

A Study on the Patentability of Inventions related to Human Embryonic Stem Cells in Korea

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1 Historical Background of Biopatenting and its Legislation System

1.1 Promotion of Biotechnology and Biopatent in Korea

The Korean government has been supporting R&D in biotechnology since legislating the “Genetic Engineering Promotion Law” in 1983. In 1993, the government initiated the National Biotechnology Development Program¹, an ambitious 14-year plan to promote biotechnology. The program aims at making Korean’s science and technology sector competitive with that of the world’s leading countries and also accelerating the technological transfer of biotechnology research to commercial applications. Since the late 1990s, the government has viewed the bio-industry as a key industry for the 21st century and has undertaken unsurpassed efforts for technological advances in related fields. Since 2000, the government’s annual budget for biotechnology has increased each year by an average of 30 percent. In addition the government is providing even more research and development support, financial support, and industrial basis support.

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¹ It is called “Biotech 2000 Program”.

The history of granting patents for microorganisms and natural extracts in Korea began in 1987 when the “Record of Understanding on Intellectual Property Rights”² was signed between Korea and the U.S. The microorganisms referred to in the Record include both newly discovered natural strains of microorganisms and genetically altered microorganisms. In 1990, food products were added to the list of patentable subject matter in addition to microorganisms and natural extracts. During the last 10 years, the number of Biopatent applications has rapidly increased.

1.2 Legislation System

Korean laws are more inclusive than the minimum requirement level specified by the provisions of TRIPs Article 27.3(b). Even though the provisions of TRIPs allow member countries to exclude animals and plants from patentability, any biotechnological invention of microorganisms, animals or plants is patentable subject matter in Korea. An ethical restriction on the patentability of biotechnological inventions is strictly judged under Patent Law Article 32, which provides that inventions liable to contravene the public order or morality or cause injury to the public health shall not be patentable. Based on this provision, the Korean Intellectual Property Office (KIPO) has stipulated unpatentable subject matter related to biotechnological inventions in the Patent Examination Guideline for Biotechnological Inventions (PEGBI), which was established in 1998.

2 Unpatentable Subject Matter of Biotechnological Invention

2.1 Microorganism Invention

Korea abides by the international standards for the protection of microorganism inventions. Microorganism inventions include both the microorganism itself and the use of new or known microorganisms. Microorganisms are defined as viruses, bacteria, protozoas, yeast, fungi, mushrooms, unicellular algae, actinomyces, etc. In addition, non-specialized cells of animals or plants as well as tissue culture are included in the definition of Microorganism.³ The requirement and procedure for the deposition of microorganisms was specified in the Regulation of Patent Law, Article 2 to Article 4.

² Section B, “Patent rights”: (1) a comprehensive bill to amend the patent law to include patent coverage for chemical and pharmaceutical products and new uses of chemical and pharmaceutical products will be introduced to the National Assembly by the end of September 1986. The Government of the Republic of Korea will give its best effort to secure enactment of the bill by the end of 1986. Regulations, guidelines and other administrative mechanisms will be formulated so that applications for patents may be accepted by the Office of Patents administration no later than July 1, 1987. (...) (5) Patent protection for new microorganisms will be effective at the same time as for chemical products and pharmaceuticals. (6) Korea will accede to the Budapest Treaty in 1987.

³ ‘Patent Examination Guideline for Biotechnological Invention’, KIPO, p. 24.

Microorganism inventions are deemed to be unpatentable under Article 32, in the following instances:⁴

- (1) The invention is liable to destroy the ecosystem
- (2) The invention is liable to cause environmental contamination
- (3) The invention is liable to hurt human beings

2.2 Animal Invention

An animal invention is a non-naturally occurring, non-human multicellular animal that includes inventions related to parts of animal, production methods, and usage.⁵ Korea has achieved much success in this field and understands the importance of patent protection for encouraging technical advancement. In 2000, the first two patents for multicellular animals were issued. These patents claimed a transgenic mouse deficient in T-cells⁶ and a diabetes-inducing transgenic mouse⁷. The patents were applied for in 1994 but were rejected during the examination process for failure to deposit an embryo. However, the Tribunal board of KIPO reversed the decision of the examination office by declaring that deposition of an embryo is not essential for these inventions. The patents for these inventions were granted in the U.S. and Japan in 1998⁸. The deposition of an embryo during the examination process is considered to be an essential prerequisite for granting animal patents. The Korean Collection for Type Culture (KCTC) is approved by the WIPO as an International Depository Authority (IDA) for the deposition of embryos.

The unpatentable subject matter for animal inventions under the Patent Law Article 32 is listed below as it states in the PEGBI⁹:

- (1) The invention is liable to destroy the ecosystem;
- (2) The invention is liable to cause environmental contamination;
- (3) The invention is liable to hurt human beings;
- (4) The invention is liable to cause abhorrence;
- (5) The invention is liable to cause severe cruelty to animals compared to the benefit to human beings;
- (6) The invention includes human beings as subject matter;

⁴ 'Patent Examination Guideline for Biotechnological Invention', KIPO, p. 28-29.

⁵ 'Patent Examination Guideline for Biotechnological Invention', KIPO, p. 42.

⁶ KR94-030675, "Transgenic mouse deficient in T-cells" is provided by fusing human heat shock protein (Hsp) gene with H2K promoter and transferring it to a mouse. Transgenic mouse line with a shrunken thymus and edficient in T-cells not having mature T-cells can be obtained.

⁷ KR94-030676, "A diabetes-inducing transgenic mouse" is a transgenic mouse containing recombinant DNA including a promoter and a heat shock protein 70 gene attached downstream of the promoter. Transgenic mice line inducing non-insulin dependent diabetes having a blood glucose level of 300 mg/dl was obtained.

⁸ KR94-030675: US5847357(98.12.8), JP2771494(98.7.2).

⁹ 'Patent Examination Guideline for Biotechnological Invention', KIPO, p. 45.

- (7) The invention is a process for cloning human beings; products and processes for modifying the germ line genetic identity of human beings;¹⁰
- (8) The invention is related behavior or R&D products that are prohibited by the “Bioethics and Biosafety Act”.¹¹

However, any invention whose R&D results are approved by the provisions of the “Bioethics and Biosafety Act” is patentable.¹²

2.3 Genetic Engineering Invention

The patentable subject matter of genetic engineering inventions includes genes, DNA fragments, antisense, vectors, recombinant vectors, transformants, fused cells, monoclonal or polyclonal antibodies, proteins or recombinant proteins, etc. In addition, the inventions related to microorganisms, plants or animals taking advantage of genetic engineering technology are included in this category of inventions.¹³

The following cases are not deemed to be complete under Patent Law Article 29.1:

- (1) When corresponding to a mere discovery; or
- (2) Inventions directed to a gene, vector, recombinant vector, transformant, fused cell, monoclonal antibody, protein, or recombinant protein, where specific production methods thereof are not described in sufficient detail in the specification.

However, an invention is deemed to be complete when the gene or protein is artificially isolated and identified from a living thing, and its function is clarified.¹⁴ In the case of an Expressed Sequence Tag¹⁵ (EST) with an unknown function and unspecified utility, it is not patentable because of its deficiency in industrial applicability and the enablement requirement.

Genetic engineering inventions are deemed to be unpatentable under Patent Law Article 32 in the following instances:¹⁶

- (1) The invention is liable to destroyed the ecosystem
- (2) The invention is liable to cause environmental contamination
- (3) The invention is liable to hurt human beings or cause a result denigrating the dignity of human being

¹⁰ The inventions under (6) and (7) were recently added to the guideline in Dec. 2003 as part of the second amendment.

¹¹ The inventions under (8) were recently added to the guideline in May 2005 as part of the third amendment.

¹² It was recently added to the guideline in May 2005 during the third amendment.

¹³ ‘Patent Examination Guideline for Biotechnological Invention’, KIPO, p. 1.

¹⁴ ‘Patent Examination Guideline for Biotechnological Invention’, KIPO, p. 11-12.

¹⁵ EST is the gene fragments having 300-500 base pairs which are mostly obtained through the Human Genome Project.

¹⁶ ‘Patent Examination Guideline for Biotechnological Invention’, KIPO, p. 10 – 11.

- (4) The invention for a transformant failed to exclude human beings as subject matter¹⁷
- (5) Behavior related to the invention or the R&D product is prohibited by the “Bioethics and Biosafety Act”.¹⁸

However, any invention that results from R&D that is approved by the provisions of the “Bioethics and Biosafety Act” is patentable.¹⁹

3 Patentability of inventions related to Embryonic Stem Cell (ESC) research

3.1 Ethical rule for ESC inventions

Even though there are several laws related to the life of human beings in Korea, they do not regulate research on human embryos directly. In 2004, the Korean government prepared the Bioethics and Biosafety Act (BBA) to control the ethical issues of biotechnological research including human ESC. The objective of the BBA is to enhance the health of human beings and the quality of human life by creating conditions that allow for the development of life sciences and biotechnologies that can be used to prevent or cure human diseases. Additionally, this act aims to protect human dignity and to prevent harm to human beings by ensuring that these life sciences and biotechnologies are developed safely and in accordance with the principles of bioethics.²⁰ This Act regulates the research of human embryos or ESC.

To cope with the promulgation of the BBA, the KIPO amended the PEGBI in 2005. According to the amended PEGBI, any invention related to a behavior or an R&D product that is prohibited by the BBA is unpatentable. However, it should be noted that any invention that is approved by the National Bioethics Committee is excluded from the unpatentable subject matter under Art. 32 of the Patent Law. Therefore, the BBA is now a critical means of determining the patentability of research related human ESC in Korea.

¹⁷ The inventions under (4) were recently added to the guideline in Dec 2003, as part of the second amendment.

¹⁸ The inventions under (5) were recently added to the guideline in May 2005, as part of the third amendment.

¹⁹ It was recently added to the guideline in May 2005, as part of the third amendment.

²⁰ Article 1 of the Acts.

3.2 Major provisions of “Bioethics and Biosafety Act” related ESC research

Major provisions that are directly related to ESC research are outlined below.

3.2.1 The Establishment of National Bioethics Committee and Institutional Review Boards

A National Bioethics Committee, which is responsible to the President, should be established to review the following items concerning bioethics and biosafety in the life sciences and biotechnologies: Policies concerning national bioethics and biosafety; and the type, subject, and extent of research involving left-over embryos and somatic cell nucleus transfer (Art. 6). In addition, research institutions are required to set up their own Institutional Review Boards in order to ensure bioethics and bioethical safety in the life sciences and biotechnologies (Art. 9).

3.2.2 Prohibition on Human Cloning and the Transfer of Embryos between Two Different Species

Article 11 of the BBA prohibits implanting a somatic cell embryo clone into a uterus, maintaining a cloned embryo within a uterus, or giving birth when the pregnancy results from the act of implanting a somatic cell embryo clone into a uterus. Anyone who implants a somatic cell embryo clone into a uterus, maintains a cloned embryo within a uterus, or gives birth when the pregnancy results from the act of implanting a somatic cell embryo clone into a uterus will be sentenced with up to 10 years of imprisonment (Art. 49).

In addition, it is forbidden to implant a human embryo in the uterus of an animal; or to implant an animal embryo into a human uterus (Art. 12). Anyone who implants a human embryo into an animal's uterus or an animal embryo into a human's uterus shall be sentenced with up to 5 years of imprisonment (Art. 50).

3.2.3 Producing Embryos

According to Art. 13, no one shall produce embryos for a purpose other than a pregnancy. Any medical institution that wishes to collect and preserve sperm or oocytes for artificial fertilization or to generate embryos through fertilization must be authorized to do so by the Minister of Health and Welfare and designated as an Embryo Producing Medical Institution (Art. 14). The storage period of embryos should be five years; shorter storage periods are possible when the consenters agree to it (Art. 16).

3.2.4 Research on Remaining Embryos

Remaining Embryos that have passed the storage period outlined in Article 16 may be utilized for the following purposes, but only until the embryological primitive streaks appear in their developmental process: to conduct research aimed at developing contraception and infertility treatments; to conduct research aimed at curing rare or incurable diseases as decreed by the President; to conduct other research approved by the President after being reviewed by the Committee. How-

ever, in order to use a remaining embryo that has been stored for less than five years, a new consent, for this new purpose, is required from the consenters (Art. 17).

Any one who wishes to do research on remaining embryos under Article 17 must meet the facility and manpower requirements set by the Ministry of Health and Welfare and be registered with the Ministry as an Embryo Research Institution (Art. 18). When an Embryo Research Institution, registered with the Ministry of Health and Welfare, wishes to do research on embryos, it must submit an Embryo Research Protocol for approval by the Minister of Health and Welfare (Art. 19).

3.2.5 Somatic Cell Embryo Clones

Article 22 of the Act strictly prohibits somatic cell nucleus transfer other than for the purpose of conducting research aimed at curing rare or currently incurable diseases. The type, subject, and extent of allowed research on somatic cell nucleus transfer is decided by the President after review by the Committee. Anyone wishing to produce or research somatic cell embryo clones must register with the Ministry of Health and Welfare and satisfy the Ministry's requirements concerning facilities and personnel (Art. 23).

3.2.6 Interim Measures on Embryo & ESC Research

Until the embryological primitive streaks emerge, remaining embryos may be utilized under any of the following conditions: if the remaining embryos are produced before this Act takes effect; if a period of five years has passed since the remaining embryos were created; or, if a written consent was obtained from the consenters, but the consenter's whereabouts is unknown.

Anyone who is engaged in embryonic stem cell research at the time this Act takes effect may continue his or her research, with the approval of the Minister of Health and Welfare, under either the following conditions: the researcher has been engaged in embryonic stem cell research for at least three years or the researcher has published at least one research paper on embryonic stem cell research in a related academic periodical.

4 Future Aspects Related to Patentability Issues of Human ESC Research

In Korea, more than 60 patent applications related to human ESC inventions were submitted from 2000 to 2005, with some still being in the middle of the examination process.²¹ In the actual examination process, Patent Law Article 32 would be a critical basis for determining the patentability of inventions related to human ESC. Even though there is a positive view towards human ESC research because of its potential to save life, Korean tradition rejects financial exploitation of human embryos. The major moral argument regarding the patentability of ESC inventions is related to the destruction of the human embryos themselves. If a human embryo

²¹ 'Trends of Biotechnological Patents in Korea', KIPO, 2004.

is considered to be a human being, inventions related to ESC research should be unpatentable under Patent Law Article 32.

However, it is still undecided whether a human embryo is a human being. According to the Korean Supreme Court Decision in 1985²², the life of a human being starts at pregnancy. In other words, the life of a human being begins when the embryo is implanted in the wall of the uterus. Thus, an embryo itself, which is not imbedded in the uterus, would not be regarded as a human being. Accordingly, human ESC inventions, which are not directly related to human cloning, would be not included in the unpatentable subject matters under Article 32.

In this situation, it would seem very convenient and efficient for the Patent Examiner at the KIPO to rely on the BBA to determine the patentability of ESC inventions. Indeed, any invention, even if it is directly related to human cloning, can be excluded from Article 32 if approved by the BBA. Insofar, due to this direct applicability of the BBA, one may also say that ethical law has a much greater impact on the patentability of human ESC inventions in Korea than in any other country.

In a recent survey²³ regarding ESC research, more than 94 percent of the population in the survey supported providing patent protection for human ESC inventions. This reflects both the expectations and the concerns of the general public regarding the potential of human ESC research. However, steps need to be taken to set up clearer guidelines in the BBA and the PEGBI. Even though somatic cell nucleus transfer is strictly prohibited by the BBA, research aimed at curing rare or currently incurable diseases could still be allowed by the President after it has been reviewed by the National Bioethics Committee. Since the stipulation for the guideline and standard of review process by the Committee has not been provided by the BBA, adverse criticism of the Committee's decision might be possible in special cases. Furthermore, this kind of debate would negatively affect the examination practice of related inventions at the KIPO.

Recently, Congress has approved amending the BBA.²⁴ The revised BBA involves several issues critical to human ESC research. **The revised BBA contains a number of important amendments, inter alia, new provisions on the establishment, status and work of the mentioned Institutional Review Boards (Art. 10.2), the prohibition of the implantation of a nucleus of human somatic cell into an animal ovum, the nucleus of which has been removed (Art. 12.2), and the registration or use of the established ES cell lines (Art. 20).** Obviously, the amendments in BBA are directed at reinforcing the prohibition of cloning between two species and supervising the utilization human ES cell lines. It is noticeable that anyone who establishes or imports the human ES cell line should register the ES cell lines to the Ministry of Health and Welfare. For transferring the registered cell line to the third person for the purpose of R&D, the review and approval of the Institutional Review Boards (IRB) is required. The registered cell lines should be

²² Supreme Court Decision 1985Da1958 (11.6.1985).

²³ The survey was conducted with 297 university students in 2005.

²⁴ May of 2008.

strictly used only *in vitro* or outside of the body, and plans for utilizing R&D with the registered ES cell lines should be reported and approved by the Ministry as well as by the IRB.

Even with the direction of the revised BBA pointing towards reinforcing the supervision of human ESC research, the reviewing process of the Committee is still not clear enough. However, it is encouraging that the revised BBA involves the new provisions related to the support of the IRB, including the investigation and the evaluation of the IRB by the Ministry of Health and Welfare, and the education of the IRB members. If the stipulation for the guideline and standard of reviewing process by each IRB is well planned and monitored, the function and the reviewing process of the Committee is expected to be more transparent. Then, it would be possible to set up the legal standard for the patentability of a human ESC invention more clearly and definitely.

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