

(Tentative Translation)

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Chapter I General Provisions

Section 1 Purpose

These Guidelines pertain to research contributing to the improvement of assisted reproductive technology treatment, in which human fertilized embryos are produced. In view of the importance of such research, the purpose of these Guidelines is for this research to be conducted appropriately, by stipulating the matters to be observed by persons involved in such research, based on such ethical viewpoints as the respect for human fertilized embryos.

Section 2 Scope of Application

These Guidelines shall apply to all research pertaining to fertilization, the development and growth of embryos and implantation, research pertaining to the improvement of preservation techniques for gametes and human fertilized embryos, and other research that contributes to the improvement of assisted reproductive technology treatment, in which human fertilized embryos are produced (hereinafter collectively referred to as “research”).

Section 3 Definitions

In these Guidelines, each of the following terms shall be defined as follows.

(1) Gamete

The term “gamete” shall mean a human ovum or sperm.

(2) Donor

The term “donor” shall mean the donor of a gamete used in research.

(3) Informed consent

The term “informed consent” shall mean consent regarding the provision and handling of a gamete, which a donor gives on the basis of his/her free will after receiving adequate prior explanations from a researcher, etc. with regard to the research and after understanding the significance, objectives and method of the research, the expected results and the disadvantages.

(4) Research institution

The term “research institution” shall mean an organization conducting research using donated gametes.

(5) Donor facility

The term “donor facility” shall mean an organization receiving donation of a gamete used in research from a donor.

(6) Research director

The term “research director” shall mean a person at a research institution who carries out research as well as supervises the operations related to the research.

(7) Research investigator

The term “research investigator” shall mean a person at a research institution who is involved in research, receiving direction from the research director.

(8) Organization representative, etc.

The term “organization representative, etc.” shall mean the representative of a business operator or organization, such as the head of an administrative organ, or the representative of a corporation that has a donor facility.

(9) Ethics review committee

The term “ethics review committee” shall mean a council-type body established within each individual organization as an advisory board to the director of a research institution or donor facility for the purposes of discussing the propriety of conducting, continuing or changing research and other related matters, involving both ethical viewpoints and scientific viewpoints.

(10) Personal information

The term “personal information” shall mean information about a living individual donor which can identify the donor by name, date of birth or other description contained in such information (including such information as will allow easy reference to other information and will thereby enable the identification of the donor; where information related to a deceased person is, at the same time, information about a living individual such as a surviving family member, it should be considered the personal information about the living individual donor in question).

(11) Anonymization

The term “anonymization” shall mean to remove, in part or in whole, from the personal information accompanying a donated gamete, information through which a specific individual could be identified and to give instead a symbol or a number that has no relevance to the donor.

Anonymization would be implemented either of the following ways:

(i) Anonymization in a linkable fashion

Anonymization based on a method where an index table of symbols or numbers attached to donors is maintained so that the donors may be identified as necessary.

(ii) Anonymization in an unlinkable fashion

Anonymization based on a method where no index table of symbols or numbers attached to donors is maintained so that individual donors cannot be identified

Chapter II Acquisition of Gametes

Section 1 Acquisition of Gametes

1. Fundamental principles

- (1) Donors shall be limited to persons who have sufficient capacity to consent; the donation of gametes shall not be accepted from minors and other persons who lack the capacity to consent.
- (2) The donation of gametes shall be without compensation, except for an amount equivalent to

the actual costs incurred as a result of the donation.

2. Ova which may be accepted for donation

For the time being, ova may be accepted for donation, but only those listed in any of the following items:

(1) An ovum stored frozen for the purpose of using it in assisted reproductive technology treatment (including future assisted reproductive technology treatment), but which can no longer be used for assisted reproductive technology treatment

(2) A non-frozen ovum which corresponds to the following:

(i) An ovum used in assisted reproductive technology treatment but which was not fertilized

(ii) An ovum collected for the purpose of using it in assisted reproductive technology treatment, which corresponds to the following:

(a) An ovum which, in the end, cannot be used in assisted reproductive technology treatment due to such reasons as a morphological abnormality

(b) An ovum other than one described in (a), for which the donor has voluntarily offered to donate to research

(iii) An ovum collected from an ovary (including a section thereof), extracted for such purpose as the treatment of a disorder, and which is not expected to be used in assisted reproductive technology treatment

Section 2 Informed Consent

1. Informed consent

(1) The donation of a gamete shall be accepted upon obtaining the informed consent of the donor in writing. The person obtaining the informed consent shall be the director of the research institution.

(2) Informed consent pertaining to the donation of a gamete shall not be acquired at a stage when a concrete research protocol has not yet been established.

2. Explanation on informed consent

The explanation on informed consent shall be provided in writing using as simple terminology as possible in order to obtain an adequate understanding regarding the research objectives and method, the possible disadvantages arising from the handling and provision of donated gametes and produced human fertilized embryos (including, in cases where the donation of ova listed in paragraph 2(2)(ii)(b) of Section 1 is accepted, the fact that there is a possibility that the decrease in the number of ova available for the primary treatment (assisted reproductive technology treatment) may lead to a decline in the treatment outcomes), the methods for protecting personal information, and other necessary matters.

3. Donation of ova by donors in the course of medical treatment

Where the offer of an ovum from a donor is accepted either in the course of assisted reproductive technology treatment or in the course of treatment for a disorder that is not assisted reproductive technology treatment, the research director shall, in obtaining the informed consent, endeavor to secure a necessary environment and shall designate a person other than the attending physician, who satisfies both of the following requirements, as someone to assist in explaining about informed consent, so that the donor can make a decision voluntarily based on an adequate understanding and without being subjected to psychological pressure:

- (i) The person should not be directly involved in the medical treatment of the donor.
- (ii) The person should be someone who has an in-depth knowledge concerning assisted reproductive technology treatment and research on assisted reproductive technology treatment.

4. Revocation of informed consent

- (1) While a gamete that a donor has provided or a human fertilized embryo produced from that gamete is being preserved, the donor may revoke his/her informed consent given to the donor facility.
- (2) Upon receipt of an application from a donor for revocation, the director of the donor facility shall notify the director of the research institution of that effect.
- (3) Upon receipt of a notification set forth in (2), the director of the research institution shall dispose of the donated gamete (excluding cases where the donor requests that the gamete be used in his/her own assisted reproductive technology treatment) or the human fertilized embryo produced from that gamete, and shall notify the director of the donor facility in writing of that effect. This shall, however, not apply to any of the following cases:
 - (i) When the gamete or human fertilized embryo has been anonymized in an unlinkable fashion
 - (ii) When continuation of the research has been authorized by the ethics review committee and approved by the director of the research institution

Chapter III Handling of Human Fertilized Embryos

Section 1 Restriction of Production

The production of human fertilized embryos shall be limited to the minimum necessary to conduct the research.

Section 2 Period of Handling

Produced human fertilized embryos may be handled, but only during the period until the primitive streak starts to form. However, with regard to human fertilized embryos in which the primitive streak does not start to form during the 14-day period calculated from the day on which the human fertilized embryo is produced, these shall not be handled after the 14 days have elapsed. In cases

where a human fertilized embryo is stored frozen, this period of frozen storage shall not be included in the period of handling.

Section 3 Prohibition of Transplantation into Uteri

- (1) Produced human fertilized embryos shall not be transplanted into a human or animal uterus.
- (2) Research shall not be conducted in a room that is equipped with facilities allowing human fertilized embryos to be transplanted into a human or animal uterus.

Section 4 Transfer to Other Institutions

A research institution shall not transfer produced human fertilized embryos to other institutions. However, in cases where research is conducted collaboratively at multiple research institutions, produced human fertilized embryos may be transferred, but only between these research institutions.

Section 5 Disposal at the Completion of Research

Where a research protocol has been completed or where the period of handling for a human fertilized embryo set forth in Section 2 has elapsed, the research institution shall promptly dispose of the produced human fertilized embryo.

Chapter IV Research System

Section 1 Research Institutions

1. Standards, etc. for research institutions

- (1) A research institution shall conform to the following standards:
 - (i) The research institution should have sufficient facilities and equipment for producing and cultivating human fertilized embryos.
 - (ii) The research institution should have a sufficient track record in the handling of gametes and human fertilized embryos and in the production of animal fertilized embryos or human fertilized embryos.
 - (iii) The research institution should have in place rules and a management system concerning the handling of gametes and human fertilized embryos.
 - (iv) The research institution should have an ethics review committee in place.
 - (v) The research institution should have in place an education and training program needed to maintain and improve its technical capability and ethical awareness with regard to the research.
 - (vi) At least one medical doctor should participate in the research.
- (2) A research institution shall prepare and keep records on the handling of gametes and human fertilized embryos.

- (3) A research institution shall cooperate in submitting materials, accepting investigations and any other measures found to be necessary by the Minister of Education, Culture, Sports, Science and Technology concerning the research.

2. Director of research institutions

- (1) The director of a research institution shall perform the following duties:
 - (i) Confirm the propriety of a research protocol and any change to a research protocol, and approve the implementation thereof;
 - (ii) Ascertain the research progress and results and the handling of any produced human fertilized embryos, and where necessary, give instructions to the research director regarding any matters such as relevant points of concern and points for improvement; and
 - (iii) Formulate an education and training program set forth in paragraph 1(1)(v), and implement education and training based on it.
- (2) The director of a research institution may not simultaneously hold the position of a research director or research investigator; provided, however, this shall not apply to cases where a person who performs the duties of the director of the research institution on their behalf has been appointed pursuant to the rules prescribed in 1(1)(iii).

3. Research directors, etc.

- (1) A research director shall be a person who has both sufficient ethical awareness regarding research on assisted reproductive technology treatments and sufficient expert knowledge and experience regarding the production of animal fertilized embryos or human fertilized embryos.
- (2) A research investigator shall be a person who is well-experienced in the handling of gametes or fertilized embryos of animals or humans.
- (3) In cases where a research director is not a person who has sufficient experience regarding the production of human fertilized embryos, at least one of the research investigators shall be a person who has such experience.

4. Research institution ethics review committees

- (1) The ethics review committee of a research institution shall satisfy all of the following requirements:
 - (i) The ethical review board should consist of experts in biology, reproductive medicine and law, persons having adequate insight to state opinions on bioethics and persons capable of stating opinions from the standpoint of the general public so as to be able to comprehensively review the scientific and ethical propriety of a research protocol.
 - (ii) The members of the ethical review board should include two or more persons who do not belong to the research institution.
 - (iii) The members of the ethical review board should include two or more men and two or more women.

- (iv) Any interested persons of the research director or research investigator, and any relatives of the research director up to the third degree of kinship should not take part in the review.
- (v) An appropriate administrative procedure that would guarantee the freedom and independence of the activities of the ethics review committee should be set in place.
- (2) The proceedings of ethics review committee meetings shall be disclosed, except in cases where doing so would impede the protection of intellectual property rights and personal information, etc.

Section 2 Donor Facilities

1. Standards, etc. for donor facilities

(1) Gamete donor facilities

A gamete donor facility shall conform to the following standards:

- (i) The gamete donor facility should be either a hospital as prescribed in Article 1-5(1) of the Medical Care Act (Act No. 205 of 1948) or a clinic as prescribed in Article 1-5(2).
- (ii) The gamete donor facility should have an ethics review committee in place.
- (iii) The gamete donor facility should have taken adequate measures for the protection of personal information of donors.

(2) Ovum donor facilities

In addition to the standards listed in paragraph (1), an ovum donor facility shall conform to the following standards:

- (i) The ovum donor facility should have an egg retrieval room that satisfies the following requirements; provided, however, that this shall not apply in cases where provision of an ovum set forth in paragraph 2(2)(iii) of Section 1, Chapter II is accepted:
 - (a) The egg retrieval room should have facilities and equipment of the same standard as an operating room prescribed in Article 20(iii) of the Ordinance for Enforcement of the Medical Care Act (Ordinance of the Ministry of Health and Welfare No. 50 of 1948).
 - (b) The egg retrieval room should be equipped with an oxygen inhaler, aspirator, patient monitoring system and other medical devices necessary for resuscitation.
- (ii) The ovum donor facility should have in place rules and a management system concerning the collection and preservation of ova.
- (iii) An obstetrician or gynecologist with adequate clinical experience should belong to the ovum donor facility.

(3) Sperm donor facilities

In addition to the standards listed in paragraph (1), a sperm donor facility shall conform to the following standards:

- (i) The sperm donor facility should have in place rules and a management system concerning

the collection and preservation of sperm.

- (ii) An obstetrician, gynecologist or urologist with adequate clinical experience should belong to the sperm donor facility.

2. Donor facility directors

The director of a donor facility shall perform the following duties:

- (1) With regard to a research protocol, in addition to the procedures for informed consent, the director of the donor facility should confirm the propriety of the research protocol from the perspective of the donor facility, and should approve the implementation thereof.
- (2) The director of the donor facility should ascertain the provision of a gamete, and, where necessary, should provide guidance and supervision to the attending physician and to other persons involved in the provision of the gamete.

3. Donor facility ethics review committees

- (1) The ethics review committee of a donor facility shall confirm that informed consent is being obtained appropriately (in cases where donation of ova set forth in paragraph 2(2)(ii)(b) of Section 1, Chapter II is accepted, including confirmation, both before and after accepting the donations, that ova required for primary treatment (assisted reproductive technology treatment) are not being used in the research, and that the patients are not being subjected to any invasion greater than that invasion accompanying the primary treatment), and shall review the scientific and ethical propriety of research protocols conducted by the research institution from the perspective of the donor facility.
- (2) The ethics review committee of a donor facility shall satisfy all of the following requirements:
 - (i) The ethical review board should consist of experts in biology, reproductive medicine and law, persons having adequate insight to state opinions on bioethics and persons capable of stating opinions from the standpoint of the general public so as to be able to comprehensively review the scientific and ethical propriety of a research protocol.
 - (ii) The members of the ethical review board should include two or more persons who do not belong to the donor facility.
 - (iii) The members of the ethical review board should include two or more men and two or more women.
 - (iv) Any interested persons of the research director or research investigator, any relatives of the research director up to the third degree of kinship, the attending physician and any other persons involved in the provision of the gamete should not take part in the review.
 - (v) An appropriate administrative procedure that would guarantee the freedom and independence of the activities of the ethics review committee should be set in place.
- (3) The proceedings of ethics review committee meetings should be disclosed, except in cases where doing so would impede the protection of intellectual property rights and personal

information, etc.

Section 3 Requirements for Directors of Institutions, etc.

Where the Research Institution and the Donor Facility are One and the Same In cases where the research institution and the donor facility are one and the same, the director of the said institution, the research director and the research investigator shall not serve concurrently as the attending physician of the donor.

Chapter V Research Process

Section 1 Implementation of Research Protocols

1. Approval of the directors of research institutions

- (1) When conducting research, a research director shall prepare a research protocol, and shall seek the approval of the director of the research institution for implementation of the research protocol.
- (2) The director of the research institution, whose approval is sought in paragraph (1), shall seek the opinion of the ethics review committee of the research institution on the propriety of implementing the research protocol, and shall confirm the conformity of the research protocol with these Guidelines based on that opinion.
- (3) With regard to the implementation of a research protocol, of which conformity with these Guidelines has been confirmed pursuant to paragraph (2), the director of the research institution shall obtain the approval of the director of the donor facility; provided however, that this shall not apply to cases where the research institution and the donor facility are one and the same.
- (4) When giving approval for the implementation of a research protocol set forth in paragraph (3), the director of the donor facility shall hear the opinion of the ethics review committee of the donor facility. When giving approval to the implementation of a research protocol, the director of the donor facility shall notify the director of the research institution by attaching documents indicating the process and results of the review by the ethics review committee of the donor facility.

2. Confirmation, etc. by the Minister of Education, Culture, Sports, Science and Technology and the Minister of Health, Labour and Welfare

- (1) When giving approval for implementation of a research protocol, the director of the research institution shall receive confirmation from the Minister of Education, Culture, Sports, Science and Technology and the Minister of Health, Labour and Welfare with regard to the conformity of the research protocol with these Guidelines.
- (2) When seeking the confirmation set forth in paragraph (1), the director of the research institution shall submit the following documents:

- (i) The research protocol
- (ii) A copy of the research institution's rules concerning the handling of gametes and human fertilized embryos
- (iii) Documents indicating the process and results of the review by the ethics review committee of the research institution, and documents describing matters pertaining to the ethics review committee
- (iv) A copy of the donor facility's rules concerning the collection and preservation of gametes
- (v) Documents indicating the process and results of the review by the ethics review committee of the donor facility, and documents describing matters pertaining to the ethics review committee of the said institution

3. Research protocols

A research protocol shall contain the following matters:

- (i) The name of the research protocol
- (ii) The name and address of the research institution, and the name of the director of the research institution
- (iii) The names, brief backgrounds, research achievements and records of education and training of the research director and the research investigators, and their respective roles to be played in the research
- (iv) The method of acquiring gametes used in the research
- (v) The purpose and necessity of the research
- (vi) The method and period of the research
- (vii) An explanation concerning the standards of the research institution
- (viii) An explanation concerning informed consent
- (ix) The name and address of the donor facility, and the name of the director of the donor facility
- (x) An explanation concerning the standards of the donor facility
- (xi) Any other necessary matters

Section 2 Alteration of Research Protocols

- (1) When intending to alter a research protocol (excluding the matters prescribed in paragraphs 3(ii), (ix) and (xi) of Section 1), the research director shall first prepare a written amendment to the research protocol, and shall seek the approval of the director of the research institution. The same shall also apply when making alterations pertaining to the addition of donor facilities.
- (2) The director of the research institution shall, when requested to give approval for an alteration set forth in paragraph (1), seek the opinion of the ethics review committee of the said institution on the propriety of the alteration, and shall confirm the conformity of the alteration with these

Guidelines based on that opinion.

- (3) When confirming the conformity with these Guidelines pursuant to paragraph (2), in cases where the contents of the alteration to the research protocol pertain to a donor facility, the director of the research institution shall obtain the approval of the director of the donor facility for the said alteration.
- (4) When giving the approval set forth in paragraph (3), the director of the donor facility shall hear the opinion of the ethics review committee of the said institution.
- (5) When giving approval for an alteration set forth in paragraph (1), the director of the research institution shall receive confirmation from the Minister of Education, Culture, Sports, Science and Technology and the Minister of Health, Labour and Welfare with regard to the conformity of the said alteration with these Guidelines.
- (6) When proposing to receive the confirmation set forth in paragraph (5), the director of the research institution shall submit the following documents to the Minister of Education, Culture, Sports, Science and Technology and the Minister of Health, Labour and Welfare:
 - (i) A written amendment to the research protocol
 - (ii) Documents indicating the process and results of the review by the ethics review committee of the research institution regarding the said alteration
 - (iii) In cases that fall under paragraph (3), documents indicating the process and results of the review by the ethics review committee of the donor facility regarding the said alteration
- (7) When any changes have been made to the matters listed in paragraphs 3(ii), (ix) or (xi) of Section 1, the director of the research institution shall notify the Minister of Education, Culture, Sports, Science and Technology and the Minister of Health, Labour and Welfare to that effect.

Section 3 Reports on Research Progress

- (1) During the period in which research is conducted, the research director shall, at least once a year, prepare a research progress report that describes the progress of the research (including the handling of gametes and human fertilized embryos), and shall submit this to the director of the research institution.
- (2) Upon receiving the submission of a report set forth in paragraph (1), the director of the research institution shall promptly submit a copy thereof to the ethics review committee of the research institution and to the Minister of Education, Culture, Sports, Science and Technology and the Minister of Health, Labour and Welfare.

Section 4 Completion of Research

- (1) When the research is completed, the research director shall promptly prepare a research completion report including a statement to that effect and describing the results of the research,

and shall submit this to the director of the research institution.

- (2) Upon receiving the submission of a report set forth in paragraph (1), the director of the research institution shall promptly submit a copy thereof to the Minister of Education, Culture, Sports, Science and Technology and the Minister of Health, Labour and Welfare.

Section 5 Protection of Personal Information

- (1) With regard to measures concerning the protection of the personal information of donors, the organization representative, etc. shall take measures corresponding to the Ethical Guidelines for Medical and Health Research Involving Human Subjects (Public Notice of MEXT and the Ministry of Health, Labour and Welfare, No. 3 of 2014) (in cases when conducting human genome/gene analysis research based on the Ethical Guidelines for Human Genome/Gene Analysis Research (Public Notice No. 1 of the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare, and the Ministry of Economy, Trade and Industry, 2013), those guidelines).
- (2) In cases where personal information is handled when receiving the provision of gametes in accordance with these Guidelines, the organization representative, etc. shall designate a privacy officer within the said organization for the protection of that personal information.
- (3) The privacy officer shall take measures for anonymization before transferring the donated gamete to a research institution (in cases where the research institution and the donor facility are one and the same, before the donated gamete is handled by a research division within the said organization).

Section 6 Disclosure of Research Results

A research institution shall disclose its research results unless this would impede the protection of intellectual property rights and personal information, etc.

Chapter VI Miscellaneous Provisions

Section 1 Public Announcement of Nonconformity to the Guidelines

When research is found to have been conducted at variance with the standards provided by these Guidelines, the Minister of Education, Culture, Sports, Science and Technology and the Minister of Health, Labour and Welfare shall make a public announcement to that effect.

Section 2 Revision

These Guidelines shall, where necessary, be revised by taking into consideration such factors as the progress of related research and changes in social circumstances regarding the handling human embryos.

Section 3 Effective Date

These Guidelines shall come into effect as of April 1, 2011.