutical Markets: India’s Catching-up Policy

The patent system has the nature of public goods as we have already pointed out. The latecomers such as the developing nations would like to emphasize the public goods nature of the patent. To join the WTO, the developing nations have to provide patent protection for any invention, whether it is a product (such as a medicine) or a process (such as a method of producing the chemical ingredients for a medicine), while allowing certain exceptions. If a patent system which provides the least narrow privilege to investors is introduced, it is considered as the most appropriate for these nations. Up until 2005 India was one of such countries by having adopted the process patent system.
India, along with other developing countries, had adopted "process patenting regime" by introducing the Patents Act of 1970, which was basically a copy of the U.K. Patents Act of 1949. The Act of 1970 had been granting "process patents" on drugs in combination with extensive use of fertilizers and pesticides. While it is expensive, complicated, and time consuming to duplicate an airplane, it is relatively simple to perform a chemical analysis of a pill and reproduce it (Scherer, 2002). Furthermore, India had emergent needs to advance its agriculture and the health of the people. These practices, it is believed, brought not only low drug prices but also extended life expectancy and the end of frequent famines.

The patent system under the Act of 1970 allowed Indian pharmaceutical companies to copy drugs patented abroad by merely changing their manufacturing process, because no patent had been granted for the new substance which was brought to the market by spending multi-million dollars. In this situation, such companies as CIPLA (The Chemical, Industrial & Pharmaceutical Laboratories), which was established by Khwaja Abdul Hamied in 1935, had pivotal roles. The company had lawfully analyzed ingredients of proprietary drugs which were invented in the developed countries, and handed the data sometimes to other local drug manufactures. These companies as together lawfully manufactured them by a different process, to which the manufactures were given the process base patent. These products were exported unlawfully under the TRIPs regime to the so-called pirate drug markets such as those in South Africa, Brazil and others, where patients were able to have access to very low cost drugs.

In 1995, the TRIPs agreement was reached in Marrakesh, Morocco, where India, along with many other countries, agreed to grant 20-year patents on pharmaceutical products from January 1, 2005. The new WTO regime effectively outlawed the Indian type of generic production of new medicines. To comply with this situation, India's Parliament approved the new law, amending the country's 1970 Patent Act, which affects everything from electronics to software to medicines. The revision has been expected for years as a condition for India to join the WTO. The patent regulations under the new laws stop local drug makers from copying new drugs developed by other, primarily Western companies.

Thus, India made a big swing from one extreme to another, moving from the 1970 law that was clearly anti-patent to the new law that is pro-patent. When India turned to the product patenting regime in 2005, they also changed their business models from pirate drug manufacturers either to manufacturers and distributors of generic drugs or to drug material producers. Under the new law, all the generic drugs already approved
in India are allowed to still be sold, as long as sellers pay licensing fees\(^8\). Thus, the assortment of generic drugs offered by Indian drugs manufacturers are just the reflection of the global markets as they have drugs with a wide coverage of diseases. For example, Cipla makes drugs to treat cardiovascular disease, arthritis, diabetes, weight control, depression and many other symptoms, and its products are distributed in more than 180 countries worldwide.

Indian generic companies have a strong competitive advantage in the drug manufacturing process thanks to the old patent system. In fact, India's generic drug companies have increased spending on research with an eye to launch low-cost drugs for the global market. As a result, India is among the world's top five drug producers in terms of volume, though its $7 billion market does not rank as high in value. India's drug exports exceed those of Japan, which has claimed its superiority in manufacturing chemicals since fiscal year ended March 2006 as shown in Figure 4. If measures such as the export-to-import ratio of a certain country denote, as Collins (1993) claims, its international competitiveness, India has certainly earned its competitiveness.

Changes in the patent system were necessary for India, which had prepared for making itself more competitive on global scale. Many of India's innovative companies welcomed the stronger patent protections. For example, Dr. Reddy's Laboratories Ltd. and Ranbaxy Laboratories Ltd. both have more than doubled their R&D expenditures to about 10% of their revenues. Furthermore, Ranbaxy launched on a proprietary drug company with the help of the venture capital division of Citicorp. With the stronger patent protection, many multinational corporations have tapped India's relatively inexpensive engineers, scientists and computer programmers for product design, drug development and clinical testing.

India's process patent system had been a disturbing factor for proprietary drug markets for many years. When the developed nations such as the United States consider legislation to create a regulatory pathway for follow-on biologics, in which the period of data exclusivity for a follow-on competitor is discussed, India simply stole the original innovations. This illegality was allowed to a certain point, probably because of the catching-up process. But this practice should not be allowed as India has opened its markets to pursue its new innovation path. Although it may be true that India's

Figure 4 India's Export of Drugs Exceeds That of Japan (unit: 100 million yen)

\(^8\) The new law states that the Controller of Patents has a series of wide-ranging discretionary powers to determine all kind of criteria like "reasonable affordability," "reasonable pricing," and "reasonable royalty." This, however, has caused many disputes between the local companies and leading pharmaceutical companies.
irregular policy had been a shrewd strategy to shorten the nation’s catching-up process, stricter new rules should govern the Indian drug industry. Discretionary powers of the Controller of Patents to allow compulsory licensing should be limited to the pandemic or the like. Otherwise, India couldn’t acquire its innovative and competitive position in the global drug industry.

5. Is There the Global Community? : A Role of Affirmative Actions by NPO and WHO

The WHO was established as a direct and coordinate authority for health within the United Nations system. It has been setting norms and standards and shaping the health research agenda by considering the global community. But very few people, if any, had imagined the existence of the global community up until 2000, when the AIDS crisis emerged. The global popular outrage provoked by crisis gathered a momentum against the tight patent regime set by the developed nations.

In an effort to enter into the HIV/AIDS treatment area, Warner-Lambert paid in 1999 $2.1 billion, by acquiring the stock of Agouron Pharmaceuticals at the value of $60 per share. The Pharmaceutical Research and Manufacturers of America (PhRMA) claims that member companies alone invested an estimated $49.4 billion in 2010 to discover and develop new medicines. Industry-wide research and investment reached a record $67.4 billion in 2010, while copy drug makers have not invested in the research.
When South African government stopped the patent rights for AIDS in 1997 and thereafter allowed the NGOs to import copy drugs for antiretroviral treatment, it was natural for big pharmaceutical companies to have filed the repeal of the order in March 2001, saying that it is impossible to develop new medicines and medical techniques without these devotions to the R&D and the patent protection. At a month before this action, namely February, 2001, however, Cipla stunned the HIV/AIDS and public health communities by announcing it would make its triple cocktail of antiretroviral drugs available to the developing countries for $350 per patient per year, a tiny fraction of $15,000 per patient ---the prices for proprietary drugs at the time. Thus, cheap generic drugs provided by Indian companies became a powerful countervailing force against the rigid patent system. They claim that the AIDS is not only emerged in the developed nations but in the global community. If the antiretroviral drugs are the need of the global community, they should be considered as quasi-public goods.

In these circumstances, big pharmaceutical companies withdrew their filing in April 2001 from humanitarian considerations and decided to offer antiretroviral drugs at the manufacturing cost of $1000. In June 2001, the UN General Assembly Special Session recognized and declared that while the AIDS epidemic had caused untold suffering and death worldwide, communities and countries could change the course of the epidemic with sufficient will and resources. At the Genova Summit in July 2001, the G8 endorsed the establishment of a Global AIDS and Health Fund, by providing political and financial backing to the UN efforts. Global Fund to Fight AIDS, Tuberculosis, and Malaria was started in January 2002 to provide appropriate treatment for unmet global medical needs.

China, the largest developing country, has experienced a rapid increase in HIV/AIDS prevalence, and at the same time it won the largest benefit from the Global Fund, which has contributed more than $400 million, making it the single largest donor for HIV/AIDS-related programs in China (Figure 5). Until 2003, China’s HIV/AIDS programs were mainly supported by international donors, but the Global Fund siphoned many bilateral, multilateral and private partnerships, which have had a major impact on the direction and success of the HIV/AIDS response in China. The process of integrating all HIV/AIDS projects into one national AIDS program in China is now regarded as a prime example of the “Three Ones” principles advocated by UNAIDS.

The contributions to the Fund so far, however, represent only part of the $15 billion, or the amount that experts estimate is needed each year to prevent and treat
AIDS, tuberculosis and malaria effectively on a global scale\(^9\). The global community is still considered by many people as a far-a-way goal to reach.

**Figure 5. Major international and domestic HIV/AIDS projects in China, 1993–2009**

- (Source) Zunyou Wu et. al. (2011) The integration of multiple HIV/AIDS projects into a coordinated national programme in China

**Further Convergence of Dual Drug Markets**

According to the IMS Institute, the demands for pharmaceuticals in the emerging markets are expected to nearly double over the next five years to $285·315 billion, or almost the equivalent to the US market, compared with $151 billion in 2010. This will be fueled by strong economic growth and governments’ commitment to expand healthcare access. When the global spending for medicines is expected to grow at the rate of 3·6 percent over the next five years to $1.1 trillion in 2015, the emerging markets has become the strategic target of the big pharmaceutical companies in the developed countries.

In other words, they have to see, from the business point of view, the medical needs of the developing nations as the BOP market advocated by Prahalad (2004). Acquisition of Wythe by Pfizer in 2009 was considered as a step into the emerging markets, as Wythe had such product lines as vaccines and distribution channels in the developing nations. So was Takeda’s acquisition of Nycomed in 2011. Most firms, however, face disincentives in conducting R&D for global health since product markets are small and uncertain, scientific problems are tough to solve, They fear that risk and reward do not match and that there is a lack of financing mechanism.

Providing low cost treatment measures for NGO such as Médecins Sans Frontières,

\(^9\) The Fund’s homepage, on 2/28/2012.
Cipla has become the world's largest manufacturer of antiretroviral drug maker in term of units. Cipla medicines are used for probably 40 percent of HIV/AIDS patients undergoing antiretroviral therapy worldwide. When the new patent law was introduced in India in 2005, many feared the increase in price due to the payment of royalties or the initial fee for licenses. The new law has its leeway, as we have already pointed out, by stipulating that a maker of generics can apply to copy a patented drug. This is possible only after it has been marketed for three years. The Indian government has some authority to step in if price rises were excessive. So, Indian generic makers have kept their position to provide low cost medicines for the developing nations.

Furthermore, the treatment of air flu created another challenge to the patent system. In 2006 the fear of an influenza pandemic spread in Southeastern Asia. Some predicted more disastrous damages than the flu pandemic which left over 40 million people dead in 1918-1919. If the highly pathogenic H5N1 avian flu virus mutates into a form transmissible between humans, it could trigger a public health crisis. Ensuring sufficient supplies of flu drugs was a central concern for public authorities at that time. Generic makers in such countries as Thailand, the Philippines, and Indonesia were encouraged to copy Tamiflu, a brand name of Roche, which bought a sole and exclusive license of oseltamivir from Gilead. As Gilead never acquired a patent for oseltamivir in those countries, it is completely lawful for them to copy it according to Thai Pharmaceutical Administration Office. Roche committed to provide 3 million tablets of Tamiflu to the WHO in case of a possible pandemic.

However, the situation in other countries such as India is closely linked to the intellectual property rights which cover these drugs. At the same time, TRIPS allows the member countries the compulsory licensing to produce the patented product without the consent of the patent owner. Indian generic makers also began to produce the copy drug of Tamiflu. In the case of Cipola, the trade name was Anitiflu. Roche asked the Indian court to stop manufacturing of Antiflu, But Roche lost the case in December 2008. Furthermore, Cipla won in May 2009 approval from the WHO certifying that its drug Antiflu was as effective as Tamiflu, and Antiflu was included in the WHO list of prequalified medicinal products.

These cases show the developments under the pressure of epidemic or pandemic. But generic makers in the developing nations have gained their powers to produce the similar drugs of the proprietary drugs. This increases the difficulty in the practice of "evergreening" of pharmaceutical patents, where patent owners allegedly try to extend patent life through grant of new patents by minor "innovations" or improvements on formulations, dosage forms or minor chemical variations of an earlier patented product.
This, in turn, makes the Indian pharmaceutical companies difficult to pursue true research-based drug companies.

Development of Hoodia: Benefit-sharing between the Drug Companies and the San

The developing nations which had been accused of pirate activities in the world drug markets condemn, in turn, the developed nations and big pharmaceutical companies for their bio-piracy. Addressing to the condemnation of bio-piracy, fair sharing practices have begun in some projects. The case of development in appetite suppress gradient of hoodia is one of such cases.

Hoodia gordonii is a small cactus that grows in the Kalahari desert. Its flesh has been eaten by the San people off the Kalahari desert for centuries to suppress appetite before they travel through the desert and the research by Council for Scientific and Industrial Research (CSIR) of South Africa isolated a molecule within the plant, given the name p57, which is believed to act as a satiety stimulator. When CSIR licensed out in 1997 the patent of p57 to Phytopharm, a UK-based biotech venture, NPO criticized the lack of fair share for the San. After starting negotiation in 1997, the San and the CSIR reached the final agreement in 2003. According to a 2003 benefit-sharing agreement the San are entitled to 6% of all royalties received by CSIR.

The development of hoodia as prescription drug and as food supplement has never been successful in spite of some 15 year collaboration with such big names as Pfizer and Unilever.

When Phytopharm tied with Pfizer in 1998, the development target was specified as a "prescription drug for obesity". However, as the development had delayed somewhat, Pfizer decided to take over the research in 2002. At that time Phytopharm planned to work on the development of a semi-synthetic version of the active molecule, leaving research and development of the naturally occurring molecule to the Natureceuticals group within Pfizer. But the Natureceuticals group was closed due to the restructuring of the whole company in July of 2003, and Pfizer returned the rights to license the Phytopharm hoodia product.

The Phytopharm and Unilever hoodia collaboration began late in 2004. Unilever considered hoodia as addition to the company's long list of consumer goods which includes the Slim Fast diet products. Indeed, Phytopharm stated that they intend to bring new "weight management products" to the market. In April of 2006, Phytopharm announced that phase 1 of the 5 stage research and development program had been
completed. It indicated years would need before any Phytopharm hoodia or Unilever hoodia products reach the market.

Unilever also dropped the joint develop project in 2009 after spending more than 20 million Euro. This was really a negative sign of hoodia products, although the company said that consumer reaction to hoodia products marketed by health supplement companies had been mostly positive. After having searched for new partners in vein, in November 2010 Phytopharm returned its commercialization rights of p57 and related patents to CSIR, concentrating its effort on the developing series of compounds, the Sapogenins, which has the potential to be a new class of therapy for neurodegenerative diseases including Parkinson’s disease, amyotrophic lateral sclerosis (ALS) and glaucoma.

As the obesity problem in the United States continues to grow, the U.S. dieters might have needed the development of an obesity drug from a traditional remedy used by Africa’s San people. But the sufferer from the abandonment of the development plan was San who are covered by the 2003 agreement This single case doesn’t tell the relevance or the usefulness of the old wisdom, but it may indicate that fair sharing is not easy to share.

Humanitarian Assistance for Neglected Diseases

Product Development Partnerships with the WHO and other non-profit initiatives have taken on much of the work in the unmet medical needs of the developing nations. For example, thirteen major research and development-based pharmaceutical companies, the Bill & Melinda Gates Foundation, the WHO, the U.S. and U.K. governments, the World Bank and governments from neglected tropical disease (NTD)-endemic countries, gave their support in January 2012 to the London Declaration, a coordinated effort to eliminate 10 NTDs by the end of this decade.

This declaration is addressing to more neglected tropical diseases, because elimination of 10 NTDs is clearly an expansion of the scope set by the Global Fund to Fight AIDS, Tuberculosis, and Malaria. According to the paper presented by staffs of African Program for Onchocerciasis Control of the WHO and scholars, "mapping is very effective for the control and elimination of NTDs such as loiasis, onchocerciasis, and lymphatic filariasis, allowing for improved quality of life for billions of individuals." In this end, the programs are to be implemented.

Onchocerciasis, also known as river blindness, is the world's second major infectious cause of blindness. It is caused by "onchocerca volvulus," a nematode that can live for up to fifteen years in human body though it can also live in other mammals. Since 1988, ivermectin has been provided free of charge by Merck & Co. through the Mectizan Donation Program (MDP). Mectizan, a trade name of ivermectin was discovered by Satoshi Ohmura, former president of Kitasato University in Japan, has been first applied to the control of parasitism of domestic animal. As it has been one of the best selling animal drugs and has expanded its applications, Merck & Co. paid some $250 million of royalty fees.

With this royalty revenue, Ohmura succeeded in constructing new hospitals and a medical research center. Leveraging on the royalty of the patent, Ohmura succeeded in renovating Kitasato Institute of Medical Research, which was established by Shibasaburo Kitasato in 1912. For example, Kitasato Medical Research Center has come to function as one of the WTO's research hubs for developing medicine for malaria by utilizing chemical data of Japanese pharmaceutical industries.

The collaboration between Ohmura and Merck led to the extension of patent life and the expansion of application of ivermectin. But it was after the end of the patent protection period when Ohmura was told that ivermectin was also applicable for the cure of the so-called river blindness. When Ohmura visited a village in Ghana, a blind old man told that he was happy because the drug Ohmura discovered had prevented children from suffering river blindness. Ivermectin does not have the power to restore the eye sight but has the power to prevent the patients from losing sight. Merck & Co. continues to provide the drug by the end of 2020, that is the WHO elimination goals.

Lymphatic filariasis, commonly known as elephantiasis, is another infectious disease occurred when filarial parasites are transmitted to humans through mosquitoes. While lymphatic filariasis is controlled with three antiparasitic agents, the supply of the medicine, DEC (diethylcarbamazine), has been in short. In line with its commitment to support the WHO’s lymphatic filariasis elimination program, Eisai and Sanofi committed to provide 2.2 billion DEC tablets to the WHO free of charge in collaboration with the Bill & Melinda Gates Foundation to deliver these tablets to some 250 million people in the developing world until 2020.

---

11 Interview with Satoshi Ohmura on March 28, 2012. He said he had written some 1100 papers and made seven commercially successful discoveries including ivermectin. At the age of 77, he is still active in research and in managing the university, because its school of marine bioscience has been suffering from the Tohoku Earthquake.

12 In Merck’s research facility in New Jersey, a statue of an old blind man who is led by a child with a sign that Merck saved many Africans from river blindness without mentioning to Ohmura.
In the cases above there are some measures to cure, but unmet needs for new drugs, vaccines and diagnostics for diseases affecting the developing countries remain as an area new research and development is required. Industry should have a unique contribution to make by applying drug discovery and pharmaceutical development capabilities to create new solutions – filling a gap between meager funding and necessary activities.

While David (2006) and Pénin and Wack (2008) proposed to use intellectual property rights to expand the commons for science or an open innovation in biotechnology, initiatives such as Alnylam's Intellectual Property (IP) contributions to the Pool for Open Innovation against Neglected Tropical Diseases show a commitment in helping to produce badly needed health technologies. The scope of Genzyme's Humanitarian Assistance for Neglected Diseases (HAND) is a little bit bigger than this, because Genzyme has committed to increasing resources beyond its areas of medical focus and commercial interest. Since the HAND program was launched in 2006, Genzyme has made available hundreds of thousands of compounds, and has dedicated tens of thousands of scientist hours annually to these collaborations.

Furthermore, Genzyme and the Drugs for Neglected Diseases initiative (DNDi) are working together to advance a treatment for African sleeping sickness. Genzyme also helps patients affected by disasters around the world by donating products, supporting the rebuilding of health-care infrastructure, and matching employee donations to relief organizations.

Non-profit organizations facilitate integration through proactive management of their network of collaborators (Pisano, 2006). In fact, the Fund for Research in Neglected Disease (FRIND) and the Global TB Alliance together with Melinda and Bill Gates Foundation seem to have functioned as virtual research headquarters to set agenda and to eliminate the duplication of many individual research projects.

Championed by Novartis, the FRIND would apply the portfolio management techniques used by private pharmaceutical firms for their mainstream drug pipelines for research in neglected disease. FRIND proposes that all available funding be pooled and then allocated by a board that represents developing countries, major funders, OECD countries and other international health stakeholders. Portfolio management teams functioning under this board would guide the R&D for a specific disease. As projects meet milestone targets, additional payments would be made for incremental successes. FRIND proposes data sharing between projects in order to promote innovation and to stop or to redirect poorly performing projects as early as possible.

---

13 The FRIND home page 2/29/2012
The TB Alliance claims that before the Alliance was established in 2000, there were no clinical-stage compounds in development to treat TB patients. Today, after a decade of advancing science and working with donors, partners, and other stakeholders, the TB Alliance has developed and manages the largest TB drug pipeline in history.

True, conquering neglected diseases is an area that biotechnology firms could play a greater role through grant financing and partnership with the NPO. New policy and financing mechanisms that can balance the investment equation and encourage biotechnology and pharmaceutical firms to include global health diseases in their R&D portfolios could unleash important advances in global health technologies.

Biosecurity and Scientific Practice

The community of scientists has expanded its geographical territories and has enhanced its voices in the global society. Their activities as scientists should expand the boundary of public goods into the commercial sphere. The publication of scientific journals such as Nature and Science is instrumental to make new information be public. After the publication of a journal, patentable new information will be turned into the interpreted information.

While the consumption of patented goods is policed by the inventor within the framework of legal protection mechanism, public goods can be collectively consumed without policing. Yoshihiro Kawaoka, Professor at the University of Tokyo and the University of Wisconsin-Madison, allegedly made a hybrid virus, fusing the hemagglutinin protein (the H in a flu virus's name) from H5N1 onto the human H1N1 virus that caused the 2009 pandemic in his laboratory at the University of Wisconsin-Madison. The paper submitted to Nature revealed the details of it. As the pace and proliferation of biological technologies is, as Carlson (2003) pointed out, very fast, it seems to be natural for Paul Keim, acting chair of the US National Science Advisory Board for Biosecurity (NSABB), to say in response to questions posed by Nature ‘no one should presume to know all the ways in which influenza virus could be misused.’

The agenda was set, however, which is bigger between the benefits of publishing sensitive data and the risks that nation states wanting mutually assured destruction options, bioterrorists or a single person's random acts of craziness use the data for making biohazard. What became clear is, as the editorial of Nature pointed out, that not only does the mammalian transmissibility threat seem greater than previously thought, but also that current avian viruses have some of the mutations identified in
the new work. In other words, there is already a substantial immediate risk to humans. If that is the case, we have to prepare for the possible pandemic by searching a proper cure method. Preparation advocated by the educated bodies such as Araz et al. (2010) and Beaton et al. (2007) is relevant. It is, therefore, rightful for Kawaoka to argue that the work he and other high level influenza scientists do to try to puzzle out why some flu viruses spread in humans is too important to be shelved, though some of biosecurity experts insist no further transmission studies on the dangerous H5N1 flu virus should be undertaken.

NSABB’s concern remained: While the biotechnology has dual aspects of drugs and weapons, there is no statutory international agent which inspects and verifies the deeds of the researchers and their laboratories. In cases of nuclear weapons and chemical weapons, the international community agreed to have both the conventions and their inspection agents, IAEA and OPCW respectively, which conduct onsite verification. As shown in Table 2, biological weapons are the easiest to acquire, yet have comparable strategic effects to nuclear weapons. Although the Biological and Toxin

<table>
<thead>
<tr>
<th>Type</th>
<th>Technology</th>
<th>Cost</th>
<th>Signature</th>
<th>Tactical Effectiveness</th>
<th>Strategic Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuclear</td>
<td>Very high</td>
<td>Very high</td>
<td>Very high</td>
<td>Very high</td>
<td>Very high</td>
</tr>
<tr>
<td>Biological</td>
<td>High</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Very high</td>
</tr>
<tr>
<td>Chemical</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>Very high</td>
<td>Low</td>
</tr>
</tbody>
</table>

(Source) US Congress, Committee on Armed Services, House of Representatives, Feb.23.1993

Convention (BWC) has totally prohibited biological weapons since 1972, there is no preventing mechanism of the biohazard. Therefore, biological weapons, Pearson (2001) argues, present the greatest danger today.

The Special Conference/VEREX Final Report in 1994 established the Ad Hoc Committee (AHC). The AHC in turn discussed appropriate measures including the establishment of a verification agent by having examined and evaluated 21 potential verification measures and some examples of possible combinations of them. Supporting such moves, President Clinton said in his address to the United Nations General assembly in 1996, that “we must better protect our people from those who would use disease as a weapon of war”. While the Bush Administration initially showed the go-further attitudes, the AHC continued to meet extensively in 2000 and early 2001 towards the better protections. Thus the moves to pursue stronger protection mechanism of biological weapons gathered its momentum. But President Bush finally
withdrew the idea of establishing verification agent as he came to think the verification process would harm the competitiveness of the U. S. biotechnology.

It may be difficult for the international community to create the verification mechanism in a short time, but the WTO might, in our opinion, be able to act as such to promote security clearance system for the relevant researchers and laboratories. Actually the NSABB took its role in March by having a two-day meeting, during which the authors explained their work and took questions from the board members. The group was presented with unpublished data showing that the mutations used in the studies are cropping up in H5N1 viruses in the wild. The NSABB voted unanimously to clear the path to publication of the revised-version paper by Professor Kawaoka of the University of Tokyo. But it voted 12 to six on a second paper by Dutch virologist Ron Fouchier from Erasmus Medical Centre in Rotterdam. The group of six concerned the publication of the latter paper, because it shows how an H5N1 virus can be pushed to become transmissible among mammals. The decision of the NSABB indicates the following. It is very difficult for both Nature and Science to publish a reduced version omitting key methods and data and make it the full version available under a certain condition. It is partly because selection of the persons who are capable of pursuing the science of making the vaccines is not easy and partly because it is also difficult to keep the information of full version paper just like trade secret for a long time.

6. Conclusion

The laws of the same concept should have mandated the behaviors of the actors involved, but rules and the executions of the laws have depended to a very large extent on the their norms about right and wrong. While the developing nations have demanded the rights to pursue the catching-up processes, the pharmaceuticals and bio-tech companies in the developed nations have tend to deny their rights. But the pharmaceutical companies have to tap the fast growing drug markets of the developing nations, if they want to continue to grow. Furthermore, both of developed and developing nations have found the common enemies such as AIDS and air flu. Thus the directions of the two parties which used to have been almost opposite interests seem to come closer than ever. We can also observe that originally broadly set the patent rights have become narrower as the results of interactions between the actors who have different interests and the maturation of the biotechnology.

Romer argues that an analysis of the interaction between rules and technologies may help explain the past economic development. He points out that some technologies
such as mobile telephony have successfully diffused globally while some others such as safe municipal water have not. The biotech-based drugs industry used to lie in the latter categories. But the progress in biotechnology and the interactions between various communities has moved its position more closely to the lines of the first categories.

Despite these facts, there remains a gap between the two. To fill this gap, non-profit organizations have been instrumental in applying a set of global patent laws as “one size fit for all” system, by offering the integration efforts in various communities in the global economy. Thus, the patent system set by the United States comes to function, though it has evolved, as the rules to govern the global biotech industry.
References
Eisenberg, R. S., (1989) “Patents and the Progress of Science: Exclusive Rights and Experimental Use,” vol.56


Prahalad, C. K., (2004)*The Fortune at the Bottom of the Pyramid* Warton Publishing
-------- and Shingo Kano (1999) “Strategies of Japanese Firms entering the Biotech
Industry—Case studies of the Pharmaceutical Industry,” paper presented at the Seminar on The Comparative Studies of the Birth of Biotech Industries in the U. S. and Japan at University of California (Berkeley) on April 2

and Fujio Namiki(2003)“Three Attempts at De-Wintelisation: Japan’s TRON Project, the US Government’s Suits against Wintel, and the Entry of Java and Linux,” Research Policy, vol.32 December


