Recent Developments in Governmental Regulation of Biomedicine in Japan

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A Law and Several Sets of Ethical Guidelines for Biomedicine in Japan

- " An Act to Regulate Human Cloning Technology" (November 30, 2000).
- "Ethical Guidelines for Human Genomic and Genetic Research" (March 29, 2001).
- "Guidelines for the Derivation and Use of Human Embryonic Stem (ES) Cells" (September 25, 2001).
- "Ethical Guidelines for Epidemiological Research" (June 17, 2002).
- "Guidelines for Clinical Research" (Its preparation was started on June 7, 2002)

History of the Human Cloning Technology Regulation Act

February 1997: A cloned sheep known as Dolly was born. It was created by the technique of somatic cell nuclear transfer (SCNT).

September 1997: The Bioethics Committee was established at the Council for Science and Technology (=advising body to the Prime Minister).

December 1999: The Bioethics Committee concluded that cloning of human beings should be prohibited by the criminal penalty.

History of the Human Cloning Technology Regulation Act

April 2000: The bill of the Act was submitted to the Parliament. It would prohibit cloning of humans under the maximum penalty of 5 years' of imprisonment and/or a fine of 5 million yen.

June 2000: The bill was strangled by the dissolution of the lower house of the Parliament.

October 2000: The bill was reintroduced into the Parliament. The maximum penalty was increased to 10 years' of imprisonment and/or a fine of 10 million yen.

November 2000: The bill was passed in both houses of the Parliament.

June 2001: The main portion of the Act came into effect.

December 2001: Specified Embryo Guidelines were enacted.

Summary of the Act

Section 4 of the Act listed the following 9 categories of embryo as “specified embryos”.

①Human somatic clone embryo

An embryo produced by transferring the nucleus of a human somatic cell into a human enucleated egg.

②Human embryonic clone embryo

An embryo produced by transferring the nucleus of a human embryonic cell into a human enucleated egg.

③Human split embryo

An embryo produced by a split of a human embryo.

④Human-animal hybrid embryo

An embryo produced by having a human gamete and an animal gamete fertilize with each other.

Summary of the Act

⑤Human-animal fused embryo

An embryo produced by transferring the nucleus of a human cell into an animal enucleated egg.

⑥Animal-human fused embryo

An embryo produced by transferring the nucleus of an animal cell into a human enucleated egg.

⑦Human-human chimerical embryo

An embryo produced by unification as a result of aggregation of a human embryo and other human embryo or cells.

⑧Human-animal chimerical embryo

An embryo produced by unification as a result of aggregation of a human embryo and an animal embryo or cells.

⑨Animal-human chimerical embryo

An embryo produced by unification as a result of aggregation of an animal embryo and human cells.

Summary of the Act

Section 3 of the Act provides that

"No person shall transfer a human somatic clone embryo, a human-animal hybrid embryo, a human-animal fused embryo or a human-animal chimerical embryo into a uterus of a human or an animal."

In addition, Guidelines for Handling of Specified Embryos enacted under the authority of the Act prohibit transferring the remaining 5 categories of Specified Embryos into the uterus of a human or an animal for the time being.

In short, at present, creation of an individual from a Specified Embryo is effectively prohibited.

Summary of the Act

Behind these provisions, there was a recognition that cloning technology and other new techniques made it possible to create

(1) humans with exactly the same genetic structure as a particular person, or

(2) a life that cannot be clearly classified as a human or an animal.

It was apprehended that these possibilities might adversely affect the conception of human dignity, the security of the human life and body, and the preservation of order of the society.

The Guidelines for Handling of Specified Embryos

Article 1

Production of a Specified Embryo shall be allowed only when the following requirements are satisfied:

1. Scientific knowledge, which cannot be acquired from research using only animal embryos or cells or other research conducted without a Specified Embryo, can be acquired with the production and utilization of such a Specified Embryo; and
2. A person who is going to produce a Specified Embryo has sufficient technical ability to study with such a Specified Embryo.

The Guidelines for Handling of Specified Embryos

Article 2

(1) Among nine categories of Specified Embryos, only an animal-human chimerical embryo shall be allowed to be produced for the time being. The purpose of its production shall be limited to the research concerning creation of organs derived from human cells that can be transplanted into a human body.

Human ES Cells Guidelines : History

November 1998: Report of successful derivation of human embryonic stem cells at the University of Wisconsin was published in *Science.*

December 1998: The Subcommittee of Human Embryo Research was established at the Bioethics Committee of the Council for Science and Technology.

March 2000: The Subcommittee published “Report on the Human Embryo Research Focused on the Human Embryonic Stem Cells.”

September 2001: The Guidelines for Derivation and Use of Human Embryonic Stem Cells was Promulgated by the Ministry of Education, Culture, Science and Technology.

Human ES Cells Guidelines: Main Requirements

◆Only basic research is permitted.

Article 2

(2) For the time being, derivation and use of ES cells shall be limited to the purpose of basic research. The following activities shall not be carried out until another set of guidelines [which are now in preparation] have been enacted:

・Clinical research applying human ES cells or cells originated from them to the human body

・Other utilization of them in medicine and in its related fields.

Human ES Cells Guidelines: Main Requirements

- Respect for Human Embryo and ES Cells

Article 3

Considering that a human embryo is the beginning of a human life and that human ES cells have the potential for developing into any type of human cell, human embryos and ES cells shall be handled carefully and conscientiously in order not to offend human dignity.

- Gratuitous Donation of a Human Embryo

Article 4

Donation of a human embryo for the purpose of derivation of human ES cells shall be gratuitous, except that the reimbursement of necessary expenses is permitted.

Human ES Cells Guidelines: Main Requirements

◆Human Embryos Used for Derivation of Human ES Cells

Article 6

The human embryo to be used for derivation of human ES cells shall satisfy the following requirements:

1. It is the human fertilized embryo which was initially been created for the purpose of infertility treatment, but is now not intended to be used for that purpose, and, the donors' intention to leave it to be destroyed has been confirmed;
2. The donors appropriately consented to it being used for the purpose of derivation of human ES cells;
3. It has been stored frozen;
4. Not more than 14 days have passed since its fertilization, excluding the days during which it has been stored frozen.

Procedure to be followed before derivation of human ES Cells is made

(1) Director of the derivation team shall prepare a derivation protocol and ask the approval for it from the head of the institution (hereinafter DI=derivation institution).

(2) The head of the DI shall seek the opinion of its ethics review committee, and based upon it, shall decide whether to certify its conformity with the Guidelines.

(3) The head of the DI shall obtain the assent to the protocol from the head of the medical facility where embryos are donated (hereinafter DMF=donation medical facility). The DMF's head, in considering the protocol, shall invite the opinion of its ethics review committee.

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Procedure to be followed before derivation of human ES Cells is made

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(4) The head of the DI, in deciding whether to approve the protocol, shall ask the confirmation of its conformity with the Guidelines from the Minister of Education, Science and Technology.

(5) The Minister shall seek the opinion of the Bioethics and Biosafety Committee of the Commission on Science and Technology, and based upon it, shall decide whether to confirm its conformity with the Guidelines.

Human ES Cells Guidelines: Informed Consent Requirements

◆Procedure of Informed Consent

Articles 22-23 (summary)

- Only married couples (excluding those who have not had their marriage registered) can donate embryos for the derivation of human ES cells.
- The informed consent to the donation shall be expressed in writing.
- Donated embryos shall not be used for the derivation for at least one month after the informed consent is given. In the meantime, the donors shall be able to withdraw the donation.
- The explanation shall be given not by physicians attending to the donors but by the persons who belong to the institution where the derivation will be made.

Human ES Cells Guidelines: Informed Consent Requirements

◆Information to be given to donors

Article 23 (summary)

- The information to be given to donors that must be in writing shall include but not be limited to the followings:
  - ✧ The purposes and methods for deriving human ES cells;
  - ✧ That the donated embryos will be destroyed in the derivation process;
  - ✧ The anticipated method to utilize human ES cells and expected outcomes;
  - ✧ That the conformity of the derivation protocol with the Guidelines has been certified by both the institution where the derivation is made and the medical facility where embryos are donated, and has also been confirmed by the Government ;

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Human ES Cells Guidelines: Informed Consent Requirements

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- That all personal information of the donors will be removed from the embryos before the derivation;
- That the donors will be never offered compensation;
- That human ES cells may be analyzed genetically;
- That the processes and outcomes of the ES cell research may be published in academic meetings and on other occasions;
- That ES cells will continue to be cultured for a long time and distributed to the user institutions gratuitously;
- That intellectual property rights or economic benefits obtained from the ES cell research will not belong to the donors;
- That donated embryos are stored for at least one month after the consent has been given and that the consent can be withdrawn in the meanwhile.

Deriving Human ES Cells in Japan

The first application for the Ministry's approval of the ES cell derivation protocol [=confirmation of its conformity with the Guidelines] was submitted at the end of December 2001 by the researchers led by Professor Nakatsuji of Kyoto University. The approval was granted in March 2002, and it has been the only ES cell derivation protocol approved by now.

In late July, four months after the Ministry's approval, Professor Nakatsuji was reported to say "the prospect is not good." At Kyoto University, as a first step, infertility doctors ask the former patients (now parents/mothers) if they want to hear the explanation about ES cells. But, very few of them answered affirmatively. Professor Nakatsuji ascribes the negative attitude to the lack of time of young parents. However, the reporter suggests other reasons: mother's special sentiment toward embryos created by in vitro fertilization.

When using human ES cells is permitted

Article 26

(1) Use of human ES cells shall be permitted only when the following requirements are satisfied:

1. Its purpose is basic research contributing to

(a) clarification of the mechanisms of human development, differentiation and regeneration, or

(b) development of a new method of diagnosing, preventing or treating diseases or development of new medicines and drugs

2. The use of human ES cells in the research is both scientifically necessary and appropriate.

(2) The human ES cells to be used shall be those which were derived in conformity with the Guidelines.

(3) Regardless of the provision in (2) above, the UI shall be able to use the human ES cells distributed from foreign institutions, when the Minister certifies that such cells have been appropriately derived in accordance with the standards of the Guidelines.

Procedure to be followed before use of human ES Cells is made

(1) Director of the use team shall prepare a use protocol and ask the approval for it from the head of the institution (hereinafter UI=use institution).

(2) The head of the UI shall seek the opinion of its ethics review committee, and based upon it, shall decide whether to certify its conformity with the Guidelines.

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Procedure to be followed before use of human ES Cells is made

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(3) The head of the UI, in deciding whether to approve the protocol, shall ask the confirmation of its conformity with the Guidelines from the Minister of Education, Science and Technology.

(4) The Minister shall seek the opinion of the Bioethics and Biosafety Committee of the Commission on Science and Technology, and based upon it, shall decide whether to confirm its conformity with the Guidelines.

Protocols using ES cells approved so far

- Kyoto University Team led by Professor Nakao: Analysis of the Mechanisms of Development and Differentiation of Blood Vessels and Its Application to the Regeneration of Blood Vessels: Approval (=confirmation of its conformity with the guidelines) applied for in January 2002 and granted in April 2002.
- Tanabe Pharmaceutical Co.: Joint research with Kyoto University Team: Approval applied for in April 2002 and granted in June 2002.
- The ES cells used in the above research are distributed from Monash University in Australia.