(Tentative Translation)

Guidelines on the Utilization of Human Embryonic Stem Cells

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Chapter I General Provisions

(Purpose)

Article 1 The purpose of these Guidelines is to provide fundamental matters to be observed in utilizing human embryonic stem (ES) cells from bioethical viewpoints so as to contribute to securing the proper utilization of human ES cells, by taking into consideration that the derivation and utilization of human ES cells involve bioethical issues, including the use of human embryos, which are the beginning of human life, and the fact that human ES cells are derived by destroying human embryos and have the potential to differentiate into any type of human cell while they have the potential to contribute significantly to the development of medicine and biology.

(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) 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")

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

(iii) Human embryonic stem (ES) cell　A cell obtained from a human embryo or produced by the division of such a cell, excluding an embryo, which has pluripotency (the capability to differentiate into endodermal, mesodermal and ectodermal cells) and retains the ability to proliferate by itself or is presumed to have an ability similar thereto

(iv) Differentiated cell　A cell differentiated from a human ES cell, which results in the cell no longer having the property of a human ES cell

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

(vi) Derivation　Production of cells with a specific property

(vii) First category derivation　Derivation of human ES cells by using human fertilized embryos prescribed by Article 2(1)(vi) of the Act (except that listed in the next item)

(viii) Second category derivation　Production of human somatic cell nuclear transfer (SCNT) embryos prescribed by Article 2(1)(x) of the Act and derivation of human ES cells by using the said human SCNT embryos

(ix) Deriving institute　An institute that derives human ES cells

(x) Distributing institute　An institute that distributes and maintains human ES cells deposited by deriving institutes for the purpose of distributing such human ES cells to third parties

(xi) Utilizing institute　An institute that utilizes human ES cells

(xii) Utilization plan　A plan concerning the utilization of human ES cells by a utilizing institute

(xiii) Utilization director　A person in a position to oversee the utilization of human ES cells in a utilizing institute

(Scope of Application)

Article 3 The utilization of human ES cells (limited to those pertaining to basic research) should be carried out appropriately pursuant to the provisions of these Guidelines.

(Consideration for Human ES Cells)

Article 4 A person handling human ES cells should handle such cells conscientiously and carefully, by taking into consideration that human ES cells have been derived by destroying human embryos, which are the beginning of human life, and have the potential to differentiate into any type of human cell.

Chapter II　Requirements for Utilization

(Requirements for Utilization)

Article 5 (1) The utilization of human ES cells derived through first category derivation should be allowed only when the following requirements are satisfied:

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

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

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

(ii) The utilization of human ES cells is scientifically rational and necessary in the research prescribed in the preceding item.

(2) The utilization of human ES cells derived through second category derivation should be allowed only when the following requirements are satisfied:

(i) The purpose of utilization is for the basic research prescribed in Article 9, paragraph (2) of the Guidelines on the Handling of Specified Embryos (Public Notice of MEXT No.83 of 2009).

(ii) The utilization of human ES cells is scientifically rational and necessary in the research prescribed in the preceding item.

(3) The human ES cells to be utilized should be limited to the following:

(i) Human ES cells that have been derived having satisfied the requirements prescribed in the Guidelines on the Derivation and Distribution of Human Embryonic Stem Cells (Public Notice of MEXT No. 156 of 2009) (in cases where they are to be utilized for the production of germ cells: human ES cells that have been derived having satisfied the requirements prescribed in the same Guidelines, including that informed consent be obtained concerning the production of germ cells).

(ii) Human ES cells that have been derived in a foreign country, and which are recognized as having been derived based on standards that are equivalent to the Guidelines on the Derivation and Distribution of Human Embryonic Stem Cells (in cases where they are to be utilized for the production of germ cells: those that are recognized as having been derived based on standards that are equivalent to the Guidelines, and for which the production of germ cells from human ES cells is not prohibited in the relevant country's national laws and regulations or guidelines equivalent thereto and in the conditions pertaining to

the provision of human ES cells).

(Prohibited Acts)

Article 6 No person handling human ES cells shall commit the following acts:

(i) Create an individual through the transplantation of embryos produced by utilizing human ES cells into a human or animal uterus or through any other method

(ii) Introduce human ES cells into a human embryo

(iii) Introduce human ES cells into a human fetus

(iv) In cases where germ cells are to be produced from human ES cells, produce a human embryo using the said germ cells.

(Distribution of Human ES Cells)

Article 7 A utilizing institute should not distribute or transfer human ES cells; provided, however, that this should not apply to the case where a utilizing institute distributes or transfers human ES cells processed in the utilizing institute through the introduction of genes or through any other method.

Chapter III Structure for Utilization

(Criteria for a Utilizing Institute)

Article 8 (1) A utilizing institute should satisfy the following requirements:

(i) The utilizing institute should have sufficient facilities, personnel and technical capability for utilizing human ES cells.

(ii) The utilizing institute should have in place rules on technical and ethical matters to be observed with regard to the utilization of human ES cells.

(iii) The utilizing institute should have in place a plan (hereinafter referred to as the “education and training plan”) for providing education and training for improving the technical capability and ethical awareness concerning the utilization of human ES cells.

(2) A utilizing institute should prepare and keep records on the utilization of human ES cells

(3) A utilizing institute should cooperate in submitting materials, accepting investigations and any other measures found to be necessary by the Minister of MEXT concerning the utilization of human ES cells.

(Head of Utilizing Institute)

Article 9 (1) The head of a utilizing institute should perform the following duties:

(i) Confirm the propriety of the utilization plan and any amendment to the utilization plan and approve the implementation thereof pursuant to Articles 12 through 15

(ii) Ascertain the progress and/or results of the utilization of human ES cells and, if necessary, give instructions to the utilization director regarding matters such as any relevant points of concern and points for improvement

(iii) Supervise the utilization of human ES cells

(iv) Communicate these Guidelines widely and thoroughly within the utilizing institute and ensure the observance thereof

(v) Formulate an education and training plan on the utilization of human ES cells and implement education and training based on it

(2) The head of a utilizing institute may not serve concurrently as the utilization director; provided, however, that this should not apply to the case where a person who acts for the head of the utilizing institute in performing the duties set forth in the preceding paragraph has been appointed pursuant to the rules prescribed in paragraph (1), item (ii) of the preceding Article.

(3) In the case referred to in the proviso to the preceding paragraph, the term "the head of a/the utilizing institute" 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 utilizing institute in performing the duties of the head of the utilizing institute."

(Utilization Director)

Article 10 (1) The utilization director should perform the following duties:

(i) Examine the scientific and ethical propriety of the utilization plan or any amendment to the utilization plan based on the materials and information available in Japan and/or abroad concerning the utilization of human ES cells

(ii) Prepare a document stating the utilization plan (hereinafter referred to as the "written utilization plan") or a document stating the contents of and reasons for any amendment to the utilization plan (referred to as the "written amendment to the utilization plan" in Article 15, paragraphs (1), (2) and (4)) based on the results of the examination set forth in the preceding item

(iii) Oversee the utilization of human ES cells, and give necessary instructions to researchers who implement the utilization plan

(iv) Confirm as needed that the utilization of human ES cells is appropriately implemented in accordance with the written utilization plan

(v) Order researchers who implement the utilization plan to participate in education and training based on the education and training plan on the utilization of human ES cells and, if necessary, implement any other education and training on the utilization of human ES cells

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

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

(Institutional Review Board)

Article 11 (1) An institutional review board (IRB) should be established within a utilizing institute for the purpose of carrying out the following operations:

(i) Comprehensively review the scientific and ethical propriety of the utilization plan or any amendment to the utilization plan and submit opinions to the head of the utilizing institute on matters such as the appropriateness of the plan or the amendment thereto and any relevant points of concern and points for improvement, in conformity with these Guidelines

(ii) Receive reports on the progress and the results of the utilization, carry out investigations if necessary, and submit opinions to the head of the utilizing institute 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 utilizing institute may use an IRB established by another utilizing institute as a substitute for the IRB set forth in the preceding paragraph.

(3) The IRB (including the IRB established by another utilizing institute 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 utilization

plan.

(ii) The members of the IRB should include two or more persons who do not belong to the juridical person to which the utilizing institute is affiliated;

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

(iv) Any researcher who implements said utilization plan, any interested persons of the utilization director or any relatives of the utilization 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 have been 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 utilization plan should have been 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　Procedure of Utilization

(Approval of Head of Utilizing Institute)

Article 13 (1) When utilizing human ES cells, the utilization director should prepare a written utilization plan in advance and seek the approval of the head of the utilizing institute for the implementation of the utilization plan.

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

(i) The title of the utilization plan

(ii) The name and address of the utilizing institute and the name of the head of the utilizing institute

(iii) The name, brief background, research achievements and record of education and training for the utilization of human ES cells of the utilization director and his/her role to be played in the utilization plan

(iv) The names, brief backgrounds, research achievements and records of education and training for the utilization of human ES cells of the researchers (except for the utilization director) and their respective roles to be played in the utilization plan

(v) The purpose and necessity of the utilization

(vi) The method and period of the utilization

(vii) The source of supply of the human ES cells to be utilized and the name of the human ES cell line

(viii) The handling of human ES cells following the termination of their utilization (including the handling of produced germ cells in cases where germ cells are to be produced)

(ix) An explanation concerning the criteria for the utilizing institute

(x) An explanation on the conditions for the derivation of human ES cells and the reception of such cells in the case where the human ES cells to be utilized are provided from foreign countries

(xi) Any other necessary matters

(Hearing of Opinion of IRB)

Article 13 The head of the utilizing institute should, when requested by the utilization director to give approval for the implementation of the utilization plan pursuant to paragraph (1) of the preceding Article, seek the opinion of the IRB on the propriety of the plan and confirm the conformity of the utilization plan with these Guidelines based on said opinion.

(Notification to the Minister of MEXT)

Article 14 (1) When giving approval for the implementation of the utilization plan, the head of the utilizing institute should notify the Minister of MEXT of the implementation of said utilization plan in advance after the completion of the procedure set forth in the preceding Article.

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

(i) Written utilization 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 11, paragraph (4), item (vi)

(iv) A copy of the rules on technical and ethical matters to be observed with regard to the utilization of human ES cells

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

(Amendments to Utilization Plan)

Article 15 (1) The utilization director should, when intending to amend any of the matters listed in Article 12, paragraph (2), items (i), (iii) and (v) through (x), prepare a written amendment to the utilization plan and request the head of the utilizing institute in advance to approve it.In this case, the head of the utilizing institute who has been requested to give the approval should seek the opinion of the IRB on the propriety of said amendment and confirm the conformity of said amendment with these Guidelines based on said opinion.

(2) The head of the utilizing institute 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 utilization plan and documents indicating the process and results of the review by the IRB on said amendment.

(3) The head of the utilizing institute should, when any amendment has been made to the matters listed in Article 12, paragraph (2), item (ii), promptly notify the Minister of MEXT to that effect.

(4) The utilization director should, when intending to amend any of the matters listed in item (iv) or (xi) of Article 12, paragraph (2), prepare a written amendment to the utilization plan and seek the approval of the head of the utilizing institute in advance.

(5) The head of the utilizing institute 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 utilization plan and notify the Minister of MEXT to that effect.

(Report on Progress)

Article 16 The utilization director should report on the progress of the utilization of human ES cells as needed to the head of the utilizing institute and the IRB.

(2) In addition to the report set forth in the preceding paragraph, at least once a year, the utilization director of a utilizing institute that produces germ cells should prepare a Germ Cell Production Report containing the status of germ cell production, and should submit this to the head of a utilizing institute.

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

(Termination of utilization of human ES cells)

Article 17 (1) The utilization director should, when the utilization of human ES cells has been terminated, promptly dispose of the remaining human ES cells based on the agreement with the deriving institute or distributing institute that has distributed said human ES cells, or return or transfer them to the deriving institute or distributing institute, and should prepare and submit to the head of the utilizing institute a Report on the Termination of Human ES Cell Utilization stating the results of the utilization.

(2) The head of the utilizing institute should, when he/she has received submission of the Report on the Termination of Human ES Cell Utilization set forth in the preceding paragraph, promptly submit a copy of the report to the deriving institute or distributing institute that has distributed said human ES cells, the IRB and the Minister of MEXT.

Chapter V Handling of Differentiated Cells

(Handling of Differentiated Cells)

Article 18 (1) A utilizing institute should, when transferring differentiated cells that it has produced, notify the transferee that the said differentiated cells originate from human ES cells.

(2) A utilizing institute that produces germ cells shall, when transferring germ cells that it has produced, in addition to giving the notification set forth in the preceding paragraph, 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

(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 institutes

(iv) An institute 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

(3) When a utilizing institute intends to transfer germ cells based on the provisions of the preceding paragraph, the utilization director of the said utilizing institute

should seek the advance approval of the head of the said utilizing institute.

(4) In giving the approval set forth in the preceding paragraph, the head of the utilizing institute should confirm that the transfer of the produced germ cells conforms to the provisions of paragraph (2).

(5) The head of the utilizing institute should, when having given the approval set forth in paragraph (3), promptly report to that effect to the IRB and to the Minister of MEXT.

(Handling of Germ Cells Following the Termination of Human ES Cell Utilization)

Article 19 (1) An institute that continues to utilize produced germ cells following the termination of human ES cell utilization shall be deemed a utilizing institute, and shall apply these Guidelines. In this case, the provisions of Article 5, paragraphs (2) and (3), Article 6, items (i) through (iii), Article 7, Article 8, paragraph (1), item (i) and paragraph (2), Article 12 paragraph (1), Article 13, Article 14, Article 16, paragraph (1), and Article 17 shall not apply, and in the provisions of Article 5, paragraph (1), Article 8 (excluding paragraph (1), item (i) and paragraph (2); the same should apply hereinafter), Article 9, paragraph (1) and Article 10, the phrase "human ES cells derived through first category derivation" in Article 5, paragraph (1) shall be deemed to be replaced with "germ cells produced from human ES cells," the phrase "human ES cells" in item (ii) of the same paragraph, Article 8, Article 9, paragraph (1), and Article 10 shall be deemed to be replaced with "germ cells produced from human ES cells," the phrase "technical and ethical" in Article 8, paragraph (1), item (ii) shall be deemed to be replaced with "ethical," the phrase "technical capability and ethical" in item (iii) of the same paragraph shall be deemed to be replaced with "ethical," and the phrase "and sufficient expert knowledge and technical capability" in Article 10, paragraph (2) shall be deemed to be replaced with "and sufficient expert knowledge."

(2) The utilization director of an institute deemed to be a utilizing institute pursuant to the provisions of the preceding paragraph should, when the utilization of germ cells has been terminated, promptly dispose of the said germ cells, and should prepare and submit to the head of the said institute a Report on the Termination of Germ Cell Utilization stating the results of the utilization of the said germ cells.

(3) The head of an institute, who has received submission of a Report on the Termination of Germ Cell Utilization set forth in the preceding paragraph, should

promptly submit a copy of the report to the IRB and to the Minister of MEXT.

Chapter VI Miscellaneous Provisions

(Disclosure of Research Results)

Article 20 (1) The research results obtained through the utilization of human ES cells should be disclosed, in principle.

(2) The utilizing institute should, when disclosing the research results obtained through the utilization of human ES cells, clearly indicate that said utilization of human ES cells has been carried out in conformity with these Guidelines.

(Coordination with Relevant Administrative Organs)

Article 21 The Minister of MEXT should closely coordinate with the Minister of Health, Labour and Welfare and the Minister of Economy, Trade and Industry by such means as providing information, by taking into consideration that the utilization of human ES cells is closely related to medicine and its related fields.

(Public Announcement of Nonconformity to Guidelines)

Article 22 The Minister of MEXT should, when there is a person whose utilization of human ES cells and germ cells produced from human ES cells 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 date of promulgation.

(Review of Guidelines)

Article 2 (1) 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.

(2) The review set forth in the preceding paragraph should be carried out based on the opinion of the Council for Science and Technology Policy.