

The Regulations for Research on Human Embryos in Japan and Germany

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Along with the development of assisted reproductive technology (ART) and embryonic stem (ES) cell research, the treatment of an embryo, the earlier stage of a fetus, has become an important theme in bioethics. I would like to compare the Japanese and German directions in regulating research on human embryos.

1. The Japanese decision in 2001: Approval of the national establishment of embryonic stem cells and prohibition of the production of human clones

It was about the time that people started to discuss research on embryonic stem cells that the human embryo became very controversial object in Japan. Japan promptly responded to the movement toward embryonic stem cell research. The Cabinet Office's Council for Science and Technology established the Subcommittee on Human Embryo Research under the Bioethics Committee in December 1998, the month after the embryonic stem cell was first established in the US. After 14 meetings, the subcommittee published, in March 2000, the "Report on Human Embryo Research, Focusing on the Human Embryonic Stem Cells," which gave approval to the launching of embryonic stem cell research in Japan. It is remarkable that Japan was one of the first countries in the world to decide to direct national funding for research not only on the utilization of embryonic stem cells but also their derivation.

After that time, the ministries and government offices were reorganized, and the Council for Science and Technology Policy (CSTP)¹ was newly established in the Cabinet Office in January 2001. Based on the "Report on Human Embryo Research", the CSTP approved the "Guidelines for Derivation and Utilization of Human Embryonic Stem Cells" in August 2001, which the Ministry of Education, Culture, Sports, Science and Technology (MEXT)² published under its auspices in September 2001. These guidelines indicated a stricter approach to research on human cloned embryos, namely, proclaiming that a human embryo is a beginning of human life and should be treated sincerely and that its dignity as a human being should not be harmed.

The main regulations were:

¹ <http://www8.cao.go.jp/cstp/english/index.html>

² <http://www.mext.go.jp/english/index.htm>

- A human embryo used for derivation of human embryonic stem cells shall be a so-called “supernumerary” embryo, be accompanied by appropriate informed consent concerning its use for the derivation of human embryonic stem cells, and have been stored frozen and used within 14 days after fertilization, not counting any time during which it has been stored frozen (Article 6).
- New production of human embryos by fertilization for the purpose of use as research material is prohibited.
- Utilization of human embryonic stem cells shall be allowed only:
 1. when its purpose is basic research contributing to:
 - (a) clarification of the functions of human development, differentiation, and regeneration, and
 - (b) development of a new method to diagnose, prevent, or treat diseases or of medicines, drugs, and so on; and
 2. when the research is both scientifically necessary and rational.

Measures to conduct the research properly were specified as follows:

- Establishment and utilization of embryonic stem cells shall be limited only to institutions with a certain standard of quality.
- Double reviewing system: Human embryonic stem cell research shall be reviewed on a case-by-case basis both by an institutional review board (IRB) and the Bioethics and Biosafety Committee of MEXT.

This regulation had the characteristic of being based on control through the guidelines made by civil service and not on laws.

Following these guidelines, embryonic stem cell research was begun in Japan, and on May 27, 2003, a research team of the Institute for Frontier Medical Sciences of Kyoto University succeeded in deriving human embryonic stem cells.

On the other hand, in November 2000, Japan enacted a law prohibiting the production of cloned humans, called “The Law Concerning Regulation Relating to Human Cloning Techniques.” This law specifies only the prohibition of the production of human cloned individuals. It called the cloned embryos “the specified embryos” and left their handling up to the guidelines determined by MEXT. Therefore, this law implied that it prohibited only the practice of transplanting a cloned embryo into a uterus and permitted on a case-by-case basis other kinds of embryonic manipulation.

In April 2001 CSTP established within the council the Expert Panel on Bioethics, for research and study relating to bioethics, in response to the rapid development of life science. Based upon Chapter 4, Section 3, of the Law

Concerning Regulation Relating to Human Cloning Techniques and Other Similar Techniques³, the Expert Panel established a project, with Professor Ida as president, for research on “specified embryos” in order to create guidelines for handling of a “specified embryo.”

The project found that only an animal-human chimerical embryo shall be allowed to be produced. This finding was quite restricted, and it disappointed those who wanted to promote research on human cloned embryos. Production of human cloned embryos was prohibited for the time being by the Guidelines for Handling of a Specified Embryo⁴ which was attached to the Law Concerning Regulation Relating to Human Cloning Techniques.

2. The German debate on stem cell research in 2001: toward importation of embryonic stem cells

In 2001, the issue of whether or not to begin embryonic stem cell research was hotly debated in Germany. At that time, I worked as a visiting fellow at the Institute of Science and Ethics(IWE)⁵ of the University of Bonn and had the opportunity to observe this debate. The establishment of human embryonic stem cells is prohibited by the Embryo Protection Act in Germany; therefore, they had to import embryonic stem cells created in foreign countries in order to conduct embryonic stem cell research.

They had a hot nationwide debate on whether to import embryonic stem cells. This issue was discussed both in the Study Commission (*Enquete-Kommission*) on the Law and Ethics of Modern Medicine⁶ of the German Parliament (*Bundestag*) and the German National Ethics Council (*Nationaler Ethikrat*)⁷. There were pros and cons to the importation of embryonic stem cells found by both the Commission and the Council. The majority of the Study Commission of the Bundestag were against importation and the majority of the National Ethics Council of the government were in favor of it. Public opinion was divided nationwide. In January 2002, the German Bundestag decided to allow the importation of embryonic stem cells, and in July 2002, it passed the Stem Cell Act (*Stammzellgesetz*), the law to regulate the importation of human embryonic stem cells.

One of the biggest focuses in these discussions was the problem of the moral status of embryos at the earlier stages. They discussed further whether it

³ http://www.mext.go.jp/a_menu/shinkou/seimei/2001/hai3/5_english.pdf

⁴ http://www.mext.go.jp/a_menu/shinkou/seimei/2001/hai3/31_shishin_e.pdf

⁵ http://www.iwe.uni-bonn.de/deutsch/index_fix.html

⁶ <http://www.bundestag.de/parlament/gremien/kommissionen/archiv14/medi/index.html>

⁷ <http://www.nationalerethikrat.de/>

was possible to balance the right to life of the younger embryos with the potential value obtained from embryonic stem cell research, such as the ability to treat serious diseases. Even if this were possible, then the embryonic stem cell research should have particularly high priority and there should be a lack of alternatives. So, the question arose as to whether the research did have such high potential and diseases lacked alternative treatments. After a hot, national debate, Germany's conclusion on importing embryonic stem cells was a product of compromise between the position that human embryos at the earlier stages also have human dignity and must be protected and the position that it is the researchers' freedom and responsibility to develop highly significant research by using supernumerary embryos which otherwise would be discarded.

Thus, in 2001, Germany and Japan were identical on the following points:

- (1) The production of human embryos for embryonic stem cell research was not permitted.
- (2) The derivation of embryonic stem cells from supernumerary embryos was approved, but in Germany is not permitted within the country.
- (3) The production of human cloned embryos was prohibited.

Japan decided point (1) based on administrative guidelines and point (3) on legislative guidelines, whereas Germany had decided both points (1) and (3) already with the Embryo Protection Act of 1991.

3. The Japanese Council for Science and Technology Policy allowed human cloned embryonic stem cell research in 2004

When the Expert Panel was established under the Council for Science and Technology Policy in April 2001, it was given not only the issue at hand of creating guidelines for handling "specified embryos" but also a broader goal, to conduct surveys and examinations of basic policies and important issues concerning bioethics. However, the panel moved toward the goal of removing the ban on the establishment of human cloned embryos for research use and the derivation of embryonic stem cells from them.

Professor Ida and Professor Shimazono, who were members of the Expert Panel, expressed their concern to the panel that it was moving so quickly when it still had a lot to discuss. In spite of their opposition, though, the majority of the panel members who wanted to promote the research steamrolled the process and forced a vote on June 23, 2004, to allow the establishment of human cloned embryos for the derivation of embryonic stem cells and the production of fertilized human eggs for fertility treatment research. On July 23, the CSTP approved the final report entitled "Basic Thinking on the Handling of the Human Embryo,"

which was finalized by the panel after 32 meetings beginning in August 2001. This was an exceptional situation in the discussion of bioethics in Japan and casts a big shadow on the way bioethics issues are discussed in Japan.

CSTP's final report positions the human embryo as follows:

- The present legal system does not treat a human embryo as a human being (person). On the basis of the present situation, in which abortion is permitted and reproductive techniques result in discarded supernumerary embryos, it is not practical at this time to change the system to one that treats human embryos as humans.
- On the other hand, a human embryo is a beginning of human life which has the potential to grow into a person and should be treated with special respect. In other words, a fertilized human egg itself is not a human being but is an entity that should be especially respected in order to maintain the fundamental social value of human dignity.
- In principle, a human fertilized embryo should not be newly created for research use, but destroying fertilized human eggs is permitted as an exception under certain conditions in order to respond to the demand of pursuing people's happiness, health, and welfare, such as in the case of research on assisted reproductive technologies or the treatment of difficult diseases.

The Report on Human Embryo Research of the Subcommittee on Human Embryo Research, published in March 2000, prohibited establishing new fertilized human embryos for research use and set a moratorium on the production of human cloned embryos, but CSTP's Final Report made an exception to this and suspended the moratorium.

4. The perspective of the German National Ethics Council concerning human cloned embryonic stem cell research

In September 2004, the German National Ethics Council made public its opinion about "cloning for reproductive purposes and cloning for the purposes of biomedical research."⁸ The Council did not reach agreement on cloning for the purposes of biomedical research but set forth the following three views:

- Position A: Retention of the prohibition on research cloning. A cloned embryo has the potential to grow into a person, and therefore its dignity and life should be protected. The derivation of embryonic stem cells by harming

⁸ http://www.nationalerethikrat.de/stellungnahmen/pdf/Stellungnahme_Klonen.pdf

cloned embryos is instrumentalization of life “as a mere means to the achievement of extraneous ends” and should not be permitted.

- Position B: Limited sanctioning of research cloning. The use of human blastocysts produced by cloning for the purposes of basic research with a therapeutic objective is acceptable in principle. There are no moral grounds for attributing the status of a person to a blastocyst created in this way, nor does the German Constitution (Grundgesetz) require it to be regarded as a subject of human dignity and possessor of the right to life.
- Position C: Prohibition of research cloning at the present time. No one knows whether transplantation of the cells derived and differentiated from the embryonic stem cells established from a patient’s cloned embryo would trigger the rejection of his own cells. It is premature to apply the argument of immunocompatibility in support of the need to obtain stem cells from cloned embryos until all questions are answered by accumulating results from analogous animal experiments.

This experiment requires large quantities of oocytes and obtaining these oocytes might entail great risks and burden to donors. Since oocytes are a scarce resource, they might be commercialized. The woman’s body would turn into merchandise. With this background, it is almost impossible to obtain proof of the voluntary nature of the donation and verify an informed consent.

Research on the formation of organs by creating ES cells derived from cloned embryos has not accumulated adequate results from animal experiments and is still at the stage of fundamental scientific knowledge. It cannot be said that the research has a high level of justification with priority and that there is no alternative.

The distribution of members was: 5 for choosing Position A, 12 for Position B, and 5 for Position C. Thus, the largest number was of those who want to promote research, but it is not the majority. With this result, the Council concluded as follows;

Joint recommendation on research cloning:

Notwithstanding the divergent positions set out above, the National Ethics Council unanimously recommends that research cloning should not be permitted in Germany at present.

If Germany wants to start research on cloning, it should revise the Embryo Protection Act, but there is no such prospect right now.

5. The year 2006: The current situation in Japan concerning research on human embryos

After CSTP approved on July 23, 2004, the final report entitled "Basic Thinking on the Handling of the Human Embryo", the Expert Panel was dismissed and the following three committees were established in order to decide the details for establishing human clones and fertilized eggs for research as described in the final report:

- 1) The Working Group for Guidelines for Research on Human Cloned Embryos was constituted under the Specified Embryo and Human Embryonic Stem Cell Research Special Committee, a branch of the Bioethics and Biosafety Council for Science and Technology of MEXT.
- 2) The Special Committee for Research on Assisted Reproductive Technologies was created under the Bioethics and Biosafety Branch.
- 3) The Special Committee for Human Embryo Research was created in the Department of Science and Technology, which belongs to the Health Sciences Council of the Ministry of Health, Labor and Welfare.

The Working Group (1) decided the procedures and the conditions for research in order to open the door for human cloned embryo research. This group held the most discussions among the three, which were summarized in June 2006 in an interim report entitled "How to Produce and Use Human Cloned Embryos for Research." During the discussions, the most important issue that was considered was the methods for obtaining the large quantity of oocytes required for the derivation of embryonic stem cells. The interim report listed the following three methods for obtaining oocytes and decided the procedures for each method:

1. Obtaining oocytes from ovaries or their parts that were surgically removed for other reasons.
2. Utilizing unfertilized eggs that are obtained for the purpose of assisted fertility treatment but are not used.
3. Utilizing unfertilized eggs that are preserved frozen but become unnecessary.

The donation of unfertilized eggs from those involved to research carries an ethical problem, as was seen in the Korean case, so the report concluded that such donations should not be accepted.

The Working Group deliberated whether it was possible, as an exception, to accept unfertilized eggs that are donated freely by volunteers, which the CSTP's Final Report in July 2004 denied in principle. As a result of this deliberation, the Working Group concluded that there should be no exception. I believe that this is

the most important point in the 92-page interim report. The report stated the reason as follows: Women will be subjected to a great deal of physical and spiritual burden and risk when they unnecessarily undergo the medical procedures needed for obtaining oocytes for research. On the other hand, the derivation of embryonic stem cells from human cloned embryos is not yet successful, and the prospect of medical treatment of difficult diseases through this method is still uncertain. Therefore, when we look at the present situation, it is difficult to accept that there is scientific and social validity for conducting research by accepting donations of unfertilized eggs from volunteers. In other words, compared with the risks and burden on women that accompanies this medical procedure, it is not yet certain whether research on human cloned embryonic stem cells would provide a worthy profit for society. It stated that the comparison did not even make sense under such circumstances from the beginning. This is very close to Position C of the German National Ethics Council's opinion on cloning in 2004.

The creation of human cloned embryos and the derivation of embryonic stem cells from them are still technically difficult, and a great number of just-obtained, fresh eggs, not frozen ones, are essential for the research. It was a crucial obstacle for promotion of the research that the interim report did not approve the donation of fresh, unfertilized eggs from volunteers.

Professor Norio Nakatsuji, Director of the Institute for Frontier Medical Sciences of Kyoto University, a member of the Working Group, and the only researcher from Japan who has established human embryonic stem cells, expressed disappointment with this conclusion. Following the issuance of the interim report, he stated that if he were to follow the interim report and conduct research on human cloned embryonic stem cells, the possibility of success would be very close to zero, so he would not be able to do research any more. On July 13, 2006, he issued a statement that his research group, the Institute for Frontier Medical Science, would not conduct regenerative medicine research using human cloned embryos for a while. The interim report intended to designate his Institute, as the recommended institute for limited research on human cloned embryos. Because this group has announced that it would retire from it, research on human cloned embryonic stem cells will not be conducted in Japan for the time being.

Professor Nakatsuji said that he would produce pluripotent stem cells in a different way than deriving them from embryonic stem cells. His outcome was published on August 11, 2006. Professor Shinya Yamanaka and Assistant Professor Kazutoshi Takahashi of Nakatsuji's Institute announced that they had successfully generated new pluripotent stem cells out of a mouse skin cell. When four particular genes were introduced, the cells developed pluripotency similar to embryonic stem cells, which they named "induced pluripotent stem (iPS)" cells.

This is a new way to bypass the ethical controversy and may overcome the problem of postoperative rejection responses.

Based upon the CSTP's "Basic Thinking" report, the Special Committee for Research on Assisted Reproductive Technologies (2) and the Special Committee for Human Embryo Research (3) were constituted in order to create guidelines for producing and using fertilized human eggs for research on assisted reproductive technologies. Committee (2) was constituted in MEXT and had its first meeting in January 2006. Committee (3) was constituted in the Ministry of Health, Labor and Welfare and had its first meeting in September 2005. As they have almost the same mission, the two committees have had joint meetings since January 2006. It might be said that it was unnecessary from the beginning to organize two committees separately in the two different ministries. They still hold joint discussions, especially on setting the framework for the production and use of fertilized human eggs and methods to obtain the oocytes needed for research on assisted reproductive technologies.

6. Japanese and German arguments concerning the regulations for human embryo research

When does a human life begin? How early does human life require human dignity? Is it possible to sacrifice the right to life of embryos for research that has the potential to save people suffering from resistant diseases? These are the themes discussed in Germany. Recently, there was a discussion also in Germany about the principle of human dignity, which their Constitution declares is not possible to infringe upon, and the discussion included some arguments which begs some fundamental questions about this principle.

Influenced by the European argument, Japan also held discussions about whether human embryo research infringes upon human dignity. However, the concept of human dignity has been used in Japan ambiguously. The principle of human dignity has the background of the worldview of Judaism and Christianity which presumes a special position for humans in the universe. We cannot say that Japanese people have an understanding of human dignity that presumes the differing status of human beings from animals. Many of us would rather believe in a dignity of life that includes all living things.

German people think that the standards of human dignity and human rights are different. They believe that "rights" can be compared but that "dignity" is beyond comparison. Japanese people believe that human dignity is quite close to the principle of the protection of human rights. It is also said in the discussions in Japan that instrumentalization of human embryos might infringe upon human dignity, but it is not discussed as seriously as in Germany. The "Basic Thinking"

document of the Japanese CSTP says, essentially, that a human embryo is not a person or a subject with rights, but it is an entity that deserves our respect as a beginning of a human being. Therefore, it is, in principle, prohibited to use human embryos as research materials, but under certain conditions there might be exceptions. It is prohibited in principle and approved case by case. Such utilitarianism is the Japanese strategy for the argument. The procedure for the approval is, as a whole, firmly in line with that of the UK.

Difference of National Concern

There is no nation that discusses as eagerly and seriously the dignity of embryos as the Germans. Not only ethicists, theologians, priests, and bioscientists, but also citizens show a great deal of interest in this area. The German national argument over embryonic stem cell research in 2001, in particular, deserves special attention. Compared to that, the Japanese argument is still limited only to experts. The citizens are not very interested. This is in contrast to the surge of national interest at the time the Cerebral Death /Organ Transplant Law was enacted in Japan in 1997. Japanese people's indifference to the question of the beginning of life requires elucidation that includes consideration of the socio-historical, religious, and cultural background of abortion.

7. Regulatory Systems Concerning Bioethics in Germany and Japan

(1) Enacting a law or setting guidelines for the regulation of biomedical research

Germany has the Embryo Protection Act, which is the strictest and most inclusive law in the world concerning the handling of embryos. This law regulates research on assisted reproductive technologies and human embryo research. Japan does not have a law that regulates the handling of fertilized human eggs outside the body. In addition, Japan has no law that regulates assisted reproductive technologies.

It is not wise to regulate everything with laws. Concerning bioethics, it is desirable to have a regulatory system that has a well-balanced combination of legal regulation, administrative guidelines, and voluntary restraint by professional groups. In Japan, people seem to depend too much on administrative guidelines. Control by guidelines has the benefit of being able to respond promptly and flexibly to the progress of scientific technologies. However, guidelines are unable to sufficiently regulate a serious crisis or infringement of rights. So, law becomes necessary. For example, enactment of the Assisted Reproductive Technologies Act and the Human Research Subject Protections Act is being demanded in Japan, but it is not probable right now.

(2) Voluntary restraint by professional groups

Concerning voluntary restraint by professional groups, the conditions of medical associations are very different in Japan and Germany. In Germany, the State Medical Society (*Landesaerztekammer*) is a legal organization and all medical doctors are required to join. The medical societies have their own courthouse, which has the legal function of sanctioning doctors. On the other hand, the Japan Medical Association is a group in which participation is voluntary. Most medical practitioners join it, but most doctors who work for big hospitals do not. It is not a system where voluntary restraint functions well enough. For example, there is neither legislation nor administrative guidelines to regulate assisted reproductive technologies. There are only guidelines created by the Japan Society of Obstetrics and Gynecology⁹. This is a critical situation to have in this area where there could be various problems that might affect relationships between parents and children and their welfare. In fact, there are already problems in that a few obstetricians openly conducted preimplantation genetic diagnosis (PGD), which is prohibited in the guidelines.

(3) Nonexistence of a standing committee

There was a time in Germany when the two ethics commissions of government and Parliament struggled with each other to achieve supremacy (May 2001-September 2005). German government decided the reorganization of the National Ethics Council to the German Ethics Council, each half of whose members are appointed by German government and the Bundestag. A Bill for the reorganization passed the Bundesrat on September 22. The Bill is under deliberation in the Bundestag.

In Japan, there is not a nationwide standing committee that discusses inclusively all bioethics issues. Even though the Expert Panel under the CSTP was an ad hoc commission, it provided a forum to discuss inclusively bioethics in general. However, it did not utilize this opportunity effectively and had an unhappy ending. Now there is not even a plan to establish a commission to take its place¹⁰. Japan has too many problems to develop systematic regulations, rather than the present patchwork-type regulations, when life-sciences are making such rapid progress in many fields, such as basic research, biomedicine, industry, agriculture, and more.

⁹ <http://www.jsog.or.jp/english/index.html>

¹⁰ Susumu Shimazono, *Inochi no hajimari no seimeirinri* (Bioethics on the Beginning of Life), shunjusha, Tokyo, 2006