Current Status and Issues on Patent Protection in a Life Science Field from a Point of Pharmaceutical Industry

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Abstract

In order to accelerate the rapid pace of innovation in the life science field, timely and appropriate patent protection and exploitation strategies are desired. This paper will discuss the current status and issues of patent protection in leading-edge medical treatment, etc., from the point of view of industry.

1. Introduction

The life sciences are one of the areas which are promoted by policies at national level emphasizing Japanese competitiveness. In this context, this paper in particular will discuss the current status and issues of patent protection in the pharmaceuticals industry of which the author is a member.

Research and development of pharmaceuticals require large investment over a long period of 10 to 15 years and are characterized by extremely low probability of market success. The majority of pharmaceuticals are low-molecular weight compounds which are relatively easy to synthesize. Moreover due to the fact that such compounds display activity at a milligram level, their production does not require large scale facilities. Thus, in the absence of protection by patent, etc., there will be few barriers to production of generic and imitative products. On the other hand, even when the active component of the pharmaceutical is a simple molecule, detailed information regarding its efficacy and safety is required for use by a wide range of patients and a high level of quality must be guaranteed to ensure the efficacy and safety. Basically, patents protecting the drugs are mainly substance patents. However in order to recover the high level of development investment and ensure further investment, the importance of each patent underpinning the product is extremely high and there is a need for high-quality patents in order to ensure a period of exclusivity.

In the upstream stages of drug discovery to explore drug candidates, screening methods are often used to select drug targets such as disease-related genes, or active components. There are also often used various materials and methods, the so-called research tools, such as genetically modified cells or model animals to evaluate the efficacy and safety of pharmaceutical candidate substances, although they do not become the drugs themselves, but effectively support the drug discovery. Except for situations in which the research tool (RT) patent is dealt as a business itself, the RT patents, in contrast to patents related to the drugs which require exclusivity, should be widely exploited so that they do not become

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impediments to drug discovery.

In recent years, the business environment surrounding drug discovery has experienced a considerable change. The expiry of the term of many patents protecting the large-sales products or block-buster drugs which have supported the growth of many pharmaceutical companies will peak at around year 2010 and the difficulties of discovering new drugs to cover the expected drop in sales is increasing year by year. The main reason for this is the existence of diseases which highly need future development of therapeutic agents, which are yet to come because the mechanism of the pathology is complex or unsolved, and the diseases involve plural pathological factors. That is to say, diseases for which there is no prospect for easy discovery of a therapeutic agent are being left. In addition, there is a fact that increasingly strict standards are applied to the safety of pharmaceuticals. The main thrust of approaches to the treatment of such diseases lies in the research and development of molecularly-targeted drugs acting with pin-point accuracy on drug-discovery targets based on analysis of information on the affected genes. In particular, in the area of anti-cancer agents and immunosuppressive agents, a business of bio-pharmaceuticals such as antibodies is expanding. As can be seen from the fact that a majority of bio-pharmaceuticals originate from venture companies, the traditional mainstream model of the so-called closed innovation for overall drug discovery including bio-pharmaceuticals, in which all processes from research to sales are handled in a single company is giving way to the so-called open innovation which stresses external alliances with upstream of drug discovery, such as a collaborative research and licenses at the initial development candidate stage with universities and venture companies.[1]

Furthermore innovation in the life science field, as can be seen in the recent establishment of the iPS cells, for example, depends to a large extent on revolutionary advances in basic science. In order to retain the competitive edge, there can be no doubt regarding the importance of suitable measures from the nascent stage of a technology for reviewing or providing a suitable intellectual property strategy which is focused on the future practical application of the technology. Furthermore the current difficulties in the development of the above-mentioned pharmaceuticals having a new mechanism of action have lead to the appearance of new pharmaceuticals which enable radical improvement in convenience, safety and efficacy due to improvements in the dosage form and method of administration of existing pharmaceuticals through development of revolutionary technologies based on the advance of science. However, the patent protection which serves as incentives for development of these are occasionally insufficient as seen in extension of the term of drug delivery system (DDS) patents, and patents on dosage regimen.

As discussed above, the research and development environment surrounding the pharmaceuticals has undergone considerable changes and a corresponding appropriate patent protection and exploitation strategies are desired. Among them, especially, important issues such as patents relating to medical treatments, extension of term of the DDS patents, RT patents, research exemption, etc., will be discussed in detail below.

2. Current Status and Issues of Patent Protection

(1) Patents Related to Medical Treatments

The whole concept of patent protection appropriate for advances in the leading-edge medical treatment including regenerative medicine and gene therapy was discussed in the "Working Group of the Sub-Committee of the Industrial Structure Council for the Patent System regarding Medical Treatment"[2] and the "Investigation Committee related to the State of Patent Protection for Acts related to Medical Treatment."[3] As a result, revisions of the examination

standards were performed on two occasions in 2003 and 2005. In particular, one of the main points of discussion was handling of inventions related to methods of treatment required by the leading-edge medical treatments. As to the propriety of the proposition that general acts related to therapy are patentable, it was thought that more discussions have to be made on the political necessity, the practical effects, etc., until a consensus can be formed" (Report dated June 3, 2003[4]) and "the techniques related to the acts of doctors have to be treated with caution in view of the characteristics of "therapy" and have been excluded from deliberation" (Report dated November 22, 2004[5]). Such inventions have been excluded from patentable subject matter on the basis of the interpretation applied up to date that they do not comply with "inventions which can be utilized industrially." On the other hand, as a result of a review of the protection for other inventions related to the leading-edge medical treatments, a revision of the examination standards in 2003 included methods of manufacturing therapeutic materials such as cultured skin sheets or pharmaceuticals such as genetically recombinant drugs within the scope of patentable subject matter even when such inventions are premised on returning the materials to the same person. The revision performed in 2005 pointed out specifically that pharmaceutical inventions specified in a form of treatment such as a combination of a plurality of therapeutic agents and a dosage interval or dosage amount are "product inventions" and therefore should be treated as "inventions which industrially applied" and in addition clarified the methods of determining patentability including novelty, inventive step, etc.

The application of stem cells to regenerative medicine including embryonic stem cells (ES cells), which have attracted a great deal of debate regarding ethical issues due to the necessity to use fertilized eggs, is being examined around the world for its proposed usefulness as a treatment for a variety of intractable diseases. Since a revolutionary path to realization of regenerative medicine which is not associated with concerns about rejection reactions or ethical problems has been opened by the emergence of induced pluripotent stem cells (iPS) which were developed by Prof. Yamanaka at Kyoto University in 2006, the need has intensified for debate about the whole concept of patent protection for leading-edge medical treatments for the purpose of increasing competitiveness in the practical application of revolutionary technologies developed in Japan in the context of fierce international competition. In the field of pharmaceuticals, the 2005 revision of the examination standards prescribed that even an invention characterized by a method of administration of a pharmaceutical was rejected, because novelty was not present as long as there was no difference in the patient population or the applicable site. Consequently there has been a problem that inventions which provide the patients with effectiveness, safety, convenience, etc., by means of new administration method cannot be proprietized. For example, in case of 5 mg Fosamax tablets, the patient could not lie down for 30 minutes after ingesting before breakfast each day in order to prevent inflammation of esophagus as a side effect, a considerable improvement in convenience and side effects was enabled for patients by the development of a new dosage regimen which administers a 35 mg tablet once a week. Such improvements in dosage regimen which exceed expectations of the experts are important for maximizing the benefit received by patients together with maximizing the value of the product. These also require investment for research and development similar to that for a new pharmaceuticals and, thus, the absence of patent protection will deaden incentives for the development of these types of useful pharmaceuticals and will create problems that more effective methods of treatment will not reach the patients.

The Investigation Committee for Patents for Leading-edge Medical Treatments[6] which held eight meetings over a period from November 2008 to May 2009 collected actual examples (including the situation in the United States which recognizes patents for methods of treatment) which required acquisition of patents both domestically and overseas

and heard testimony from researchers related to the whole concept of suitable patent protection in the field of leading-edge medical treatments including technologies related to iPS cells. The Committee also considered a range of issues including sufficient consideration of public interest and the characteristics of treatments directly related to the life and health of the general population. As a result, a report[7] was issued prescribing that the "methods of treatment" remained excluded from patentable subject matter due to the paucity of actual examples of inventions only expressed in the form of a "method of treatment" which was initially thought necessary to be dealt with, that the examination standards were to be clarified by addition of a large number of examples to assist understanding of applicants, who do not realize that a matter may be handled by patent protection as a "product" because the examination standards are not clear. The report also included support, etc., for the acquisition of patents regarding the leading-edge medical treatments as a response to the lack of understanding of patentable subject matter and patent application strategies in universities, etc., the lack having been made clear through the course of the testimony. Support was also included for an expansion of patentable subject matter to include inventions not currently capable of protection ("inventions characterized by novel dosage and administration of cells or a pharmaceutical agent" and "inventions for data collection relating to the human body for the purpose of assisting the final diagnosis").

The results of the considerations on this occasion can be regarded as contributing to the strengthening of patent protection for the support of commercialization of regenerative medical treatments by the development of iPS cell related technologies where competitiveness of Japan can be expected. In particular, the inclusion of inventions characterized by new-dosage and administration having a usefulness which exceeds expectation of experts is thought to have a great significance for regenerative medicine and cell therapies which are optimized by various improvements in a clinical setting to a greater extent than the conventional pharmaceuticals. Furthermore, the revision of the examination standards is expected to include a large number of examples to facilitate understanding of the patentable subject matter by patent applicants regarding inventions in which there are difficulties in specifying the cells such as in a cell population which is not uniform but varies over time and inventions characterized by combination of cells, pharmaceutical agents and physical means (devices producing a strong magnetic field) and, moreover, when respective elements have characteristics in terms of time or the position. It is to be welcomed that in the fields related to pharmaceuticals, inventions characterized by dosage and administration which had traditionally been excluded from patent protection can now be protected and that patentable subject matter has been clarified by the addition to the examination standards of examples related to inventions characterized by combinations of existing products. The details of the revised examination standards are eagerly awaited. Therefore, the present situation where creation of revolutionary new pharmaceuticals is becoming difficult, a path has been opened to added values of the existing drugs as large as that of a new drug and revival of products, which had been removed from development, as a new drug. This approach should result in increased possibilities for achieving more useful drugs for patients. On the other hand, although conclusions with respect to conditions for patent registration were expressed substantially along the lines hoped for by industry, characteristics of a "method" are strong as the basic property of invention in the case of inventions characterized by dosage and administration and, thus, it is desired that rights are respected as an invention for a "product" appropriate for the reality of pharmaceuticals which require for the stable exercise of legal rights. Furthermore, it is thought that there should be an option left to reconsider the protection of patents for "methods of treatment", which were not examined because of low needs. This should be done with public interest taken into account, in response to materialization of the needs at the

commercialization stage of the regenerative treatments or technical innovation in the field of leading-edge medical treatments in which innovations are actively generated with developments in science.

(2) System for Patent Term Extension

Research and development of pharmaceuticals take a long period of 10 to 15 years and the pharmaceuticals cannot be sold until approval is obtained pursuant to the Pharmaceutical Affairs Law. Thus, even when patents related to the pharmaceutical are granted, there is usually a period in which exploitation is not possible. In a situation in which the term of the patent is eroded in this manner, even if a pharmaceutical which requires a large amount of development investment is successfully brought to market, the incentive for further investment in research and development, and recovery of investment will be deadened when the period of exclusivity is limited to 20 years after application, resulting in a situation in which superior pharmaceuticals are not developed. From this standpoint, a system under which a maximum of five years could be recovered from the period eroded due to the requirement of the Pharmaceutical Affairs Law was introduced in 1988 for the purpose of promoting research and development of pharmaceuticals. The system of patent term extension in Japan differs from the systems employed in Europe and the United States, and is characterized in that a plurality of patents may be extended a plurality of times corresponding to each approval for a pharmaceutical. This system has an excellent aspect of providing a strong incentive for not only development of a new active component but also development of related technologies and acquisition of additional effects which are difficult to develop. On the other hand, disposition (approval) under the system for patent term extension requires that a disposition is applied which is required for the exploitation of the patented invention, the condition of which is understood to be that this is the first disposition of the product related to the disposition. The Patent Office of Japan (JPO) makes the determination whether the disposition is the first procedure or not from a standpoint of "product (active component)" and "use (efficacy and effectiveness)". Consequently even in a case of a new pharmaceutical based on a revolutionary DDS technology, the patent for the DDS drug was not considered to be a subject matter for extension of term unless the disposition was not the first one when considered from the points of "product (active component)" and "use (efficacy and effectiveness)."

According to the policy entitled "A Fundamental Review of the Extension of Term System for Patent Rights" in the Intellectual Property Promotion Plan 2008, studies were commenced by the Working Group for the Extension of Term System for Patent Rights[8] of the Sub-Committee of the Industrial Structure Council for the Patent System from October 2008. The relationship to the Cartagena Law was also considered but problems to be studied in relation to pharmaceuticals are described below. Discussion were made on (1) the whole concept of the system including conditions for extension, number and frequency of patent rights to be extended and the effective scope of extended patent rights, and (2) whether or not to add revolutionary pharmaceuticals which differ only in a dosage form using a epoch-making DDS technology to the subject matter for extension. With respect to (1), comparisons were made with the system employed in Europe and the United States under which, in principle, patent may be extended only once. As stated in an opinion brief[9] by the Japan Pharmaceutical Manufacturers' Association, the Japanese system is a unique one based on a patent system of a code different from Europe and the United States, and having a correspondingly befitting legislative intent. Furthermore, since such a system is necessary for the improvement of the health and welfare of the Japanese people and the future development of the entire pharmaceutical industry in Japan, a consensus was achieved with the opinion of the Japan Pharmaceutical Manufacturers' Association that pursuit of a system appropriate for Japan

should be continued instead of simply harmonizing with the systems in Europe and the United States. On the other hand, with respect to (2), an idea[10] was submitted with respect to a new system enabling extension of patents for the DDS drugs from the JPO and the Japan Pharmaceutical Manufacturers' Association. However, it still has many problems and a consensus has not been reached.

In connection with point (2) above, the Intellectual Property High Court handed down three decisions[11] on May 29, 2009, in contrast to previous judgments, approving extension of terms for drug formulation patents based on approval of new pharmaceutical drug formulations. Although the JPO is currently appealing the decisions and it is necessary to wait for the decision of the Supreme Court including acceptance of appeal, it is to be noted that the decision stated that even when there is a prior pharmaceutical approval with the same conventional "product (active component)" and "use (efficacy and effectiveness)" with respect to the conditions for registration, that fact alone is not a sufficient reason to reject an application for extension of the patent term. The deliberations related to the current problems by the Working Group is expected to be halted until the Supreme Court hands down its decision., However, as is proposed in the new system proposal submitted by the Japan Pharmaceutical Manufacturers' Association, future deliberations are expected to be made in order to realize a system enabling term extension of patents for DDS drugs, etc., while maintaining the excellent characteristics of the current system in order to maintain the incentive for the continued creation of useful new pharmaceuticals.

(3) Research Tool Patents

Regarding the problems associated with impediments to drug discovery activities stemming from monopolization of or requisition of big fees for patents covering research tools which cannot be substituted and which may be exemplified by genes, etc., acting as drug targets, there have been various discussions since about year 2000. Previously the Hamamatsu University Case[12] regarding the Oncomouse patent is well known. More recently, the Euroscreen Case[13] involving a screening method patent using the CCR5 receptor or the Cellectis Case[14] involving a method of genetic recombination have been before the courts. In both cases, a large amount of claim amounting to approximately ¥1 billion in damages was sought. These demonstrate that problems regarding the RT patents have fundamentally not been resolved yet.

In order to solve these problems, discussions were conducted under the auspices of the Working Group of the Sub-Committee of the Industrial Structure Council for the Patent System regarding Patent Strategy Planning[15] and other specialist investigatory bodies in 2003. There were considered a range of ideas including use of exceptional provision for experimentation and research, and compulsory licenses, abolition of applications for injunction as prescribed under the Swiss Patent Act and determination of remuneration by the court when the license negotiations do not go well. However, at the present time, a concrete solution requiring amendments to current law has not been laid down. As pointed out in the "Introduction" with respect to the open innovation in upstream drug discovery, the important point when considering this problem is to strike a balance between the benefit to a pharmaceutical manufacturer which effectively implements drug development and drug discovery by using RT patents, and protection of business models of the universities and venture capital companies which create the RT patents or drug related technologies using the RT patents, the fact that in the absence of such a business model, point beyond which activation of upstream drug discovery would become difficult. The Intellectual Property Committee of the Japan Pharmaceutical Manufacturers' Association

has formulated Guidelines[16] with respect to this problem. As is proposed therein, in view of the character of RT patents that it is important that they are widely used, it is ideal that licenses are typically granted on rational terms to promote their use while respecting rights. Regarding promotion of the use of RT patents, OECD has issued Guidelines[17] and the Council for Science and Technology Policy has published a "Guideline Related to Facilitation of Use of Research Tool Patents in Life Sciences."[18] These recommend the wide facilitation of use of RT patents. Furthermore, the JPO commenced operation of a "Research Tool Patent Database"[19] in April 2009 as a tool for promoting use of RT patents. Since many of the holders of RT patents are foreign corporations, a practical solution to this problem is dissemination of the above guidelines and database to foreign countries for promotion of a system whereby utilization of RT patents under rational conditions including the fees.

(4) Research Exemption

Characteristics of the life science field include an intimate relationship between the results of leading-edge research in the biological sciences and promotion of research activities in the upstream drug discovery using those results and mutual use of research results by both sides which becomes a key to further innovation. Thus, the whole concept of appropriate utilization of these research results becomes an issue. Although utilization of research results applied for as a patent has already been discussed above in relation to the RT patents, other solutions to the problem may be enabled by application of the exception rule of experimentation and research. Although this topic was discussed during the sessions of the Intellectual Property Strategy Working Group[15] referred to above regarding the promotion of the use of RT patents, at present, the prevailing interpretation is the Someno Theory[20] in which the scope of application of the exception rule is limited to research for the purpose of improvement or functional experimentation of the patented invention itself for the purpose of improvement or further development of the technique. Furthermore even a university may be subject to an action for patent infringement by acting as a "business entity."

However in addition to the fact that there is no concrete judicial precedent on this point, when considering the current state of promotion of open innovation or stimulation of innovation in the universities as mentioned above, it is necessary to reconsider the range of Article 69(1) of the Patent Act. For example, in relation to the use of RT patents, it is necessary to consider the practice of contracts including licensing at no charge for academic research and that it is difficult to think that the interests of the patent holder will be unfairly damaged by use of an RT patent in provisional drug screening for the purpose of suitable verification of a drug target in the stage of upstream drug discovery and, therefore, permission of such use will result in future acceleration of broad use. Furthermore, the recent trend in industry is more often not to conduct all research alone but rather to use group companies which span off from its research support functions and outside research such as research commissioned companies and universities which possess special technologies. It is submitted that there is scope within Aritcle 69(1) of the Patent Act for application to situations in which commissioning the synthesis and evaluation of the patented compound of another party for use as a reference agent in comparing the properties of a product under development.

There is a decision of the Supreme Court[21] triggered by litigation about a generic product regarding the application of Article 69(1) of the Patent Law to experimentation required for obtaining an approval for a pharmaceutical pursuant to the Pharmaceutical Affairs Law. Although application of that decision to the development of a new drug is not entirely clear, there is a decision of the Tokyo Regional Court[22] which supports this. Further clarification of this

point would benefit the promotion of new pharmaceuticals development. Meanwhile, in the United States, the position is clearly stated by the Bolar Provision (S. 271(e)(1)). However, in Europe, the provision is limited to generics depending on the country.

Other problems include exemption of medical doctors, which arise often when discussing the patent protection related to leading-edge medical treatments. At present, although there is no judicial precedent for filing a suit for patent infringement against acts of medical treatment performed by a doctor, only a part of acts are exempted in Article 69(3) of the Patent Act. Thus, there may be a need to clarify a general exemption for the acts of medical treatment by doctors in view of the characteristics of medical treatment, which is directly associated with the life and health of the general population. It is hoped that this will lead to discussions focused on important points other than this issue, when discussions become necessary about patent protection of the inventions related to methods of treatment which are required for leading-edge medical treatments.

(5) Other Problems

When importance of patents in the life science field is considered, it is important that stable patents with high predictability of exercising of rights are established globally as a similar right and there is a considerable significance to the improvement in quality through comparative research of examination practices in the Trilateral Patent Offices. However, as discussed below, examination in Japan is in part more rigorous than Europe or the United States mainly in the field of biotechnology. Thus, further improvement would be desirable. Whereas more than 80% of applications in the United States and Europe for novelty of a protein or a gene of a similar structure in which there is a difference of 1 to several amino acids are judged to be novel, in Japan 64% are judged not to be novel, demonstrating severity of the examination standard for novelty.[23] Furthermore, the inventive step for human antibodies is allowed in the United States and Europe on the basis of a comparison of neutralization activity with a known human monoclonal antibody. In Japan, a pronounced effect with respect to a humanized known monoclonal antibody is required, for example, to display more than 10 times the affinity, demonstrating the high hurdle placed on the inventive step in Japan.[24] In Europe and the United States, there are examples of admission of the inventive step based on assertions based on results of clinical trials conducted after application or on assertions that there is no rational expectation for success. Furthermore there are examples where the inventive step was allowed based on assertions that trying something which is neither suggested nor shown in a citation is obvious is not the standard for obviousness. In Japan, in the absence of a basis in the specification as originally filed, presentation of clinical results may be determined that they cannot be taken into consideration as a new matter and there are many cases[25, 26] in which assertions of the inventive step as above in the United States and Europe are not recognized and the applications are refused. Thus Japanese examination practice which does not allow later filing of pharmacological data and strict determination of the inventive step is thought to be a problem, which is not limited to the field of biotechnology.

In order to promote innovation and strengthen international competitiveness, a framework is thought to be required, which provides suitable protection to revolutionary basic inventions. In particular, there are many examples of basic inventions in which the prior art is limited or abundant embodiments cannot necessarily be submitted. In order to promote such inventions, it is necessary that broad rights should be given within a rational scope without limitation to the embodiments. In the area of pharmaceuticals, this corresponds to use patents written using functional expression

without limitation of the compounds. However it goes without saying that there is a necessity to avoid unnecessary disruption which may be produced in relation to other patents, by devising ways such as the definition of a basic invention and the determination of rational scope of rights from the relationship with the embodiments. Furthermore, at the same time, consideration should be given to the whole concept of protection in view of the nature of a basic patent that it will be widely utilized and elimination of adverse effects that arise from a broad scope of rights.

3. Conclusion

Current status and issues of patent protection in the life science field was reviewed, particularly from a viewpoint of the pharmaceutical industry. In the patent protection of leading-edge medical treatments, the discussions held at The Investigation Committee for Patents for Leading-edge Medical Treatments have lead to policies including revision of the examination standards enabling protection of inventions characterized by dosage and administration of pharmaceuticals and cells, and clarification of examination standards conforming to the need that the practical application of the regenerative medicine should be facilitated. It is strongly hoped that the policies will be suitably implemented and timely reviewed in response to future needs. In this paper, the following were mainly discussed. The revision of the system for the extension of patent term should retain the excellent characteristics of the current system and, at the same time, continue to pursue a system of patent term extension which protects revolutionary technologies such as DDS. As for the RT patents, realization of an environment should be planned, where both patentee and user can obtain benefits by spreading domestically and overseas the guidelines and database for the promotion of use of RT patents. Further, the exception to experimentation and research need to be reviewed corresponding to the change in the environment for drug discovery. Concerning the whole concept of examination of patent applications, an improvement in predictability of patent protection on a global level was hoped by pointing out strictness in some areas of examination in Japan, compared to examination performed at other Trilateral Patent Offices. The whole concept of basic patent protection was also discussed.

In order to effectively support the pharmaceutical business which is low in success rate for R&D and requires a large investment and a long development period until a product reaches the market, there is no change in the importance of a high-quality patent, but it has become necessary to the whole concept of patent protection which not only provides a simple monopolistic exclusionary right but also promotes active use according to the phase, as prompted by the changes in environment such as the open innovation in upstream drug discovery. All of the above points are issues which correspond to such changes and it is necessary to consider continually reexamining the whole concept of suitable protection in accordance with the existing situation of the pharmaceutical business.

Notes

1 http://www.inpit.go.jp/jinzai/study/pdf/46_ronbun2.pdf
2 http://www.jpo.go.jp/cgi/link.cgi?url=/shiryou/toushin/shingikai/sangyou_kouzou.htm
3 http://www.kantei.go.jp/jp/singi/titeki2/tyousakai/iryou/index.html
4 http://www.jpo.go.jp/shiryou/toushin//toushintou/pdf/iryou_report.pdf
5 http://www. kantei.go.jp/jp/singi/titeki2/tyousakai/iryou/torimatome.pdf
6 http://www. kantei.go.jp/jp/singi/titeki2/tyousakai/kyousou/index.html
7 http://www. kantei.go.jp/jp/singi/titeki2/tyousakai/ kyousou/houkoku/090529/090529_ tokkyohogo.pdf

[8] http://www.jpo.go.jp/cgi/link.cgi?url=/shiryou/toushin/shingikai/sangyou_kouzou.htm
[9] http://www.jpo.go.jp/cgi/link.cgi?url=/shiryou/toushin/shingikai/sangyou_kouzou.htm
[10] JPO proposal: http://www.jpo.go.jp/cgi/link.cgi?url=/shiryou/toushin/shingikai/sangyou_ kouzou.htm
Japan Pharmaceutical Manufacturers' Association Proposal:
http://www.jpo.go.jp/cgi/link.cgi?url=/shiryou/toushin/shingikai/sangyou_kouzou.htm
[11] Intellectual Property High Court 2008 (Gyo-Ke) No. 10458, No. 10459, No. 10460
[12] Tokyo High Court 2002 (Ne) No. 675
[13] Osaka District Court 2006 (Wa) No. 7760
[14] http://www.cellectis.com/fileadmin/Cellectis/Communiques_de_Presse/clspr-gb-080509.pdf
[15] http://www.jpo.go.jp/shiryou/toushin/shingikai/strategy_wg_menu.htm
[16] http://www.jpma.or.jp/about/basis/guide/pdf/guideline_j.pdf
[17] http://www.oecd.org/dataoecd/39/38/36198812.pdf
[18] http://www8.cao.go.jp/cstp/output/iken070301.pdf
[19] http://www.ryutu.inpit.go.jp/RTPatents/
[20] AIPPI, 33 (1988) 138 - 143
[21] Supreme Court April 16, 1999
[22] Tokyo District Court 1996 (Wa) No. 8627
[23] Chizai Kanri Vol. 57, No. 4, 589 – 607 (2007)
[24] Chizai Kanri Vol. 58, No. 7, 873 – 898 (2008)
[25] Chizai Kanri Vol. 58, No. 7, 873 – 898 (2008)
[26] Chizai Kanri Vol. 59, No.8, 971 – 991 (2009)