(Tentative Translation)

Guidelines on the Distribution and 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 handling human embryonic stem (ES) cells from bioethical viewpoints so as to contribute to securing the proper handling of human ES cells. The Guidelines fully take into consideration that ES cells involve bioethical issues, including the use of human embryos, which are the emerging potential 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 should be as prescribed in the following 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 fertilized embryo	A human fertilized embryo prescribed in Article 2, Paragraph (1), Item (vi) of the Act
(iv) Human somatic cell nuclear transfer (SCNT) embryo	A human somatic cell nuclear transfer embryo prescribed in Article 2, Paragraph (1), Item (x) of the Act
(v) 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
(vi) 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
(vii) Germ cell	Any cell from a primordial germ cell to a spermatozoon or an ovum
(viii) Derivation	Production of cells with a specific property
(ix) First category derivation	Derivation of human ES cells by using human fertilized embryos (except as listed in the next item)
(x) Second category derivation	Production of human SCNT embryos and derivation of human ES cells by using produced human SCNT embryos
(xi) Deriving institute	An institute that derives human ES cells
(xii) Distributing institute	An institute that distributes and maintains human ES cells (limited to those intended to be used for basic research) deposited by deriving institutes for the purpose of distributing such human ES cells to third parties
(xiii) Utilizing institute	An institute that utilizes human ES cells to carry out basic research (except overseas utilizing institutes)
(xiv) Utilizing clinical institute	An institute that utilizes human ES cells following procedures established for the utilization of such cells for the purpose to use such in medical care (including clinical research and trials) in accordance with laws and regulations. An institute that utilizes human ES

	cells for basic research, however, is not considered as a utilizing clinical institute
(xv) Overseas utilizing institute	An institute that utilizes human ES cells for basic research at their places of business outside Japan
(xvi) Overseas distribution plan	A plan concerning the distribution of human ES cells (limited to those intended to be used for basic research) to an overseas utilizing institute by a distributing institute
(xvii) Utilization plan	A plan concerning the utilization of human ES cells by a utilizing institute
(xviii) Distribution director	A person in a position to oversee the distribution of human ES cells in a distributing institute
(xix) Utilization director	A person in a position to oversee the utilization of human ES cells in a utilizing institute
(xx) Informed consent	Consent given out of one's own free will based on the provision of sufficient explanation

(Scope of Application)

Article 3 These Guidelines shall apply to the distribution of human ES cells (excluding that carried out by a deriving institute) and the utilization of such for basic research.

(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 emerging potential of human life, and have the potential to differentiate into any type of human cell.

Chapter II Distribution of Human Embryonic Stem Cells

Section 1 Requirements for Distribution

(Requirements for Human ES Cells to be Distributed)

Article 5 Human ES cells to be distributed should be limited to those that satisfy the following requirements:

(i) The human ES cells should be those that have been derived based on the Guidelines on the Derivation of Human Embryonic Stem Cells (Public Notice of MEXT and MHLW No. 2 of 2014; hereinafter referred to as the "ES Derivation Guidelines") or those that have been distributed from overseas based on these Guidelines (limited to those intended to be used for basic research).

(ii) The human ES cells should be those that have been distributed, deposited and transferred gratis, except for necessary expenses.

(Requirements for Distribution to Utilizing Institute)

Article 6 (1) The distribution of human ES cells to a utilizing institute may be carried out only when the following requirements are satisfied:

(i) Human ES cells should be distributed only to utilizing institutes that implement a utilization plan based on these Guidelines.

(ii) Human ES cells should be distributed gratis, except for necessary expenses.

(2) A distributing institute should, when a request for the distribution of human ES cells has been made by a utilizing institute that implements a utilization plan based on these Guidelines, distribute the human ES cells unless there are unavoidable circumstances.

(Requirements for Distribution to Utilizing Clinical Institute)

Article 7 The distribution of human ES cells from a utilizing institute to utilizing clinical institute may be carried out only when such human ES cells are not distributed by a distributing institute and the following requirements are satisfied:

(i) In order to ensure that the following requirements are satisfied, the utilizing institute has concluded in writing a contract with the utilizing clinical institute.

(a) The utilizing clinical institute should not 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, introduce human ES cells into a human embryo or human fetus, or produce germ cells from human ES cells.

(b) The utilizing clinical institute should not redistribute or transfer the human ES cells that it has received by distribution to any other institutes.

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

(d) The utilizing clinical institute should have in place a plan for providing the education and training for improving ethical knowledge concerning the utilization of human ES cells.

(e) The utilizing clinical institute should have taken sufficient and appropriate measures to protect personal information.

(f) The utilizing clinical institute should, in the event of violating the requirements prescribed in this article, return or transfer human ES cells to the utilizing institute that has distributed the human ES cells.

(g) The utilizing clinical institute should, when transferring differentiated cells that it has produced, notify the transferee that the said differentiated cells originate from human ES cells.

(h) The utilizing clinical institute should, when it has terminated the utilization of human ES cells, dispose of the remaining human ES cells, or return or transfer them to the utilizing institute that has distributed such human ES cells.

(ii) Human ES cells should be distributed gratis, except for necessary expenses.

(Requirements for Distribution to Overseas Utilizing Institute)

Article 8 The distribution of human ES cells to an overseas utilizing institute may be carried out only when the following requirements are satisfied:

(i) Human ES cells should be distributed only to overseas utilizing institutes that have concluded a contract based on an overseas distribution plan that has been confirmed by the Minister of Education, Culture, Sports, Science and Technology as prescribed in Article 20, Paragraph (7).

(ii) Human ES cells should be distributed gratis, except for necessary expenses.

Section 2 Distributing Institute

(Criteria for Distributing Institute)

Article 9 A distributing institute should satisfy the following requirements:

(i) The distributing institute should have sufficient facilities, personnel, technical and managerial capabilities and finances for carrying out the distribution, etc. (the distribution, receipt of deposits and maintenance; the same should apply hereinafter) of human ES cells.

(ii) The distributing institute should have in place rules on technical and ethical matters to be observed with regard to the distribution, etc. of human ES cells and on matters concerning the management of human ES cells.

(iii) The distributing institute should have established an ethical review board.

(iv) The distributing institute should have a track record concerning the distribution of animal or human cells.

(v) The distributing 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 knowledge concerning the distribution, etc. of human ES cells.

(Operations of Distributing Institute)

Article 10 (1) In addition to the distribution, etc. of human ES cells, a distributing institute should carry out the following operations:

(i) Receive already-distributed human ES cells that have been processed by a utilizing institute, and distribute and maintain such processed human ES cells (limited to the cases that are reasonable for the development of research utilizing human ES cells).

(ii) Provide technical training on the handling of human ES cells to persons who implement utilization plans (limited to those in which human ES cells that have been distributed by the said distributing institute are utilized).
(2) The distributing institute should prepare and keep records on the distribution, etc., return and receipt of human ES cells.
(3) The distributing institute should 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 distribution, etc., return and receipt of human ES cells.

(Head of Distributing Institute)
Article 11 (1) The head of a distributing institute should perform the following duties:
(i) Confirm the propriety of the overseas distribution plan and approve the implementation thereof pursuant to Article 20.
(ii) Ascertain the status of the distribution, etc. return and receipt of human ES cells and, if necessary, give instructions to the distribution director regarding matters such as any relevant points of concern and points for improvement.
(iii) Supervise the distribution, etc. of human ES cells.
(iv) Communicate these Guidelines widely and thoroughly within the distributing institute and ensure the observance thereof.
(v) Regularly report on the actual results of the distribution of human ES cells received by deposit from a deriving institute to the head of the said deriving institute.
(vi) Formulate an education and training plan on the distribution, etc., of human ES cells and implement education and training based on this plan
(vii) Establish an implementation system for the technical training prescribed in Paragraph (1), Item (ii) of the preceding article.
(2) The head of a distributing institute may not serve concurrently as the distribution director.

(Distribution Director)
Article 12 (1) The distribution director should perform the following duties:
(i) Oversee the distribution, etc. of human ES cells, and give the necessary instructions to researchers.
(ii) Confirm as needed that the distribution, etc. of human ES cells is appropriately implemented.
(iii) Make the necessary reports to the head of the distributing institute and the ethical review board of the distributing institute on the status of the distribution, etc., return and receipt of human ES cells.

(iv) Order researchers who implement a plan concerning the establishment of the said distributing institute (hereinafter referred to as the "establishment plan") or an overseas distribution plan to participate in education and training based on the education and training plan on the distribution, etc. of human ES cells and, if necessary, provide any other education and training for the distribution, etc. of human ES cells.
(v) Provide the technical training prescribed in Article 10, Paragraph (1), Item (ii).
(vi) Prepare a document containing the overseas distribution plan (hereinafter referred to as the "written overseas distribution plan").
(vii) In addition to what is prescribed in the preceding items, take any necessary measures for overseeing the distribution, etc. of human ES cells.
(2) One distribution director should be assigned in each distributing institute, and the director 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.

(Establishment Review Board)
Article 13 (1) An ethical review board concerning the establishment of a distributing institute (hereinafter referred to as the "establishment review board") should carry out operations to comprehensively review the propriety of the establishment plan and submit opinions to the head of the institute intending to establish a distributing institute on matters such as the appropriateness of the plan and any relevant points of concern and points for improvement, in conformity with these Guidelines.
(2) The establishment review board should prepare and keep records on the process of the review set forth in the preceding paragraph.
(3) The establishment review board should satisfy the following requirements:
(i) The establishment review board 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 propriety of the establishment plan.
(ii) The members of the establishment review board should include two or more persons who do not belong to the juridical entity to which the institute that intends to establish a distributing institute belongs.
(iii) The members of the establishment review board should include two or more men and two or more women.
(iv) Any researcher who implements the said establishment plan, any interested persons of the distribution director or any relatives of the distribution director up to the third degree of kinship should not take part in the review.
(v) An appropriate administrative procedure that can guarantee the freedom and

independence of the activities of the establishment review board should be set in place.
(vi) Rules on the constitution, organization and administration of the establishment review board, disclosure of the contents of its meetings and other necessary procedures required for reviewing an establishment plan should be set in place and disclosed.
(4) When administering the establishment review board, 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.

(Procedure Concerning Establishment of Distributing Institute)
Article 14 (1) The head of an institute that intends to become a distributing institute should prepare a document containing the establishment plan (referred to as the "written establishment plan" in Paragraph (3) and Paragraph (4), Item (i)) and receive confirmation from the Minister of Education, Culture, Sports, Science and Technology with regard to the conformity of the establishment plan with these Guidelines.
(2) The head of the institute that intends to receive the confirmation set forth in the preceding paragraph should establish an establishment review board in advance and seek its opinion with regard to the propriety of the establishment plan.
(3) A written establishment plan should contain the following matters:
(i) The name and address of the distributing institute and the name of its head.
(ii) The organization and personnel framework for carrying out the distribution, etc. of human ES cells.
(iii) The name, brief background, track record regarding the handling of human ES cells or research achievements concerning human ES cells and record of education and training of the distribution director and his/her role to be played in the distributing institute.
(iv) The names, brief backgrounds, track records regarding the handling of human ES cells or research achievements concerning human ES cells and records of education and training of the researchers and their respective roles to be played in the distributing institute.
(v) The facilities and equipment for handling the distribution, etc. of human ES cells and the management framework thereof (including the floor plans of the facilities and arrangement plans of the equipment for handling the distribution, etc. of human ES cells and the arrangement plan of the management system).
(vi) An explanation concerning the human ES cells to be received by deposit or transfer.
(vii) An explanation concerning the rules on technical and ethical matters to be observed with regard to the distribution, etc. of human ES cells and on matters concerning the management of human ES cells.
(viii) The framework of the ethical review board.
(ix) The contents of the education and training plan on the distribution, etc. of human ES cells.

(x) Any other necessary matters.
(4) The head of the institute that intends to receive the confirmation set forth in Paragraph (1) should submit to the Minister of Education, Culture, Sports, Science and Technology the following documents:
(i) A written establishment plan.
(ii) Documents indicating the process and results of the review by the establishment review board.
(iii) Documents containing matters concerning the establishment review board, and a copy of the rules prescribed in Paragraph (3), Item (vi) of the preceding article.
(iv) Documents containing matters concerning the ethical review board of the distributing institute, and a copy of the rules prescribed in Paragraph (3) Item (vi) of the preceding article as applied mutatis mutandis by replacing terms pursuant to the provisions of Article 16, Paragraph (2).
(v) A copy of the rules on technical and ethical matters to be observed with regard to the distribution, etc. of human ES cells and on matters concerning the management of human ES cells.
(vi) Documents indicating the financial basis for continuously carrying out the distribution, etc. of human ES cells.
(vii) Documents detailing the track record concerning the distribution of animal or human cells.
(5) The Minister of Education, Culture, Sports, Science and Technology should, when requested to provide the confirmation set forth in Paragraph (1), seek the opinion of the Bioethics and Biosafety Commission under the Council for Science and Technology on the conformity of the establishment plan with these Guidelines, and provide confirmation based on the said opinion.
(6) The Minister of Education, Culture, Sports, Science and Technology should, when having provided the confirmation set forth in the preceding paragraph, make a public announcement to that effect.

(Change to the Establishment Plan)
Article 15 (1) The head of a distributing institute should, when intending to change any of the matters listed in Paragraph (3), Item (ii), (iii), (v) or (vi) of the preceding article, receive confirmation from the Minister of Education, Culture, Sports, Science and Technology with regard to the conformity of the said change with these Guidelines after hearing the opinion of the ethical review board of the distributing institute on the propriety of the said change in advance. In this case, the head of the distributing institute should submit to the Minister of Education, Culture, Sports, Science and Technology a document containing the contents of, and reasons for, the said change and documents indicating the process and results of the

review by the ethical review board pertaining to the said change.
(2) The Minister of Education, Culture, Sports, Science and Technology should, when requested to provide the confirmation set forth in the preceding paragraph, seek the opinion of the Bioethics and Biosafety Commission under the Council for Science and Technology on the conformity of the said change with these Guidelines, and provide confirmation based on the said opinion.
(3) The head of a distributing institute should, when any change has been made to any of the matters listed in Paragraph (3), Items (i), (iv) and (vii) through (x) of the preceding article, notify the Minister of Education, Culture, Sports, Science and Technology to that effect. In this case, when the said change pertains to alterations to any of the matters listed in Items (iv) and (vii) through (ix) of the said paragraph, the head of the distributing institute should seek the opinion of the ethical review board of the distributing institute on the propriety of the said change in advance.
(4) The Minister of Education, Culture, Sports, Science and Technology should, when a notification set forth in the preceding paragraph (except those pertaining to change to any of the matters listed in of Paragraph (3) Item (i) of the preceding article) 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.

(Ethical Review Board of Distributing Institute)
Article 16 (1) The ethical review board of a distributing institute should carry out the following operations:
(i) Comprehensively review the propriety of a change to the establishment plan and submit opinions to the head of the distributing institute on matters such as the appropriateness of the change and any relevant points of concern and points for improvement, in conformity with these Guidelines.
(ii) Comprehensively review the propriety of the overseas distribution plan and submit opinions to the head of the distributing institute on matters such as the appropriateness of the plan and any relevant points of concern and points for improvement, in conformity with these Guidelines.
(iii) Receive reports on the status of the distribution, etc., return and receipt of human ES cells, carry out investigations if necessary, and submit opinions to the head of the distributing institute on matters such as any relevant points of concern and points for improvement.
(2) The provisions of Article 13, Paragraphs (2) through (4) should apply mutatis mutandis to the requirements and administration of the ethical review board of a distributing institute. In this case, the term “establishment review board” in these provisions should be deemed to be replaced with “ethical review board of the distributing institute,” the term “propriety of

the establishment plan" with "propriety of a change to the establishment plan and the overseas distribution plan," the term "institute that intends to establish a distributing institute" with "distributing institute," the term "any researcher who implements the said establishment plan" with "any researcher who implements the said establishment plan or overseas distribution plan," and the term "reviewing an establishment plan" with "changing an establishment plan and reviewing an overseas distribution plan."

(Report on Progress of Distribution)

Article 17 (1) The distribution director should report on the status of the distribution, etc., and return and receipt of human ES cells as needed to the head of the distributing institute and the ethical review board of the distributing institute.

(2) The head of a distributing institute should report on the status of the distribution, etc., return and receipt of human ES cells to the Minister of Education, Culture, Sports, Science and Technology at least once a year.

(Termination of Operations of Distributing Institute)

Article 18 (1) The head of a distributing institute should, when intending to terminate or suspend the operations of the distributing institute, seek the opinion of the ethical review board of the distributing institute and receive confirmation from the Minister of Education, Culture, Sports, Science and Technology with regard to the handling of human ES cells after the termination or suspension.

(2) The Minister of Education, Culture, Sports, Science and Technology should, when requested to provide the confirmation set forth in the preceding paragraph, seek the opinion of the Bioethics and Biosafety Commission under the Council for Science and Technology on the propriety of the handling of human ES cells after the termination or suspension of the operations of the distributing institute, and provide confirmation based on the said opinion.

(3) The Minister of Education, Culture, Sports, Science and Technology should, when having provided the confirmation set forth in Paragraph (1), make a public announcement to the effect that the said operations have been terminated or suspended.

Section 3 Distribution to Overseas Utilizing Institutes

(Criteria for Overseas Utilizing Institute)

Article 19 For the time being, an overseas distribution plan should be formulated for distribution to an overseas utilizing institute that satisfies the following requirements:

(i) The overseas utilizing institute should observe the national laws and regulations or guidelines equivalent thereto of the country where such overseas utilizing institute is located with regard to the handling of human ES cells and differentiated cells.

(ii) The overseas utilizing institute should not redistribute or transfer the human ES cells that it has received by distribution to any other institutes.
(iii) The overseas utilizing institute should, when it has terminated the utilization of human ES cells, dispose of the remaining human ES cells based on the agreement with the distributing institute that has distributed the said human ES cells, or return or transfer them to the distributing institute that has distributed the said human ES cells.
(iv) The overseas utilizing institute should not 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, introduce human ES cells into a human embryo or human fetus, or produce human embryos using germ cells produced from human ES cells.
(v) The overseas utilizing institute should not utilize human ES cells for a commercial purpose.
(vi) The overseas utilizing institute should not carry out clinical research applying human ES cells or cells originating therefrom to the human body or utilize human ES cells in medicine and in its related fields.
(vii) The overseas utilizing institute should have taken sufficient measures to protect personal information.
(viii) The overseas utilizing institute should take any other necessary measures for the appropriate handling of human ES cells.
(ix) The overseas utilizing institute should, in the event of violating the criteria for an overseas distribution plan prescribed in this article, return or transfer human ES cells to the distributing institute that has distributed the human ES cells.

(Procedure for Distribution to Overseas Utilizing Institute)
Article 20 (1) When distributing human ES cells to an overseas utilizing institute, the distribution director should prepare a written overseas distribution plan in advance and seek the approval of the head of the distributing institute for the implementation of the overseas distribution plan.
(2) The written overseas distribution plan should contain the following matters:
(i) The name of the overseas distribution plan.
(ii) The name and address of the distributing institute and the name of its head.
(iii) The name of the distribution director.
(iv) The name and address and the name of the country of the location of the overseas utilizing institute to which human ES cells are to be distributed.
(v) The method of distribution.
(vi) The period of utilization by the overseas utilizing institute to which human ES cells are to be distributed.
(vii) The source of supply of the human ES cells to be distributed and the name of the human

ES cell line.
(viii) An explanation concerning the criteria for the overseas utilizing institute.
(ix) Any other necessary matters.
(3) The distribution director should attach to the written overseas distribution plan a copy of a document indicating that the utilization of human ES cells by the overseas utilizing institute to which the cells will be distributed has been approved based on the national laws and regulations or guidelines equivalent thereto of the country where such overseas utilizing institute is located, and Japanese translations thereof.
(4) The head of a distributing institute should, when requested to give the approval set forth in Paragraph (1), seek the opinion of the ethical review board of the distributing institute on the propriety of the plan and confirm the conformity of the plan with these Guidelines based on the said opinion.
(5) When giving approval for the implementation of an overseas distribution plan, the head of a distributing institute should seek the consent of the head of the deriving institute that has derived the said human ES cells with regard to the distribution under the said overseas distribution plan.
(6) The head of a deriving institute should give the consent set forth in the preceding paragraph unless there are unavoidable circumstances.
(7) When giving approval for the implementation of an overseas distribution plan, the head of a distributing institute should receive confirmation from the Minister of Education, Culture, Sports, Science and Technology with regard to the conformity of the said overseas distribution plan with these Guidelines after the termination of the procedures set forth in Paragraphs (4) and (5).
(8) In the case referred to in the preceding paragraph, the head of the distributing institute should submit to the Minister of Education, Culture, Sports, Science and Technology the following documents:
(i) The written overseas distribution plan.
(ii) Documents indicating the process and results of the review by the ethical review board of the distributing institute.
(9) The Minister of Education, Culture, Sports, Science and Technology should seek the opinion of the Bioethics and Biosafety Commission under the Council for Science and Technology on the conformity of the overseas distribution plan with these Guidelines, and provide confirmation based on the said opinion.

Chapter III Utilization of Human Embryonic Stem Cells

Section 1 Requirements for Utilization

(Requirements for Utilization)

Article 21 (1) The utilization of human ES cells derived through first category derivation should be allowed only when the following requirements are satisfied:

(i) The 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 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 ES Derivation Guidelines (limited to 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 ES Derivation Guidelines (limited to 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 ES Derivation Guidelines, and for which the production of germ cells from human ES cells is not prohibited in the national laws and regulations or guidelines equivalent thereto of the country where such overseas utilizing institute is located, and in the conditions pertaining to the provision of human ES cells).

(Prohibited Acts)

Article 22 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 23 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 and the case prescribed in Article 7.

Section 2 Utilization System

(Criteria for Utilizing Institute)

Article 24 (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 an education and training plan on 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 Education, Culture, Sports, Science and Technology concerning the utilization of human ES cells.

(Head of Utilizing Institute)

Article 25 (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 28 through 31.

(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 this plan.

(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 26 (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 31, 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 the director 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.

(Ethical Review Board of Utilizing Institute)
Article 27 (1) An ethical review board 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 ethical review board established by another utilizing institute as a substitute for the ethical review board of his/her utilizing institute set forth in the preceding paragraph.
(3) The ethical review board of a utilizing institute (including the ethical review board 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 ethical review board of a utilizing institute should satisfy the following requirements:
(i) The ethical review board of a utilizing institute 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 ethical review board of a utilizing institute should include two or more persons who do not belong to the juridical entity to which the utilizing institute is affiliated;
(iii) The members of the ethical review board of a utilizing institute should include two or more men and two or more women.
(iv) Any researcher who implements the 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 can ensure the freedom and independence of the activities of the ethical review board of a utilizing institute should have been set in place.
(vi) Rules on the constitution, organization and administration of the ethical review board of a utilizing institute, 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 ethical review board of a utilizing institute, 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.

Section 3 Utilization Procedure

(Approval of Head of Utilizing Institute)
Article 28 (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 its head.
(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 receipt of such cells in the case where the human ES cells to be utilized are provided from foreign countries.
(xi) Any other necessary matters.

(Seeking Opinion of Ethical Review Board of Utilizing Institute)
Article 29 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 ethical review board of the utilizing institute on the scientific and ethical propriety of the plan and confirm the conformity of the utilization plan with these Guidelines based on the said opinion.

(Notification to the Minister of Education, Culture, Sports, Science and Technology)
Article 30 (1) When giving approval for the implementation of the utilization plan, the head of the utilizing institute should notify the Minister of Education, Culture, Sports, Science and Technology of the implementation of the 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 Education, Culture, Sports, Science and Technology the

following documents:
(i) Written utilization plan.
(ii) Documents indicating the process and results of the review by the ethical review board of the utilizing institute.
(iii) Documents containing matters concerning the ethical review board of the utilizing institute, and a copy of the rules prescribed in Article 27, 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 Education, Culture, Sports, Science and Technology 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 Utilization Plan)
Article 31 (1) The utilization director should, when intending to amend any of the matters listed in Article 28, 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 ethical review board of the utilizing institute on the scientific and ethical propriety of the said amendment and confirm the conformity with these Guidelines based on the 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 Education, Culture, Sports, Science and Technology to that effect by attaching the written amendment to the utilization plan and documents indicating the process and results of the review by the ethical review board of the utilizing institute on the said amendment.
(3) The head of the utilizing institute should, when any amendment has been made to the matters listed in Article 28, Paragraph (2), Item (ii), promptly notify the Minister of Education, Culture, Sports, Science and Technology to that effect.
(4) The utilization director should, when intending to amend any of the matters listed in Article 28, Paragraph (2), Item (iv) or (xi), 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 ethical review board of the utilizing institute to that effect by attaching the written amendment to the utilization plan and notify the Minister of Education, Culture, Sports, Science and Technology to that effect.

(Report on Progress of the Utilization)

Article 32 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 its ethical review board.
(2) In addition to the report set forth in the preceding paragraph, at least once a year, the utilization director of the 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 the utilizing institute.
(3) The utilization director who distributes the human ES cells to the utilizing clinical institute should, in each instance, prepare a report that describes the distribution status and submit the said report to the head of the utilizing institute.
(4) On receipt of submission of a Germ Cell Production Report set forth in Paragraph (2) or (3), the head of the utilizing institute should promptly submit a copy of the report to the ethical review board of the utilizing institute and to the Minister of Education, Culture, Sports, Science and Technology.

(Termination of Utilization of Human ES Cells)
Article 33 (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 the 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, having 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, distributing institute or utilizing institute that has distributed the said human ES cells, the ethical review board of the utilizing institute and the Minister of Education, Culture, Sports, Science and Technology.

(Disclosure of Research Results)
Article 34 (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 the said utilization of human ES cells has been carried out in conformity with these Guidelines.

Section 4 Handling of Differentiated Cells

(Handling of Differentiated Cells)

Article 35 (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) Notwithstanding the provisions of the preceding paragraph, the utilizing institute may not transfer the germ cells to the utilizing clinical institute.

(4) When a utilizing institute intends to transfer germ cells based on the provisions of Paragraph (2), the utilization director of the said utilizing institute should seek the advance approval of the head of the said utilizing institute.

(5) 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).

(6) The head of the utilizing institute should, when having given the approval set forth in Paragraph (4), promptly report to that effect to the ethical review board of the utilizing institute and to the Minister of Education, Culture, Sports, Science and Technology.

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

Article 36 (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 21, Paragraphs (2) and (3), Article 22, Items (i) through (iii), Article 23, Article 24, Paragraph (1), Item (i) and Paragraph (2), Article 28, Paragraph (1), Article 29, Article 30, Article 32, Paragraph (1), and Article 33 shall not apply, and in the provisions of Article 21, Paragraph (1), Article 24 (excluding Paragraph (1), Item (i) and Paragraph (2); the same should apply hereinafter), Article 25, Paragraph (1) and Article 26, the term “human ES cells derived

through first category derivation" in Article 21, Paragraph (1) shall be deemed to be replaced with "germ cells produced from human ES cells," the term "human ES cells" in Item (ii) of the same paragraph, Article 24, Article 25, Paragraph (1), and Article 26 shall be deemed to be replaced with "germ cells produced from human ES cells," the term "technical and ethical" in Article 24, Paragraph (1), Item (ii) shall be deemed to be replaced with "ethical," the term "education and training plan" in Item (iii) of the same paragraph shall be deemed to be replaced with "a plan (hereinafter referred to as the "ethical education and training plan") for providing the necessary education and training (hereinafter referred to as the "ethical education and training") for improving ethical awareness," the term "education and training plan" in Article 25, Paragraph (1), Item (v) and Article 26, Paragraph (1), Item (v) shall be deemed to be replaced with "ethical education and training plan," the term education and training" in those same Items shall be deemed to be replaced with "ethical education and training" and the term "and sufficient expert knowledge and technical capability" in Article 26, 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 ethical review board of the said institute and to the Minister of Education, Culture, Sports, Science and Technology.

Chapter VI Miscellaneous Provisions

(Coordination with Relevant Administrative Organs)

Article 37 The Minister of Education, Culture, Sports, Science and Technology 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 handling of human ES cells is closely connected to medicine and its related fields.

(Public Announcement of Nonconformity to Guidelines)

Article 38 The Minister of Education, Culture, Sports, Science and Technology should,

when there has been a person or entity whose handling of human ES cells and germ cells produced from human ES cells was 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 shall come into effect as of November 25, 2014.

(Repeal of Guidelines on the Utilization of Human Embryonic Stem Cells)

Article 2 The Guidelines on the Utilization of Human Embryonic Stem Cells (Public Notice of MEXT No. 87 of 2010; referred to as the "old Guidelines" in Article 4 of the supplementary provisions) should be repealed.

(Transitional Measures)

Article 3 An establishment plan or overseas distribution plan that has been confirmed by the Minister of Education, Culture, Sports, Science and Technology pursuant to the provisions of the Guidelines on the Derivation and Distribution of Human Embryonic Stem Cells (Public Notice of MEXT No. 156 of 2009) at the time of the enforcement of these Guidelines should be deemed to have received the confirmation set forth in Article 14, Paragraph (1) or Article 20, Paragraph (7), respectively.

Article 4 A utilization plan that has been notified to the Minister of Education, Culture, Sports, Science and Technology pursuant to the provisions of the old Guidelines at the time of the enforcement of these Guidelines should be deemed to have been notified in accordance with Article 30, Paragraph (1).

(Review of Guidelines)

Article 5 (1) The Minister of Education, Culture, Sports, Science and Technology 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, Technology and Innovation.