Comparative Analysis of Issues on Patent Laws for Medical Invention on Recent Drug Development between Japan and Europe (*)

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Recent drug development is expected to develop new drugs at low cost. Universities, venture companies, etc. increasingly carry out exploring drug candidate substances instead of pharmaceutical companies in order to reduce the cost. Drug repositioning (DR), finding new effects on existing approved drugs and developing them as new therapeutic agents for other diseases is expected as a promising drug discovery system with low cost. For drug development, monopolizing the market by acquiring patents is important as an incentive. However, in DR development, patent issues may arise between the new drug and a patented drug. This is because the scope of the patent right of the drug with a new indication of an already patented substance is unclear and the effect obtained by the patent right differs among countries. Therefore, in DR development, problems and differences of the current patent system between Japan and Europe are found by comparative analysis of the impact of patent systems and legislations to DR development and comparative analysis of patent laws and legislations relating to technology transfer. Moreover, the possibility of introducing the necessity of international harmonization of patent law in order to promote DR development is analyzed. If the international harmonization is necessary to be introduced, a new system suitable therefor is also analyzed.

I. Introduction

In recent years, a new approach to drug development and improving the productivity of drug research and development[1] are desired. As measures, technology transfer by industry-university collaboration and drug repositioning (DR), effectively utilizing existing drugs and so on,[2] are included.

Patent law is deeply involved in pharmaceutical development as well as pharmaceutical legislation, but neither patent law nor pharmaceutical legislation is internationally unified.

In this research, comparative analysis between Japan and Europe is carried out on issues of patent laws relating to medical patents and technology transfer for DR development. Based on the analysis, the possibility of introducing a new system or the necessity of international harmonization

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[1] Pharmaceutical Industry Policy Institute 'Current Status and Issues Surrounding the Pharmaceutical Industry - To Deliver Better Medicines to the World - Part 1 Innovation and New Drug Creation' Industrial Report No.5, (December 2014) p.26

[2] Reuters, Thomson 'The Changing Role of Chemistry in Drug Discovery,' International Year of Chemistry, (2011); Sleigh, Sara H., and Cheryl L. Barton 'Repurposing Strategies for Therapeutics,' Pharmaceutical Medicine, vol.24, no.3 (2010) p.151-159; 'Current Status and Issues Surrounding the Pharmaceutical Industry,' p.28-30; Reuters, Thomson 'Knowledge-Based Drug Repositioning to Drive R&D Productivity,' White Paper (2012)

of patent law is examined in order to promote DR development.

II. Current Situation of Drug Development

The impact of the patent system on the pharmaceutical industry is enormous in Japan. The impact of the patent system on drug development is therefore discussed finding problems in the current pharmaceutical industry. Understanding a historical approach based of the pharmaceutical industry in Japan improves the discussion.

1. Historical Approach

From the Meiji era to the present, several national policies were introduced in the pharmaceutical industry and the patent system triggered the development. Under World War I, patent rights of the opponent countries were withdrawn and domestic companies could manufacture medicines thereof. After World War II, overseas technology for manufacturing drugs was introduced to Japan, and the introduction of the medical substance patent system dramatically improved the technology for developing new drugs[3]. In this way, the Japanese pharmaceutical industry has been developed by introducing different kinds of patent systems according to the degree of maturity of industry.

2. Current Topics of Pharmaceutical Industry

Conventional pharmaceutical development had problems such as a regularized drug price reduction, and an increase of the burden of clinical trials necessary for approval, thereby increasing the cost of drug development. In order to overcome these problems, pharmaceutical companies shifted the product development strategy from modifying existing drugs to innovative new drugs[4]. Among innovative new drugs, the development of "blockbusters" with international competitiveness was one pharmaceutical business model in the 1990s[5]. However, recent problems

[3] Hara, Hiroshi ‘European and American Pharmaceutical Companies in Japan: Historical Overview,’ National Economic Journal vol.196, no.1 (2007) p.91-107

[4] Endo, Hisao; Tanaka Shinro Tanaka ‘Present state and possibility of international competitiveness of our pharmaceutical industry,’ Medical and Society vol.7, no.1 (1997) p.46-71; Pharmaceutical Industry Policy Research Institute ‘Toward Strengthening Competitiveness as "Place of Drug Discovery"- Current status and problems of the pharmaceutical industry,’ (November 2005) p.25-42

[5] ‘Toward Strengthening Competitiveness,’ p.55-60; Tomita, Kenji ‘Outline of New Drug Development from Business Viewpoint (77th Celebration of Professor Tetsuo Ukai),’ Doshisha Commercial Science, Vol.65, no.6 (2014) p.978-994; Cuatrecasas, P.‘Drug Discovery in Jeopardy,' The Journal of Clinical Investigation, vol.116, no.11 (2006) p.2837-2842; Jorgensen, W. L. 'The Many Roles of Computation in Drug Discovery,' Science (New York, N.Y.) vol.303, no.5665 (2004) p.1813-1818

are the decrease in the number of blockbusters and drastic sales reduction thereof after the expiration of the blockbuster's patent period[6].

In order to promote drug discovery cycles, pharmaceutical companies tend to shift targets of drug discovery to drugs in new areas where therapeutic drugs are strongly desired[7].

Among them, recently, attention has been drawn to drag repositioning (DR), effectively utilizing existing drugs, having already been approved for production, or medicinal active ingredients whose development has been discontinued.

3. Drug Repositioning

In DR development, reliable safety has been already obtained because the efficacy and safety of candidates for pharmaceutical active substances have already been proved. Moreover, since the results of clinical trials necessary for obtaining the approval have already been obtained, implementation of these tests can be omitted and the period and cost of drug development can be reduced[8].

Drug re-profiling is the recent trend of DR, finding a new indication of a known pharmaceutical active substance by comprehensively analyzing the functions using the latest science technology[9].

However, when the pharmaceutical active substance applied in DR has already been patented, problems may occur against the existing patent right.

III. Pharmaceutical Patent System

As an incentive for drug development, monopolization of the market by patent acquisition is important. In this chapter, the patentability, patent right, and patent protection, etc. of drug inventions completed by DR development is determined.

1. Medical Use Invention by DR Development

An invention relating to a novel effect of a known substance is referred to as a medicinal use invention in Japan and as a second medicinal use invention in Europe. For obtaining a patent for a

[6] Alazraki M. 'The 10 biggest-selling drugs that are about to lose their patent,' DailyFinance, 27.2.2011 www.dailyfinance.com/2011/02/27/top-selling-drugs-are-about-to-lose-patent-protection-ready/ retrieved on 16.8.2017
[7] Tomita p.978-994; 'Current Status and Issues Surrounding the Pharmaceutical Industry,' p.1-42
[8] Mizushima p.47-98
[9] Mizushima, Tohru 'Crisis of Drug Development,' Kodansha (2015) p.99-140

medical use invention, the medical use invention has to satisfy novelty and inventive step as requirements of patentability. In both Japan and Europe, a DR medicinal use invention satisfies novelty when the indication is novel even if the substance is known and satisfies inventive step when a person skilled in the art could not achieve the new indication from known prior arts[10].

2. Scope of Patent Right of DR Medical Use Invention by Development

In Japan, patentability is examined within the scope of the medical use specified by the claim of the medicinal use invention during the examination for granting patent. On the other hand, since the scope of patent right is practically decided in patent infringement litigation[11], the scope of the patent right of the medical use invention is not yet clear. Therefore, the scope of patent examination does not necessarily correspond with the scope of patent right.

Under the European Patent Convention (EPC), Article 69 stipulates the extent of the protection conferred by a European patent, or that a European patent application shall be determined by the claims and the description and drawings shall be used to interpret the claims. However, the scope of patent right is left to the judgment of each country. For example, in Germany, the scope of the patent right of a second medicinal use invention covers the whole of the claimed substance whereas the scope is limited to the claimed medical use in the UK. The scope of patent right of a second medicinal use invention is not therefore unified among countries[12].

3. Other Protections of Patent Right of DR Medical Use Invention

During the preparation period of the application for obtaining approval necessary for launching a new drug to market, a patented invention cannot be carried out and each country takes measures for recovering this eroded 'period which patented invention cannot be carried out.'

(1) Extension of Patent Protection Period

The extension system of the duration of patent protection was introduced for the first time in the US Hatch Waxman Act in 1984, which was a legislation combining recovery of eroded patent periods and simplification of application for approval of generic drugs. In 1987, the same system

[10] JPO Examination Guideline Division 'Examination Guideline of Life Science etc.,' (2017.1)
[11] Japan Patent Law Articles 68, 70; IIP 2004 Report p.90-104
[12] EPC Article 69; AIPPI Law Series

was introduced in Japan. In response to this movement of Japan and the United States, the demand for the establishment of the same system increased in Europe due to concern that research bases would move to non-MSs with greater protection. Since it is difficult to revise the EPC, the European Commission set a supplementary protection certificate (SPC)[13] separately from the EPC and introduced the extension system[14].

The Japan Patent Law Article 67-2 stipulates that the period during which the patented invention could not be implemented because of preparation of clinical trial data for obtaining approvals defined by the Pharmaceutical Affairs Law shall be extended by a period not exceeding 5 years.

The 'description of the disposition designated by Cabinet Order' should be submitted on filing a request for the registration of extension of the duration[15]. When one patent has plural approval dispositions, since the implementation period and the extent of the extended patent right differ for each disposal, the extension registration can be applied for each disposition[16]. This means, an approval disposition of a patented invention for a DR new indication can be filed for extension registration separately from approval disposition of patented invention of already approved medicine. The application for extension registration is examined in terms of whether it is necessary to obtain approval for the implementation of the patented invention[17]. "Implementation of patented invention" is an activity of manufacturing, etc. of a medicinal product specified by "subjective matters of the invention" described in the approval document, it is decided by comparing the present disposition with a cited disposition directly relevant to examination matters on the substantial identity as a medicinal product of the patented invention[18] and determining whether the medicine receiving the disposition falls within the scope of the patented invention[19]. DR drug patents relating to new indications of the same ingredient can receive a disposition at this point.

In Europe, the extension period during which the patented invention could not be implemented because of preparation of clinical trial data for obtaining approvals can be obtained by a period not exceeding 5 years within 15 years from the date on which the initial approval is obtained. "First approval" is examined on the basis of the ingredients of the approved medicinal products and the indication is not taken into consideration[20]. The problem is whether the extension period of the patent right of second medicinal use invention can be allowed or not. When the patent right of the

[13] REGULATION No 469/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 6 May 2009 concerning the supplementary protection certificate for medicinal products
[14] IIP 'Research on Extension Registration System of the Duration of Patent Rights of Pharmaceuticals, etc. and Its Implementation,' IV. Extension System of Overseas Patent Rights and Related System (March, 2015) p.91-120
[15] Japan Patent Law Article 67-2
[16] Yoshifuji et al., p.552-561
[17] Japan Patent Law Article 67-3 para.1 no.1
[18] H26 (Gyo-Hi) 356
[19] H21 (Gyo-Ke) 10092
[20] CJEU C-202/05

original medicine does not fall within the scope of the patent right of the second medicinal use invention, the patent right of the second medicinal use invention can be protected by SPC[21]. In other words, the patent period of a DR second medicinal use invention can be extended.

Both Japanese and European legislations share the following common features: the purpose of the institution; the maximum period of the extension is 5 years; and the extension of the patent right of the DR medical use invention can be allowed separately from the basic patent right. In conclusion, this system has been harmonized in some degree between Japan and Europe.

(2) Data Exclusivity

Pharmaceutical companies desire to protect the data submitted to obtain approval. On the other hand, the implementation of the same clinical tests imposes a huge economic cost if generic companies have to carry them out[22]. Clinical data necessary for approval is therefore protected for a certain period. The TRIPS Agreement includes a provision on data protection at the international level[23]; however, since no internationally unified rule is defined, the provision of data protection varies among Contracting States.

The fundamental difference of data protection systems between Japan and Europe is that the Japanese system aims at "reaffirming safety and effectiveness" while the European system aims at "clinical trial data protection to monopolize new drug markets." However, even in Japan, a drug for which clinical data has been submitted can be exclusively sold before the reexamination period expires. Therefore, the data protection period is substantially the monopolization period of sales of the drug both in Japan and Europe.

Regarding the data protection period of DR medicines, although the method of calculation of the protection period is different between Japan and Europe, both protection periods approved are about 11-12 years.

IV. Industry-Academia Collaboration and Technology Transfer in Drug Development

Technology transfer as a means of improving drug development efficiency will be discussed

[21] CJEU C-130/11
[22] Ramlall, Vishva, 'Data Protection in the Pharmaceutical Industry: Comparative Study between Japan and Canada,' 2003 (IIP 2004) p.4
[23] TRIPS Article 39

from the viewpoint of DR development. Technology transfer has developed separately in Japan and Europe, and is diverse within European countries. In this chapter, the historical approach of technology transfer and national policy in each country and the legal framework relating to technology transfer are examined and comparison thereof is carried out to confirm the necessity of institutional harmonization and institution building.

1. Historical Approach and National Strategy of Technology Transfer

For the analysis of technology transfer in Japan, analysis of the United States, which Japan has followed as, a developed country of technology transfer, is indispensable. The United States had declined in international competitiveness and introduced the pro-patent policy proposed in the "Young Report" in the 1980's. The Bayh-Dole Act[24] enacted in 1980 stipulated that patent rights acquired by universities which are obtained by government funds belong to universities, and by Federal Technology Transfer Law enacted in 1986, the joint research and development system was established by intellectual property right, etc for the first time. provided by universities and industry[25]. It functions as a major mechanism in technology transfer in the United States.

The Japanese Bayh-Dole Act, the 'Act on Special Measures for Industrial Revitalization[26]' was enacted in 1999, about 20 years after the establishment of the Bayh-Dole Act, and patent rights which are the result of national research expenses belong to researchers of universities and the universities support the operation of their patent rights[27]. Furthermore, national universities were turned into independent agencies in 2004, and the university system changed. Since then, inventions completed by the researchers of national universities are owned by Technology Licensing Organizations (TLO) which are responsible for technology transfer of university inventions.

Regarding technology transfer in Europe, universities also own intellectual property rights completed by researchers of universities. However, the situation of technology transfer has diversified under the influence of national innovation policies and science and technology policies of each country.

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[24] Patent and Trademark Act Amendments of 1980

[25] Cooperative Research and Development Agreement; Ministry of Internal Affairs and Communications 'Technology transfer policy in the US,' 11.12 2009 http://www.soumu.go.jp/main_content/000048596.pdf retrieved on 17.1.2018; Ministry of Economy, Trade and Industry 'Efforts of past industrial technology policy in the US,' http://www.meti.go.jp/policy/innovation_policy/powerpoint/hpn/gikankyokukosein/genjotokadain/tsld010.htm retrieved on 17.1.2018

[26] It was transferred to the Industrial Technology Enhancement Law in August 2007; Hanawa, Hiroyuki, 'Changing Japanese Bayh-Dole Act,' Industry-Academia-Government Collaboration Journal December 2007 https://sangakukan.jp/journal/journal_contents/2007/12/articles/0712-07/0712-07_article.html retrieved on 24.1.2017

[27] Takahashi, Nobuo, et al., 'Approach to technology transfer-For universities and researchers belonging to universities,' Akamon Management Review - 2 vol. 10 (October 2003)

2. Legal framework on technology transfer of DR development in Japan and Europe

Technology transfer is carried out by the licensing of patent rights[28]. Licensing is subject to agreement between the parties based on the principle of freedom of contract but the content of the contract should be competitive[29]. Japan and European countries have provisions on license in their patent laws[30]. Some European countries have a Licensing of Right (LOR) system, allowing the reduction of patent fees when patent holders declare their intention to contract licenses to third parties[31]. Germany and the UK have agreement models for industry-academia collaboration practically indicating the contents of a contract in detail[32].

Regarding anti-competitive activity, the Antitrust Act is applied in Japan and the Fair Trade Commission is responsible for its operation. The Act defines a patent as exempt from anti-competition; however, in certain cases the antitrust law is applied[33]. The European Competition Law is Article 101, etc., of the European Function Treaty (TFEU), and Article 101, paragraph 1 prohibits restrictive competition agreements, while paragraph 3 does not apply paragraph 1 to certain categories of agreements, the so-called block exemption regulation. This block exemption regulation is directly applied to domestic laws of the Member States[34]. The block exemption regulation relating to the licensing agreement of pharmaceutical patents developed by DR is the research and development block exemption regulation, R & DBER[35]. Although licensing activities relating to pharmaceutical patents developed by DR are not basically anti-competitive both in Japan and Europe, handling of the anti-competitive behavior of the obligation to challenge the validity of intellectual property rights is different between Japan and Europe.

V. Conclusion

In this chapter, the possibility of introducing a new system or the necessity of international harmonization of patent law in order to promote DR development is analyzed.

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[28] Ishida, Masayasu, 'Technology Transfer and Licensing,' (2011) p.2. https://www.jpo.go.jp/torikumi/kokusai/kokusai2/training/textbook/pdf/Technology_Transfer_and_Licensing2011_jp.pdf retrieved on 2.2.2018

[29] Jiyoung Han, 'Study on Intellectual Property Licensing under Antimonopoly Law in the U.S., Europe, and Japan,' (IIP 2005) p.1-5

[30] Japan Patent Law Articles 34-2,34-3, 77, 78 etc.; Takahashi p.74

[31] German Patent Law Article 23(1). UK Patent Law article 46

[32] Heinz Goddar 'University/Industry Cooperation in Europe,' Goddar, Presentation description in LES Taipei 2017 (1.9.2017); Interview with Prof. Dr. Goddar

[33] Antitrust Act Article 21; Fair Trade Commission 'Guidelines on the Antimonopoly Act on Utilization of Intellectual Property,' No. 1-1 Competition Policy and Intellectual Property System; No.1-2 the Object of this Guidelines; and No. 2-1 Antitrust Law and Intellectual Property Law http://www.jftc.go.jp/dk/guideline/unyoukijun/chitekizaisan.html retrieved on 4.2.2018

[34] TFEU Article 288 para.2

[35] Research and Development Block Exemption Regulation No.1217/2010 http://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32010R1217 retrieved on 7.2.2018

The scope of patent right of a DR medicinal use invention differs among countries including the United States and this point requires harmonization. From the viewpoint of incentive for drug development, it is preferable that the medicinal use invention is classified as a substance invention, by which sufficiently enforcement is possible. The DR medicinal use invention is clearly specified with new indications, and the scope of the patent right is sufficient to be limited to the new indication.

In the extension system of the patent protection period, if the examination period stipulated by the Pharmaceutical Affairs Law differs among each country, since the period may not be able to be fully recovered in five years, prompt examination is therefore desired. Although this is not a problem to be solved by the patent law, it is necessary to provide a broad-ranging analysis including the viewpoint of DR development in the future.

The data protection system can protect drugs uncovered by patent rights and drugs for which the extension was not allowed. Since the application for approval of generic drugs cannot be allowed during the data protection period, the data protection system is valuable to complement the abovementioned patent system under the current situation that the scope of patent rights of medicinal use inventions is not internationally harmonized.

The LOR system is worthwhile to widely ask for licensees of patented inventions such as active ingredients whose drug development has been discontinued as a target of LOR. Matching licensees and patentees in technology transfer is also an important element of the promotion of DR development. Therefore, the introduction of the LOR system is worth considering. The matching in technology transfer is preferable to be carried out extensively and internationally. Since ‘patent specifications attached to patent applications are expected to be used as technical literature[36]’, it is reasonable to willingly utilize the patent specification for matching in technology transfer.

When a complicated agreement is contracted in licensing, communication does not always proceed smoothly between parties, especially in international agreements. It is therefore useful to prepare an international agreement model of technology transfer in order to avoid unnecessary conflicts.

[36] Yoshifuji et al., p.247-8