(Tentative Translation)

Public Notice of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) No. 88 of May 20, 2010

Chapter I General Provisions

(Purpose)

Article 1 Research on germ cell production has the potential to help clarify causes of infertility and congenital diseases or syndromes that originate in germ cells. At the same time, such research also has the potential to lead to the creation of individuals by using germ cells produced from human iPS cells or from human tissue stem cells. In view of such possibilities, the purpose of these Guidelines is to stipulate the fundamental matters to be observed from bioethical perspectives, such as the appropriate management of the said germ cells, thereby contributing to ensuring that research on germ cell production is conducted properly.

(Definitions)

Article 2 In these Guidelines, the meanings of the terms listed in the following items should be as prescribed respectively in those items:

(i) Germ cell A cell from a primordial germ cell to a spermatozoon or an ovum

(ii) Research on germ cell production Research on producing germ cells from human iPS cells or human tissue stem cells (excluding germ lines; hereinafter the same in Article 3 and Article 7, paragraph (1)), which pertains to basic research

(iii) Embryo An embryo prescribed in Article 2, paragraph (1), item (i) of the Act on Regulation of Human Cloning Techniques (Act No. 146 of 2000; hereinafter referred to as the "Act")

(iv) Human embryo An embryo of a human being (including an embryo with the genetic information of a human being)

(v) Research institution An institution that conducts research on germ cell production (including

an institution that accepts offers of cells from donors)

(vi) Informed consent Consent given out of one's own free will based on the provision of a sufficient explanation

(Scope of Application)

Article 3 Research on germ cell production should be carried out appropriately pursuant to the provisions of these Guidelines.

Chapter II Requirements for Research on Germ Cell Production

(Requirements for Research on Germ Cell Production)

Article 4 Research on germ cell production should be allowed only when the following requirements are satisfied:

(i) The purpose of the research is for basic research contributing to either of the following:

(a) Clarification of the function of human development, differentiation and regeneration; or

(b) Development of a new diagnosis method, preventive method or treatment method or development of such products as medicines.

(ii) The production of germ cells is scientifically rational and necessary in the research prescribed in the preceding item.

(Requirements for Research Institutions)

Article 5 (1) The research institution should have in place rules on ethical matters concerning the production of germ cells, which are to be observed by persons who conduct research on germ cell production.

(2) The research institution should have persons who conduct research on germ cell production undertake courses and other necessary education on ethics concerning the production of germ cells.

(3) A research institution should cooperate in submitting materials, accepting investigations and any other measures found to be necessary by the Minister of MEXT concerning the production of germ cells.

(Prohibited Acts)

Article 6 A person handling germ cells that have been produced shall not produce human embryos using the said germ cells.

(Handling of Germ Cells)

Article 7 (1) A research institution shall, when transferring germ cells that it has produced from

human iPS cells or human tissue stem cells, confirm that the following matters for the handling of the said germ cells are ensured in a contract with the transferee or by other means:

(i) Germ cells should be used for basic research that contributes to either of the following:

(a) Clarification of the function of human development, differentiation and regeneration; or

(b) Development of a new diagnosis method, preventive method or treatment method or development of such products as medicines.

(ii) Germ cells should not be used to make human embryos.

(iii) Germ cells should not be transferred to other institutions.

(iv) A research institution that has transferred germ cells should, as needed, be able to request a report from the transferee on the status of the handling of germ cells listed in each of the preceding items.

(2) When a research institution intends to transfer germ cells based on the provisions of the preceding paragraph, the person who is in a position overseeing research on germ cell production at the said research institution (hereinafter referred to as the "research director") should seek the advance approval of the head of the said research institution.

(3) In giving the approval set forth in the preceding paragraph, the head of the research institution should confirm that the transfer of the produced germ cells conforms to the provisions of paragraph (1).

(4) The head of the research institution should, when having given the approval set forth in paragraph (2), promptly report to that effect to the institutional review board and to the Minister of MEXT.

Chapter III Structure for Research on Germ Cell Production

(Head of Research Institution)

Article 8 (1) The head of a research institution should perform the following duties:

(i) Confirm the propriety of the plan concerning research on germ cell production which is conducted by the research institution (hereinafter referred to as the "research plan") and any amendment to the research plan, and approve the implementation thereof pursuant to Articles 11 through 14;

(ii) Ascertain the progress and/or results of the research on germ cell production and, if necessary, give instructions to the research director regarding matters such as any relevant points of concern and points for improvement;

(iii) Supervise the research on germ cell production; and

(iv) Communicate these Guidelines widely and thoroughly within the research institution and ensure the observance thereof.

(2) The head of a research institution may not serve concurrently as the research director; provided,

however, that this should not apply to cases where a person who acts for the head of the research institution in performing the duties set forth in the preceding paragraph has been appointed pursuant to the rules prescribed in paragraph (1) of the Article 5.

(3) In the case referred to in the proviso to the preceding paragraph, the term "the head of a/the research institution" in the provisions of these Guidelines (excluding the preceding paragraph) shall be deemed to be replaced with "a person who acts for the head of a/the research institution in performing the duties of the head of the research institution."

(Research Director)

Article 9 (1) The research director should perform the following duties:

(i) Examine the scientific and ethical propriety of the research plan or any amendment to the research plan based on the materials and information available in Japan and/or abroad concerning the research on germ cell production;

(ii) Prepare a document stating the research plan (hereinafter referred to as the "written research plan") or a document stating the contents of and reasons for any amendment to the research plan (referred to as the "written amendment to the research plan" in Article 14) based on the results of the examination set forth in the preceding item;

(iii) Oversee the research on germ cell production, and give necessary instructions to persons who conduct the said research on germ cell production (excluding the research director) (hereinafter referred to as "researchers");

(iv) Confirm as needed that the research on germ cell production is conducted appropriately in accordance with the research plan; and

(v) In addition to what is prescribed in the preceding items, take any necessary measures for overseeing the research plan.

(2) One research director should be assigned to each research plan, and he/she should have ethical awareness and sufficient expert knowledge regarding the production of germ cells, and be capable of performing precisely the duties listed in the items of the preceding paragraph.

(Institutional Review Board)

Article 10 (1) An institutional review board (IRB) should be established within a research institution for the purpose of carrying out the following operations: (i) In accordance with these Guidelines, comprehensively review the scientific and ethical propriety of the research plan or any amendment to the research plan, and submit opinions to the head of the research institution on matters such as the appropriateness of the plan or the amendment thereto and any relevant points of concern and points for improvement; and

(ii) Receive reports on the progress and the results of the research on germ cell production, carry

out investigations if necessary, and submit opinions to the head of the research institution on matters such as any relevant points of concern and points for improvement.

(2) Notwithstanding the provisions of the preceding paragraph, the head of a research institution may use an IRB established by another research institution as a substitute for the IRB set forth in the preceding paragraph.

(3) The IRB (including the IRB established by another research institution prescribed in the preceding paragraph; the same should apply hereinafter) should prepare and keep records on the review set forth in paragraph (1), item (i).

(4) The IRB should satisfy the following requirements:

(i) The IRB should consist of experts in biology, 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 the research plan.

(ii) The members of the IRB should include two or more persons who do not belong to the juridical person to which the said research institution belongs.

(iii) The members of the IRB should include two or more men and two or more women.

(iv) Any researcher who implements the said research plan, any interested persons of the research director or 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 ensure the freedom and independence of the activities of the IRB should be set in place.

(vi) Rules on the constitution, organization and administration of the IRB, disclosure of the contents of its meetings and other necessary procedures required for reviewing a research plan should be set in place and disclosed.

(5) When administering the IRB, the contents of its meetings should be disclosed except for the matters that are specified to be kept undisclosed pursuant to the rules prescribed in item (vi) of the preceding paragraph.

Chapter IV Procedures for Research on Germ Cell Production

(Approval of Head of Research Institution)

Article 11 When conducting research on germ cell production, the research director should prepare a written research plan in advance and seek the approval of the head of the research institution for the implementation of the research plan.

(2) The written research plan should contain the following matters:

(i) The title of the research plan;

(ii) The name and address of the research institution and the name of the head of the research

institution;

(iii) The name, brief background and research achievements of the research director;

(iv) The names, brief backgrounds and research achievements of the researchers;

(v) The purpose and necessity of the research on germ cell production;

(vi) The method and period of the research on germ cell production;

(vii) An explanation on the cells to be used for producing germ cells;

(viii) An explanation concerning informed consent; and

(ix) Any other necessary matters.

(Hearing of Opinion of Institutional Review Board)

Article 12 The head of the research institution should, when requested by the research director to give approval for the implementation of the research plan pursuant to paragraph (1) of the preceding Article, seek the opinion of the IRB on the propriety of the plan and confirm the compliance of the research plan with these Guidelines based on the said opinion.

(Notification to the Minister of MEXT)

Article 13 (1) When giving approval for the implementation of the research plan, the head of the research institution should notify the Minister of MEXT of the implementation of the said research plan in advance after the completion of the procedures set forth in the preceding Article.

(2) In the case referred to in the preceding paragraph, the head of the research institution should submit to the Minister of MEXT the following documents:

(i) Written research plan;

(ii) Documents indicating the process and results of the review by the IRB;

(iii) Documents containing matters concerning the IRB, and a copy of the rules prescribed in Article 10, paragraph (4), item (vi); and

(iv) A copy of the rules prescribed in Article 5 paragraph (1).

(3) The Minister of MEXT should, when a notification under paragraph (1) has been given, report on the matters pertaining to the said notification to the Bioethics and Biosafety Commission under the Council for Science and Technology.

(Amendments to the Research Plan)

Article 14 (1) The research director should, when intending to amend any of the matters listed in Article 11, paragraph (2), items (i), (iii) and (v) through (viii), prepare a written amendment to the research plan and request the head of the research institution in advance to approve it. In this case, the head of the research institution who has been requested to give the approval should seek the opinion of the IRB on the propriety of the said amendment and confirm the compliance of the said

amendment with these Guidelines based on the said opinion.

(2) The head of the research institution should, when having given the approval set forth in the preceding paragraph, promptly notify the Minister of MEXT to that effect by attaching the written amendment to the research plan and documents indicating the process and results of the review by the IRB on the said amendment.

(3) The head of the research institution should, when any amendment has been made to the matters listed in Article 11, paragraph (2), item (ii), promptly notify the Minister of MEXT to that effect.

(4) The research director should, when intending to amend any of the matters listed in item (iv) or (ix) of Article 11, paragraph (2), prepare a written amendment to the research plan and seek the approval of the head of the research institution in advance.

(5) The head of the research institution should, when having given the approval set forth in the preceding paragraph, promptly report to the IRB to that effect by attaching the written amendment to the research plan and notify the Minister of MEXT to that effect.

(Report on Progress)

Article 15 (1) At least once a year, the research director should prepare a Germ Cell Production Report containing the status of germ cell production, and should submit this to the head of the research institution.

(2) On receipt of submission of a Germ Cell Production Report set forth in the preceding paragraph, the head of the research institution should promptly submit a copy of the report to the IRB and to the Minister of MEXT.

(Termination of Research on Germ Cell Production)

Article 16 (1) The research director should, when the research on germ cell production has been terminated, promptly dispose of the produced germ cells, and should prepare and submit to the head of the research institution a Research Termination Report stating the results of the research on germ cell production.

(2) The head of the research institution should, when he/she has received submission of the Research Termination Report set forth in the preceding paragraph, promptly submit a copy of the report to the IRB and to the Minister of MEXT.

Chapter V Provision of Cells Able to be Used for the Purpose of Producing Germ Cells

(Requirements for Cells that can be Used for the Purpose of Producing Germ Cells)

Article 17 Cells that can be used for the purpose of producing germ cells in research on germ cell production (in cases where the said cells are human iPS cells: including human somatic cells to be utilized for the production of the said human iPS cells; the same should apply hereinafter in this

Chapter) should be limited to the following:

(i) Cells for which informed consent pertaining to the fact that germ cells will be produced has been received in writing; and

(ii) In cases where cells are to be provided from a foreign country, those for which the production of germ cells from the said cells is not prohibited in the relevant country's national laws and regulations or guidelines equivalent thereto and in the conditions pertaining to the donation of the said cells

(Procedure of Informed Consent)

Article 18 (1) The research institution should, when providing an explanation pertaining to informed consent to cell donors, do so in an easy-to-understand manner by presenting a written explanation containing the following matters:

(i) The purpose of receiving the donation of cells and the method of research;

(ii) Concrete methods for protecting the personal information of donors;

(iii) The fact that donors will receive no reward in the future;

(iv) In cases where the donated cells may be analyzed genetically, that fact, and the fact that such genetic analysis will not identify specific individuals;

(v) The fact that any germ cells produced will not be used to produce human embryos;

(vi) The possibility that the research results obtained from the donated cells may be disclosed at such occasions as academic meetings;

(vii) The possibility that, in cases where useful results have been obtained from the donated cells, patent rights, copyrights or other intangible property rights or economic interests may arise from those results and the fact that these will not belong to the donors;

(viii) The fact that the manifestation of an intention to donate or not to donate does not bring any advantage or disadvantage to the donor;

(ix) The method and procedures for revoking informed consent; and

(x) Any other necessary matters

(2) When obtaining the informed consent of donors, the research institution shall not take unfair advantage of the situation of the donors.

(3) The research institution should, when it needs to receive the donation of cells from a minor or other donor who lacks the capacity to consent, receive the informed consent of a person who shall become the proxy for consent (meaning a person who has parental authority over the said donor, the spouse or guardian of the said donor, or any other person equivalent thereto).

(Protection of Personal Information)

Article 19 Any representatives of juridical persons that have research institutions, and any business

operators and representatives of organizations, who are heads, etc. of administrative organs, should take measures pertaining to the protection of cell donors' personal information, which are equivalent 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) (or in cases where human genome / gene analysis research based on the Ethical Guidelines for Human Genome / Gene Analysis Research (Public Notice of MEXT, MHLW and the Ministry of Economy, Trade and Industry, No. 1 of 2013) is conducted, the same guidelines).

Chapter VI　Miscellaneous Provisions

(Disclosure of Research Results)

Article 20 (1) The results obtained through research on germ cell production should be disclosed, in principle.

(2) The research institution should, when disclosing the results obtained through the research on germ cell production, clearly indicate that the said research has been carried out in conformity with these Guidelines.

(Public Announcement of Nonconformity to Guidelines)

Article 21 The Minister of MEXT should, when there is a person whose research on germ cell production is found not to conform to the criteria provided by these Guidelines, make a public announcement to that effect.

Supplementary Provisions

(Effective Date)

Article 1 These Guidelines should come into effect as from the day of promulgation.

(Review of Guidelines)

Article 2 The Minister of MEXT should review the provisions of these Guidelines if necessary, by taking into consideration such factors as the progress of research in life sciences and trends of society.