12 Comparative Studies on Patent Systems for Protecting High Technologies in the Advanced Medical Field

There have recently been remarkable technological innovations in the advanced medical field, including gene therapy and regenerative medicine. It has been recognized that it is necessary to clarify the present situation of protection of technologies in the this field in other countries and problems which each country is addressing to protect advanced technologies, as well as to conduct basic study on desirable systems and their operations to protect technologies in the field more appropriately in Japan. In this study, we prepared materials that can serve as a basis for discussion on systems to protect technologies in the field and their operations, etc. More specifically, we did research on how researchers and engineers expect or foresee the future trends in R&D and how they approach to intellectual property relating to technologies in the advanced medical field, relevant provisions in the patent laws of some countries and their operational guidelines, the background of establishment of such provisions and guidelines, and specific operations of the patent system of each country, based on the present situation of specific R&D relating to technologies in this field,.

In this study, we did research on the future trends in advanced medical care, including gene therapy and regenerative medicine, based on the present situation of R&D, and also surveyed basic information with regard to the patent system of some countries, and operations and backgrounds thereof, as well as that with regard to systems other than the patent system.

I Introduction

There have recently been remarkable technological innovations in the fields of gene therapy and regenerative medicine. The Institute of Intellectual Property published "Research and Study on Patent Protection for Medical Field" in March 2001. In 2003, Chapter 1 "Industrially Applicable Inventions" in Part II of the Examination Guidelines for Patent and Utility Model was revised from the viewpoint of regenerative medicine, etc.

In March 2006, the Japan Patent Office (JPO) published a report titled "Analysis of Filing of Patent Applications Based on Correlation between Trends in Articles and Patent Applications in the Advanced Medical Field." According to this report, major technological elements that constitute gene therapy include gene transfer/expression technology, target molecules/genes for gene therapy, target cells for gene transfer, target diseases, technology for controlling gene expression, technology for manipulating genes, and experimental animals for studies on human diseases. In addition, major technological elements that constitute regenerative medicine include cells (ES cells, etc.), differentiation-inducing/growth-inhibiting mechanisms, tissue engineering, tissue regeneration, cell therapy, technology for handling cells (extraction/preservation, separation, cultivation/proliferation, transport, etc.), transplant, experimental animals for studies on human diseases, imaging, monitoring, and safety/quality assessment technology.

In this study, the following surveys and research were conducted based on the present situation of specific R&D of high technologies in the advanced medical field, in Japan and abroad: a survey for leading researchers and engineers in the field on how they expect or foresee the future trends in R&D and how they approach to intellectual property; research on relevant provisions in the patent law; research on other relevant

provisions; research on the specific operations of the patent system in relation to advanced medical technology; and research on the backgrounds (discussions, etc.) of establishment of relevant provisions in patent law and operational guidelines for examination in each country.

II A Survey Concerning the Future Trends, etc. for Leading Researchers and Engineers in the Advanced Medical Field

In this study, an awareness survey was conducted for individuals and companies, etc. engaged in R&D in the advanced medical field, including gene therapy and regenerative medicine. That is, a questionnaire survey was conducted in Japan for researchers in the fields of gene therapy technology and regenerative medicine technology, and engineers and companies, etc. engaged in these technologies, in order to understand the actual conditions and their attitudes on how they regard the present situation of R&D, what kinds of technologies will attract their attentions in the future, and how they approach to intellectual property. Then, an interview survey was conducted for some of the questionnaire respondents based on their answers to the questionaire.

As a result of the questionnaire survey, many respondents cited “process or means of introducing the active ingredients of a gene therapeutic agent administered to an individual into the target cell, etc.,” as the present research target in the field of gene therapy, a noticeable research target in terms of future research trends, or a category of inventions for which they have filed patent applications. As well, many respondents cited “process or means of differentiating, inducing, proliferating or preserving cells,” as the present research target in the field of regenerative medicine, a noticeable research target in terms of future research trends, or a category of inventions for which they have filed patent applications. However, most respondents have filed no more than five patent applications in the field of gene therapy or regenerative medicine, which indicates a tendency that not many patent applications are filed in these fields on the whole. In Japan, the government has been developing measures for R&D in the advanced medical field, outside the patent system, from multifaceted perspectives, and various laws and regulations as well as guidelines have been put into force or made public. According to the survey, these laws and regulations as well as guidelines are widely recognized among researchers and companies, etc., of which, the Convention on Biological Diversity (CBD) relating to access to genetic resources, the Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of their Utilization, and the Cartagena Protocol on Biosafety, as well as laws, regulations and guidelines, etc. for implementation thereof in Japan are recognized as measures oriented toward restraining R&D as a whole. To the contrary, reduction of fees for requesting examination of patent applications and patent fees as well as accelerated examination/appeal proceedings systems are recognized as measures oriented toward promoting R&D.

In the interview survey, the respondents were asked their opinions about the fact that the definition of “industrially applicable inventions” in the Examination Guidelines for Patent and Utility Model was recently revised to stipulate that a method for manufacturing a medicinal product or medical material by utilizing raw material collected from a human being is not qualified to be placed under the category of “methods for treatment of the human body by surgery or therapy and diagnostic methods practiced on the human body,” even if the method is a method for processing the material collected from the human being based on a presupposition that the material from a human being will be returned to the same human being as part of his medical treatment and that such a method has been included in the subject matter of patent protection. In response to this question, most of the respondents positively evaluated the expansion of the subject matter of patent

protection through this time's revision. As the reasons, the respondents, for example, said that the field covered by the expansion of the subject matter of protection is the field relating to regenerative medicine, in which the industry can participate, and participation of and support by the industry are indispensable for the development of advanced medical care. On the other hand, regarding medical acts, such as a method for collecting cells, etc. from a human being and a method for returning cells, etc. to the same human being as part of medical treatment, some said that the subject matter of patent protection should be expanded to include these medical acts while others said that these medical acts should be excluded from the subject matter of patent protection, as is. Even the former cited the following as conditions for expanding the subject matter of patent protection to include medical acts: (1) medical acts shall be made immune from liability for patent infringement and (2) patent rights shall not be enforced in relation to treatment for an incurable disease or in the case of an emergency. Therefore, it can be said that the respondents, including the latter, have a common recognition of the necessity of giving consideration in patent practice to medical acts relating to advanced medical care and patients who enjoy the benefits of such medical acts. In addition, the respondents cited the following as reasons for asserting that patent protection should be expanded to include medial acts: (1) economic support from companies is essential; (2) the nature of an invention in the field of regenerative medicine using autologous cells is often a series of processes from collecting cells, etc. from a human being to injecting the cells, etc. into the same human being, (3) claiming a portion of the entire process causes discrepancy between the nature of that invention and the claim directed to the portion, and (4) even if a portion of the entire process is entitled to be patented, there will be concerns about the effectiveness of the patent. The appropriateness of these reasons remains to be verified, and it will become clear through accumulation of decisions for appeal and courts' judgments.

III Provisions Relating to Advanced Medical Technology in Patent Law and Guidelines for Their Specific Operations

In this study, research was conducted on provisions relating to advanced medical technology in the patent law of each country (requirements for patentability, description requirements, enablement requirement, etc.), their specific operations (operational guidelines for examination, examination guidelines, etc.), and backgrounds for establishment of the patent law and specific operation guidelines thereof (discussions at congress, the government, various bodies, and industrial parties).

The Japan Patent Act and the Ordinance for Operation thereof do not set any provisions specific to the technical fields directly related to advanced medical care. However, patent laws in the United Kingdom, Germany and France as well as the European Patent Convention clearly stipulate that uses of human embryos for industrial or commercial purposes shall not be the patentable subject matter. European countries have been intending to establish a common framework for patent systems relating to biotechnological inventions, including uses of human embryos, through implementation of Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the Legal Protection of Biotechnological Inventions (Biotechnology Directive) in each member country. However, there have been circumstances, problems and discussions unique to each country in terms of domestic implementation of the Biotechnology Directive.

The examination guidelines in Japan, the United States, France and South Korea do not directly refer to human embryos and human embryonic stem cells. On the contrary, the U.K. Examination Guidelines explicitly exclude human embryonic stem cells that have the potential to develop into an entire human body and methods of producing or culturing such cells from the patentable

subject matter. The present determination standards are unique to the United Kingdom and seem to be based on the implementation of the Biotechnology Directive. On the other hand, it seems that as of the time of our research, the implementation of the Biotechnology Directive had yet to be directly reflected in the examination guidelines of France and Germany. The Chinese Examination Guidelines clearly stipulate that no patent right may be granted for uses of human embryos for industrial or commercial purposes as well as human embryonic stem cells and methods for producing them.

In Japan, a chapter titled "Industrially Applicable Inventions" in the Examination Guidelines for Patent and Utility Model was recently revised to stipulate that a method for manufacturing a medicinal product or medical material by utilizing raw material collected from a human being is not qualified to be placed under the category of "methods for treatment of the human body by surgery or therapy and diagnostic methods practiced on the human body," even if the method is a method for processing the material collected from the human being based on a presupposition that the material from a human being will be returned to the same human being as part of his medical treatment. In contrast, the Guidelines for Examination of the European Patent Office (EPO) stipulate that a method of treatment of tissues or fluids removed from a human body is excluded from the patentable subject matter if they are returned to the same human body, and cite a process of blood by dialysis as an example of such invention. In a similar way, the Chinese Examination Guidelines stipulate that methods comprising returning cells or tissues to the same human body and a process of blood by dialysis fall under the category of methods of treatment, and that no patent may be granted for such processes. The Examination Guidelines of South Korea also stipulate that a method for processing the material collected from a human being based on a presupposition that the material from a human being will be returned to the same human being falls under the category of medical acts and is thus not an industrially applicable invention, and then cite a process of blood by dialysis as an example of such invention. However, the Examination Guidelines for Medical and Health Fields of South Korea stipulate that a method for processing blood, cells, etc. collected from a human being is a step that is separable from relevant medical acts and is thus industrially applicable, and cite a method of manufacturing recombinant human cells and a method of manufacturing artificial bone containing human cells, which are apparently intended to be used for gene therapy and regenerative medicine, respectively, as examples of such method. Relationships and consistency between the Examination Guidelines for Medical and Health Fields and the Examination Guidelines are not necessarily clear, and attention also must be paid to the trends of future appeal decisions and courts' judgments.

As for movements relating to gene therapy, Germany and other European countries have recently come to stipulate in their patent laws that uses of a gene disclosed in the specification shall be described in the claims directed to a genetic invention. It is necessary to carefully watch for the influence of the practice of deeming a genetic invention as an exception to an invention of a product and limiting the scope of claims directed to the product by use thereof as well as courts' judgments.

IV Decisions for Appeals and Courts' Judgments Relating to Patents Pertaining to Advanced Medical Inventions

In this study, courts' judgments and appeal decisions on cases pertaining to patents in the relevant field in each country were collected in order to analyze the examination process in specific cases and study representative appeal decisions and judgments in detail as part of research on the specific operations of the patent system for

inventions in the advanced medical field in each country. As a result, about 30 cases were extracted in which the requirements for substantive examination (industrial applicability, novelty, inventive step, enablement requirement, and description requirements, etc.) have become a point of issue on patent application claiming advanced medical inventions.

About 30 extracted cases were classified by the type of the disputed requirements. Inventive step/non-obviousness has become a point of issue in about three-fifths of all the cases extracted while eligibility for patent (industrial applicability, public order and morality, exclusion from patentable subject matter, utility, etc.) has become a point of issue in about one-fifth of all the cases. In addition, about 30 extracted cases were classified by the category of a patented invention (or an invention for which an application was filed). About half of all the cases were related to gene therapy while about one-third were related to regenerative medicine, of which, gene therapy-related inventions included therapeutic genes, vectors, antisense, combination of genes and other drugs, and gene-trapping technology, while regenerative medicine-related inventions included embryonic stem cell cultures, hematopoietic stem cells and compositions containing hematopoietic stem cells, technologies for isolating, enriching or selectively proliferating stem cells, scaffolding materials for tissue engineering, technologies for tissue regeneration using mesenchymal stem cells, compositions containing cells for skin regeneration, and technologies for separating/culturing cells.

In Europe, there has been much debate on whether or not inventions related to embryonic stem cells are excluded from the patentable subject matter. With respect to a decision of the Technical Board of Appeal of the EPO (T1374/04) over an invention of an embryonic stem cell culture, some questions of law were referred to the Enlarged Board of Appeal (G2/06). The Enlarged Board of Appeal of the EPO sought public comments from third parties, and the President of the EPO and the United Kingdom, etc., submitted their opinions. A decision on G2/06 is expected to be rendered at the end of 2007 at the earliest. On the other hand, the German Federal Patent Court rendered a judgment of partial invalidation of German Patent No. 19756864 relating to human embryonic stem cells in December 2006. In particular, it appears that claims pertaining to use of human embryonic stem cells were determined to be invalid. The said judgment had not been made public as of February 2007, and it was not possible to review the details thereof. However, this judgment attracts attention as one that may affect the outcome of the above-mentioned case of the Enlarged Board of Appeal of the EPO (G2/06).

Some decisions and judgments were also found in South Korea which has been making a remarkable rise in the field of regenerative medicine. The Supreme Court of Korea held that the industrial applicability requirement, which is required for an invention pertaining to a cell for immunotherapy under the Patent Act, may be met even if the invention is to be industrially reduced to practice in the future, but that it will not be met if the invention will become industrially applicable only after it is technically complemented through the development of relevant technology.

In cases in the United States in which non-obviousness was disputed, judgments were made mainly on the procedures followed by the examiner, including motivation to combine more than one prior art document, unacceptable hindsight, and picking and choosing among a number of options disclosed by a prior art. On the other hand, appeal decisions relating to inventive step in Japan contain those on the outstanding effect argued by the appealant and the existence of technical difficulties at the level of the art as of the filing. The decisions of the EPO relating to inventive step contain those on whether or not there was an incentive to achieve the invention in terms of prior art or the level of the art and whether or not success of the invention could be reasonably expected based on prior art.

For the United Kingdom, France, China and Hong Kong, however, neither decisions nor judgments pertaining to patents directly related to an advanced medical invention, including gene therapy and regenerative medicine, were detected. In addition, some judgments relating to the enforcement of a patent right pertaining to an advanced medical invention, including gene therapy and regenerative medicine, were found only in the United States, among countries and regions subject to the research.

V Other Relevant Provisions Relating to R&D in the Advanced Medical Field

In this study, research was conducted on provisions etc., relating to ethics/human rights, pharmaceutical affairs law/doctor law, environment/genetic resources, R&D subsidies, and fosterage of small and medium sized enterprises, as well as other relevant propulsive provisions and other relevant restraining provisions, focusing on Europe as a whole, countries in Europe, the United States, and countries in East Asia, with the aim of gaining an understanding of provisions relating to R&D in the advanced medical field other than those under the patent system.

In regard to ethics/human rights, dynamic efforts have been made in Japan and other countries to develop, improve or strengthen the regulations of establishment/transfer/import and export of human embryos and human embryonic stem cells, regulations of human genome/ handling of genetic information/genetic recombination, systems to protect test subjects in the advanced medical field and those who provide samples relating to advanced medical care (informed consent, management of personal information, etc.), and systems to examine, follow up and evaluate the plan, implementation and results of research in the advanced medical field from an ethical viewpoint (establishment of an ethics commission in a relevant organization, and clarification of its duties, etc.). In Japan, the Act on Regulation of Human Cloning Techniques has come into effect, and subsequently, the Guidelines on the Handling of Specified Embryos have been made public. In Europe, there are regulations at the domestic level, in addition to regulations at the European Union level through some EU Directives and the Oviedo Convention (Convention on Human Rights and Biomedicine). Consequently, there are differences in regulations among European countries. In the United States, there are neither laws nor regulations at the federal level that regulate specifically research on human embryos and human embryonic stem cells. However, federal regulations related thereto have been widely established, and also, state-level laws and regulations are applicable. In addition, R&D in the advanced medical field is examined and supervised by the Food and Drug Administration (FDA), which is the regulatory authority on medical products, etc., and the National Institutes of Health (NIH), while research on gene transfer is examined and supervised by the Recombinant DNA Advisory Committee (RAC) within the NIH.

Regarding pharmaceutical affairs law and doctor law, systems (laws and regulations, guidelines, relevant authorities, etc.) to regulate clinical R&D of medical products and equipment, such as those in the advanced medical field, including regenerative medicine using human embryonic stem cells and other stem cells, have recently been newly established, or reformed, improved or strengthened, in Japan and other countries studied. The research provided a glimpse into the current situation in Europe wherein the whole of Europe has been steadily increasing the efficiency of the procedures for clinical trials in the advanced medical field and promoting the establishment of common procedures for them, through implementation of EU Directive 2001/20/EC on clinical trials and GCP Directive 2005/28/EC in each country, as well as through strengthening of the European Medicines Agency (EMEA) and improvement and promotion of the EMEA's centralized procedure for approval. In Germany, it is not possible to select the

domestic procedure for approval that is implemented by the German national authorities, for medical products derived from biotechnology, and the EMEA's centralized procedure for approval is the only way to approval. In the United States, the regulatory authorities for medical products and equipment are centralized in the FDA. Also in the United Kingdom, such authorities have just been centralized in the Medicines and Healthcare Products Regulatory Agency (MHRA). While clinical trials and permission/approval for medical products and equipment are examined and supervised in a centralized manner through said regulatory authorities in the United States and the United Kingdom, clinical trials under the Pharmaceutical Affairs Act and clinical trials led by doctors coexist in Japan. In addition, the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) plays an important role in standardizing the quality of clinical trials at the international level. Development of systems is ongoing in reference to the ICH guidelines in China and other countries, as well as in Japan. In terms of measures that can promote clinical trials in the advanced medical field, various measures taken by the FDA (micro-dose study, Phase 1 GMP, etc.) attract attention.

Regarding the environment/genetic resources, it is possible to see the present situation where the above-mentioned CBD, in particular, the Cartagena Protocol on Biosafety under the CBD, plays an important role in Japan and other countries. For example, Japan, South Korea and so on have enforced laws and made guidelines to implement the Catagena Protocol to the public. In relation to the CBD, the Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of their Utilization have been published. Then, China is going on strengthening measures to prevent its own genetic resources from running off to outside the country. On the other hand, the United States has not ratified the CBD. In this manner, differences in the responses adopted by each country are relatively noticeable. In connection with genetic resources, procedures for revising the Patent Law are now ongoing in China to add provisions, such as a provision that if acquisition and use of genetic resources necessary to complete an invention claimed in a patent application violates any relevant laws and regulations in China, a patent will not be granted for the invention.

Regarding R&D subsidies, a framework adopted in the United States is distinctive. Under the administration of the incumbent President Bush, the U.S. Federal Government provides no funds (represented by NIH Funds) to research designed to newly establish human embryonic stem cells by destroying human embryos and research using human embryonic stem cells established in said manner. However, there are no federal-level regulations on the provision of private funds, and provision of state government funds differs with respect to each state. Although the framework of provision of the U.S. Federal Government's funds is expected to be maintained for the meantime under the current administration, attention has to be paid to future movements, including the possibility that the framework may be significantly changed in the case of a change of administration.

Regarding fosterage of small and medium sized enterprises, the United States has established the basis of enabling creation and fosterage of biotechnological venture companies in advance of other countries by promoting technology transfer from universities based on the Bayh-Dole Act enacted in 1980 as well as taking other measures. In recent years, other countries have been developing systems to foster small and medium sized enterprises and venture companies (promotion of technology transfer, reduction and exemption of taxes, preferential examination of patent applications, reduction and exemption of costs necessary for filing a patent application, formation of industrial clusters).

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