Albert Einstein College of Medicine

Embryonic Stem Cell Research Policy

I. Purpose

Human Stem Cells is essential to advancing fundamental scientific knowledge of cellular and developmental human biology. Such research, however, raises important scientific and ethical questions, which have resulted in restrictions on the use of federal and state funds for certain research involving such cells.

In light of these concerns and to comply with applicable federal and state laws and regulations, MMC and Einstein has established this Policy to ensure that "Covered Research" (defined herein) meets the highest scientific and ethical standards possible. The goals of this Policy are to assure that:

a. MMC/Einstein is aware of and provides oversight over and review of all research involving the procurement, derivation, banking, distribution, and use of Human Stem Cells conducted at or under the auspices of MMC/Einstein or funded by MMC/Einstein;
b. Each person working on such Covered Research will have available to them, through Einstein, to access the CITI ESCRO course for training and continuing education purposes.
c. MMC/Einstein observes the federal government's current restrictions against use of federal funds on non-registered hESC lines and any other applicable law or policy;
d. MMC/Einstein complies with any special requirements for such research imposed by research sponsors;
e. MMC/Einstein is aware of and maintains a registry documenting the sources or derivation of any Human Stem Cell lines planned for use or being used in research at MMC/Einstein; and
f. MMC/Einstein establishes oversight of the ESCRO Committee, which is charged with reviewing and approving research protocols involving the procurement, derivation, banking, distribution, or use of Human Stem Cells.

These goals are achieved in collaboration with the Institutional Review Board (IRB), the Institutional Animal Care and Use Committee (IACUC), the Executive Compliance Committee, other applicable compliance committees, and the participation of the research community.

MMC/Einstein's requirements for the conduct of research with Human Stem Cells as set forth in this Policy are based in large part on and intended to comply, as applicable, with (i) federal requirements and limitations with respect to federally-funded human stem cell research as set forth in the "National Institutes for Health Guidelines on Human Stem Cell Research" promulgated July 6, 2009, (ii) state requirements and limitations with respect to state-funded research as reflected in the Empire State Stem Cell Board Contract Policy Statements and Conditions (rev. approved 6/27/12), (iii) the recommendations of the National Academies in its 2005 report (as amended in 2007, 2008 and 2010) entitled "Guidelines for Human Embryonic Stem Cell Research", and (iv) the recommendations of the International Society of

Stem Cell Research in its 2016 report entitled "Guidelines for the Conduct of Human Embryonic Stem Cell Research", as each may be amended from time to time.

II. Scope

This Policy applies to all research involving the procurement, derivation, banking, distribution, or use of Human Stem Cells conducted at or under the auspices of MMC/Einstein or funded by MMC/Einstein, and to all other research conducted at or under the auspices of MMC/Einstein or funded by MMC/Einstein that is subject to oversight by the ESCRO Committee pursuant to law, regulation, or the terms of funding.

This Policy does not apply to research involving fetal tissue or stem cells derived from human adults, umbilical cord blood, placentas, or fetuses, or research involving any other type of human cells, unless the experiments are designed or expected to yield gametic cells or tissues or the research is otherwise subject to oversight by the ESCRO Committee pursuant to law, regulation, or the terms of funding.

III. Definitions

For purposes of this policy, the following definitions will apply:

Adult Stem Cell means an undifferentiated cell, found among differentiated cells in a tissue or organ, that can renew itself and can differentiate to yield primarily some or all of the specialized cell types of the tissue or organ, but the cell itself is not pluripotent or totipotent.

Blastocyst means a pre-implantation embryo of about 150 to 250 cells produced by successive rounds of cell division following fertilization. The blastocyst is a sphere made up of an outer layer of cells (the trophoblast), a fluid-filled cavity (the blastocoel), and a cluster of cells on the interior (the inner cell mass).

Chimera means an organism composed of cells derived from at least two genetically different zygotes. Theoretically, the zygote could be from separate species.

Cloning means the asexual production of a line of cells that is genetically identical to the originating cell.

Embryo means an organism in the early stages of growth and differentiation.

ESCRO Committee means MMC/Einstein's Embryonic Stem Cell Research Oversight Committee, established for the purpose of reviewing and approving research protocols involving the procurement, derivation, banking, distribution, or use of Human Stem Cells.

ESCRO Registration means the registration of Covered Research as described in Section IV(D) below.

hESC(s) or **human embryonic stem cell(s)** means one or more cells that are derived from the inner cell mass of blastocyst-stage human embryos, are capable of dividing without differentiating for a prolonged period in culture, and are known in appropriate conditions to develop into cells and tissues of the three primary germ layers (endoderm, ectoderm and mesoderm) as well as germ cells. These human embryos include those generated by fertilization, parthenogenic activation or somatic cell nuclear transfer.

hESC Research means research involving the procurement, derivation, banking, distribution, or use of hESCs.

Human embryo means the embryo of a human, generally defined as extending from the time of the formation of the Zygote until the end of the first eight weeks of gestation. Human embryos may be derived from fertilization, parthenogenesis, cloning, or other means from one or more gametes or human cells.

Human embryonic germ cell(s) means the cells found in a specific part of the human embryo or human fetus called the gonadal ridge that normally develop into mature gametes.

Human Stem Cell means any human embryonic stem cells, human totipotent or pluripotent cells, human neural progenitor stem cells, human gonadal progenitor stem cells, and induced pluripotent stem cells.

Covered Research means research involving the procurement, derivation, banking, distribution, or use of Human Stem Cells at or under the auspices of MMC/Einstein or any other research at or under the auspices of MMC/Einstein that is subject to oversight by the ESCRO Committee pursuant to law, regulation or the terms of funding.

iPSC(s) or **induced pluripotent stem cell(s)** means one or more human pluripotent stem cells that have been derived from non-embryonic sources, such as spermatogonial stem cells and "induced" pluripotent stem cells derived from somatic cells by introduction of genes or otherwise, and other pluripotent stem cells yet to be developed.

Intact human embryo means a human embryo that is developing in an integrated, normal fashion and continuing to progress and otherwise capable of progressing into a fully-developed human.

Morula means a solid mass of 16–32 human embryo cells that resembles a mulberry and results from the cleavage (cell division without growth) of a zygote (fertilized egg).

NIH Eligible hESC line means a stem cell line posted on the NIH hESC Registry or a stem cell line for which an institution has established eligibility for NIH funding under the NIH Stem Cell Guidelines.

NIH hESC Registry means the current list of hESC lines, as it may from time to time be revised, that are eligible for federal funding.

NIH Ineligible hESC line means any hESC line other than an NIH Eligible hESC line.

NIH Stem Cell Guidelines means the "National Institutes for Health Guidelines on Human Stem Cell Research" (2009 and subsequent updates).

Pluripotent stem cell means a stem cell having the capacity of developing cells of all germ layers (endoderm, ectoderm and mesoderm) as well as germ cells.

Provenance means sufficient documentation, on the basis of usual and customary standards within the field of Covered Research, to authenticate the history of ownership and place of origin of hESCs and/or hESC lines and/or iPSCs and/or iPSC lines.

Reproductive cloning means the use of cloning for the purpose of creating one or more adult organisms that are all genetically identical to another organism.
SCNT means somatic cell nuclear transfer, a technique that combines an enucleated egg and the nucleus of a somatic cell to make an embryo.

Spindle transfer means the process in which chromosomes from one oocyte are transferred into a recipient enucleated egg to make an embryo.

Stem cell means a cell with the ability to divide for indefinite periods in culture and to give rise to specialized cells.

Stem cell line means a mass of cells descended from and retaining at least some of the characteristics of an original stem cell.

Totipotent stem cell means a stem cell having the ability to give rise to all the cell types of the body plus all of the cell types that make up the extraembryonic tissues, such as the placenta.

Zygote means a cell formed by the union of male and female germ cells (sperm and egg, respectively).

IV. Policy

A. Compliance

All Covered Research conducted at or under the auspices of MMC/Einstein or funded by MMC/Einstein shall be conducted in compliance with (i) this Policy, (ii) all applicable federal, state, and local laws, regulations, and policies, (iii) the terms of any grant, contract, agreement, or other funding supporting the Covered Research, and (iv) all other applicable MMC or Einstein policies, including, where applicable, the policies and procedures of the Einstein IRB.

B. Prohibited Activities

No MMC or Einstein facilities, equipment or other resources, including funding, shall be used for any of the following:

1. Covered Research requiring or involving federal funds if such research is ineligible for federal support under the NIH Stem Cell Guidelines;
2. human reproductive cloning;
3. research involving in vitro culture of any post-fertilization human embryos or organized cellular structures that might manifest human organismal potential, regardless of derivation method, for longer than 14 days or until formation of the primitive streak, whichever occurs first;
4. research in which any products of research involving human totipotent or pluripotent stem cells are implanted into a human or non-human primate uterus;
5. research in which animal chimeras incorporating Human Stem Cells, including but not limited to hESCs and iPSCs, with the potential to form gametes are bred to each other; or
6. Covered Research engaged in a manner that is contrary to any applicable federal, state or local laws, rules or regulations or the terms of the grant or other support.

C. Categories of ESCRO Review

There are two types of ESCRO Committee review: ESCRO Registration and full ESCRO Committee review and approval. The type of review depends on the nature of the research activity.

ESCRO Registration entails the submission of a research protocol registration form to the ESCRO Committee, the official record of all hESC research at MMC/Einstein.

Full ESCRO Committee review is a lengthier process that requires both registering the research protocol with the ESCRO Committee and evaluation and approval of the research protocol by the ESCRO Committee.

Submission to the Office of Human Research Affairs ("OHRA") (and IACUC, as applicable) is a requirement for all such research to be reviewed.

D. Research and Activities That Do Not Require ESCRO Registration.

Unless otherwise provided in the terms of the grant, contract, agreement, or other funding supporting the research and/or other activities, the following research and/or other activities are not subject to this Policy:

1. Use of non-Human Stem Cells;
2. Use of fetal tissue or stem cells derived from human adults or umbilical cord blood, placentas, or fetuses, or research involving any other type of human cells, unless the experiments are designed or expected to yield gametic cells or tissues;
3. Transplantation of stem cells as part of a standard of care or other recognized and accepted medical treatment for a disease or condition (Transplantation of Human Stem Cells as part of a Human Subjects Research project subject to IRB review or as part of innovative care that departs in a significant way from standard or accepted practice may require ESCRO Registration (see Section IV(E) (below), ESCRO Committee review (see Section IV(F) (below)), or be prohibited (see Section IV(B) (above));
4. The creation and ex vivo passage of iPSCs. (ESCRO Registration and ESCRO Committee review and approval are required if the iPSCs are pluripotent stem cells and are transferred into an animal or human, or are used to make an embryo.); and
5. Other categories of Covered Research or activities that the Executive Dean (or designee) has made a written determination, after due consideration of relevant legal and ethical requirements, that such research or activities are appropriate for exemption from ESCRO Registration.

E. ESCRO Registration

The following categories of Covered Research are subject to ESCRO Registration only:

1. In vitro research involving hESC lines that are listed on the NIH hESC Registry;
2. In vitro research involving hESC lines or iPSC lines that have been pre-approved for such use by the ESCRO Committee;
3. In vitro research involving Human Stem Cells, if:
   3.1. Institutional Review Board (IRB) review approval has been received (i.e., the cells were obtained by a process approved by an IRB to ensure that donor(s) provided voluntary informed consent in accordance with then current federal and state law, regulations, and guidelines), **and**

3.2. The cell lines have been de-identified (i.e., the cell lines and any corresponding information are anonymous or are coded in such a manner that the donor(s) cannot be identified (by the investigators or others) directly or indirectly through identifiers linked to the donor(s), pursuant to a written agreement obtained from the source of the cell lines stating that the identity of the donor(s) will not be released to the investigator under any circumstances);

4. Research involving the transplantation of non-totipotent and non-pluripotent Human Stem Cells or cells derived from non-totipotent and non-pluripotent Human Stem Cells into human subjects (In no case shall such research involve implantation of human totipotent or pluripotent stem cells into a human uterus (See Section V(B) (above clinical research in which cells of human totipotent stem cells or iPSCs are transplanted into living human subjects requires ESCRO Committee Review (See Section (IV(F)(below).
5. Other types of Research not covered under this policy that the Executive Dean (or designee) has made a written determination, after due consideration of the likely risks and benefits of such research, that such categories are permissible without the additional review of the ESCRO Committee.

To determine whether proposed research meets the requirements of this section, the ESCRO Committee may choose to conduct an "expedited review" of such research proposals by the ESCRO Committee chair or his or her designee.

Investigators will be responsible for submitting annual progress reports for their registered studies to the ESCRO committee for re-review.

Investigators will also be responsible for amendment submissions to the ESCRO Committee for any changes, however minor, made to the protocol. The ESCRO Committee will determine if the amended study continues to meets the definition of not-human subject research and if any further actions to be taken by the principal investigator is warranted, The Committee will also determine if the study can still be classified as a registration, such as the addition of a new cell line or change in PI, or would require full committee review, due to substantive changes to the protocol.

F. ESCRO Committee Review Required

The following research activities apply to the review of human research that is non-exempt and not eligible for expedited review under federal regulations and/or institutional policy:

1. Creation of a new hESC line by any means, including through use of SCNT, human zygotes, spindle transfer, or a human embryo furnished by an in vitro fertilization clinic or other lawful source;
2. Payment to a donor solely for the purpose of creating a human embryo to be used in hESC research;
3. Research in which personally identifiable information about the donor of the blastocysts, morulae, gametes, or somatic cells from which the hESCs or iPSCs were derived is readily ascertainable or might become known to the investigator;
4. Research involving NIH Ineligible hESC lines that have not been pre-approved for such use by the ESCRO Committee;
5. iPSC research that includes experiments designed or expected to yield gametic cells and tissues;

6. Mixing human totipotent stem cells or iPSCs with pre-implantation human embryos (In no case shall such experiments be allowed to progress for more than 14 days of development in vitro, or past the point of primitive streak formation, whichever is first (See Section IV(B)(3) above));
7. Clinical research in which cells of human totipotent or pluripotent stem cells or iPSCs are transplanted into living human subjects (In no case shall such research involve implantation of human totipotent or pluripotent stem cells into a human uterus (See Section IV(B)(4) above);
8. In vitro culture of an intact human embryo;
9. Research that generates animal chimeras involving human cells, including, but not limited to, introducing hESCs, human totipotent stem cells or iPSCs into animals other than humans or primates at any stage of embryonic, fetal, or postnatal development; and
10. Research that involves the introduction of hESCs into non-human primates at any stage of fetal or postnatal development.

G. ESCRO Committee Review Procedures

1. Quorum Requirements - The MMC/Einstein ESCRO Committee shall officially conduct its review of proposed research at convened meetings at which at least fifty percent (50%) of the voting members (i.e., a quorum) of the ESCRO Committee are present, in person or by electronic conferencing. To meet quorum requirements, a majority of the ESCRO Committee members must be present at the convened meeting, including at least one scientist with relevant expertise and one ethicist. Alternate members may attend in place of absent primary members in order to meet quorum. If the Chair is absent or recused due to a conflict of interest, an experienced ESCRO Committee member may be designated to serve as meeting Chair.
2. ESCRO Committee Review of Research Proposals - Each research study requiring review and approval by the convened ESCRO Committee shall be addressed separately at ESCRO Committee meetings.
   - 2.1 Submitted protocols will be made available to ESCRO Committee members in advance of ESCRO Committee meetings to allow sufficient time for review.
   - 2.2 The primary reviewers for each protocol shall summarize the proposed research followed by an open discussion of the research by the ESCRO Committee members.
   - 2.3 The IRB Chair reminds members to recuse themselves from the confidential deliberations and vote on any protocols in which they have a conflict of interest. Members who recuse themselves due to a conflict of interest do not count toward quorum.
   - 2.4 For initial studies that require full review, representatives for protocols on the agenda (either the PI or qualified designees) are invited to attend the meeting to participate in the discussion and respond to any additional questions that arise during the board's discussion. They may participate via teleconference if they are unable to attend in person. Representatives are requested to leave before the confidential discussion and vote.
   - 2.5 The reviewers may contact the principal investigator with questions about the submitted protocol. In such cases, the principal investigator will have an opportunity to submit revisions before full ESCRO Committee review.
   - 2.6 Reviewers who are absent from a full ESCRO Committee meeting may provide written comments regarding the proposed research, but absent members shall not be counted in the ESCRO Committee vote.

3. Outcome - Studies reviewed by the ESCRO Committee may be approved, approved pending (with non-substantive revisions), deferred, tabled, or disapproved. The minutes for each agenda item will record the number in favor of, opposed to, and abstaining from the action, and those who recused themselves due to a conflict of interest:
   3.1 Approved: No changes are required to the proposed research, which is compliant with the regulatory and ethical guidelines. A majority of members' present must vote in favor of approval;
   3.2 Approved Pending: The proposed research may be granted full approval by the ESCRO Committee Chair pending principal investigator concurrence with specific revisions stipulated by the ESCRO Committee. The research may not receive full approval until such time that the research procedures have been modified to comply with the specific revisions stipulated by the ESCRO Committee and such revisions have been reviewed and approved by the ESCRO Committee Chair or a designee; The results of the review of such materials are recorded in the agenda and minutes for the ESCRO Committee members' information;
   3.3 Deferral: Approval of the proposed research requires substantive clarifications or modifications of the research design or procedures. The principal investigator must respond to the identified clarifications, modifications, or revisions and resubmit the revised research protocol for re-review by the ESCRO committee;
   3.4 Tabled: Full discussion was not able to occur (e.g. quorum was not met, the committee ran out of time, the committee did not have enough information to make a decision, or lack of representation for the study at the convened meeting). Tabled studies are rescheduled for a later meeting; or
   3.5 Disapproval: The proposed research has fundamental design problems and/or presents significant ethical, legal or regulatory compliance concerns. The principal investigator must undertake a major revision of the proposed research before it can be resubmitted for re-review by the ESCRO Committee.
4. The vote of the majority of the ESCRO Committee members present at the meeting shall determine the final determination status (i.e., Approved, approved pending, deferral, tabled, or disapproval) of the proposed research. The Albert Einstein College of Medicine Executive Dean may impose additional restrictions on approved research, but may not approve research for which approval was withheld by the ESCRO Committee.
5. The ESCRO Committee shall notify the investigators in writing of the Committee's decision to approve, defer, or withhold approval of the research, or of the Committee-directed changes required to secure ESCRO Committee approval of the research.

H. Processes for Protocols Following ESCRO Committee Vote

1. Protocols Granted Full Approval

For research granted full approval by the ESCRO Committee, the principal investigator will be notified. The principal investigator shall be responsible for ensuring that all other applicable institutional requirements are met (e.g., IRB, IACUC, IBC, or COI approval).

2. Protocols Approved Subject to Concurrence with ESCRO Committee-Directed Changes

If the convened ESCRO Committee decides to approve the proposed research pending concurrence with ESCRO Committee-directed changes, the principal investigator will be provided:

2.1. Notification addressing the specific revisions stipulated by the ESCRO Committee in order to obtain full approval of the research;
2.2. Notification instructing the investigator to revise the research to concur with the specific revisions stipulated by the ESCRO Committee and to resubmit for full approval; and
2.3. Notification specifying that the principal investigator must respond to the ESCRO Committee's request for revisions within six (6) weeks of the date of the notification, and that failure to respond within this six (6) week period may result in termination of the respective research submission.

For research approved by the ESCRO Committee pending concurrence with ESCRO Committee-directed changes, the revised research submitted in response to the specific revisions stipulated by the ESCRO Committee shall be reviewed by an ESCRO Committee Chair or his/her designee and, based on an appropriate response, granted full approval. Any problems or concerns related to the principal investigator's response shall be communicated, in writing or by e-mail, to the principal investigator. In the event that the principal investigator does not agree with certain specific revisions stipulated by the ESCRO Committee, the research proposal (to include any ESCRO Committee-directed changes agreed on by the principal investigator) and the investigators justification for not complying with certain of the ESCRO Committee-directed change(s) shall be referred to convened meeting review. The investigator shall be notified that s/he will be afforded an opportunity to appear in person at the ESCRO Committee meeting during which the research will be reconsidered.
ESCRO-only studies will have an ESCRO determination in iRIS in which they will also have an annual review, regardless if they are a registration or a full review submission. ESCRO studies that require an IRB determination will have two applications in the iRIS system.

3. Protocols Deferred or Not Approved

If the ESCRO Committee decides to defer or disapprove the proposed research, the principal investigator will be provided, in writing:

3.1. The primary reason(s) for the ESCRO Committee's decision to defer or withhold approval of the research;
3.2. A listing of additional problems or deficiencies identified by the ESCRO Committee;

4. Continuing Oversight
4.1 Approved research shall be reviewed by the ESCRO Committee every year, or more frequently, as determined by the ESCRO Committee on a case-by-case basis. The investigator is responsible for submitting the renewal application in a timely manner as specified by the ESCRO Committee, but no later than 2 weeks prior to the expiration date. Failure to submit the application by the deadline may result in withdrawal of approval.
4.2 Progress Reports and Adverse Event Reports pertaining to ESCRO Committee approved research and submitted to the IRB, IACUC, and/or IBC must also be submitted to the ESCRO Committee. Additionally, reports of adverse or unexpected outcomes that raise new ethical issues with respect to ESCRO Committee approved research shall be submitted to the ESCRO Committee.

4.3 Amendment submissions are required for substantive changes to the protocol during the course of the study. The ESCRO Committee will determine if the amended study continues to meets the definition of not-human subject research and if any further actions to be taken by the principal investigator.

4.4 No modification(s), however minor, to ESCRO Committee approved research shall be implemented prior to ESCRO Committee approval of the modification(s), except when a deviation is necessary to prevent imminent harm. Such deviations should be reported to the ESCRO Committee within 5 business days. The ESCRO Committee has the authority to review and approve, require modifications of, or withhold approval of all proposed modifications to ESCRO Committee approved research prior to the implementation of such modifications.

4.5 The principal investigator must notify the ESCRO Committee upon his/her termination of the ESCRO Committee approved research.

5. Monitoring of ESCRO Committee Approved Research

5.1 The ESCRO Committee or its representatives shall have the authority to observe the conduct of any research activity subject to ESCRO Committee oversight. This function includes the authority to review all records associated with the conduct of the research.

6. Restrictions, Suspension, and Termination of Research

6.1 The ESCRO Committee shall have the authority to place restrictions on research activities that fall under its jurisdiction. The ESCRO Committee will notify other relevant committees (e.g., IRB, IACUC, Institutional Biosafety Committee (IBC), Conflict of Interest (COI)) of any such restrictions.

6.2 The ESCRO Committee shall have the authority to suspend or terminate its approval of research that falls under its jurisdiction and that is not being performed in compliance with ESCRO Committee requirements, applicable governmental regulations, and/or institutional policies. The ESCRO Committee will notify the applicable institutional official(s), as well as other relevant committees (e.g., IRB, IACUC, IBC, COI) of any suspension or termination.

6.3 If an Einstein or MMC researcher is conducting ESCRO related research at any external site under auspices of Einstein/MMC, this research must receive ESCRO review at Einstein/MMC. Any and all Covered Research requires local ESCRO registration or Committee review unless expressly approved otherwise by the Institutional Official (IO). If this happens, the ESCRO Committee reserves the right to terminate the participation of Einstein/MMC researchers if that research is not in compliance with Einstein ESCRO Committee requirements. In such cases, the Einstein ESCRO Committee will inform the responsible institutional official(s) at Einstein and MMC and the relevant official at each institution other than Einstein/MMC involved in the research of the termination. If an Einstein/MMC researcher chooses to rely on another institution's ESCRO Committee, the researcher must seek permission from the Einstein ESCRO Committee in order to so.

7. Review of Research within the Jurisdiction of the ESCRO Committee by Other Committees or Officials

7.1 Research requiring ESCRO Committee review ordinarily will be submitted for review and approval by the ESCRO Committee concurrently with submission of the research to any other entity (e.g., IRB, IACUC, IBC, COI) that may have responsibility for oversight of

other aspects of the research. Note that COI review must occur prior to the review of two separate applications in iRIS for both an IRB and ESCRO determination.

7.2 Research activities approved by the ESCRO Committee may be subject to further review, modification of, approval and/or disapproval by all relevant bodies, such as the IRB, IBC and IACUC. However, those committees and officials may not approve the conduct of research within the ESCRO Committee's jurisdiction if approval was previously withheld by the ESCRO Committee.

8. Principal Investigator Responsibilities

The ESCRO requires that the principal investigator (PI) of an ESCRO application must be a faculty member at Albert Einstein College of Medicine appointed to the ranks of:

- Instructor
- Assistant Professor
- Principal Associate
- Senior Associate
- Associate Professor; or
- Professor

The PI is responsible for conducting Covered Research in compliance with all applicable federal regulations, state and local laws and institutional policies, including the following:

8.1 Obtaining ESCRO/IRB approval (if applicable) or an exempt determination prior to initiating the research, and ceasing all research activities if approval expires before continuing review and approval occur;

8.2 Ensuring that all members of the study team have a) been trained to conduct the study in accordance with the approved protocol, b) if applicable, completed mandatory human research training as required by the Office of Human Research Affairs (“OHRA”),

8.3 Completed all required conflict of interest disclosures in accordance with Einstein and MMC policies on conflicts of interest;

8.4 Obtaining Department/Division approval and applicable ancillary committee approval in accordance with institutional policies;

8.5 Overseeing the conduct of the research, managing data collection to ensure adequate and accurate records, storage, security and backup, and ensuring accurate analysis of study data;

8.6 Ensuring that the research is conducted in accordance with the study’s ESCRO/ IRB-approved protocol, and any conditions that are set in order to receive ESCROIRB approval;

8.7 Obtaining and documenting informed consent (if applicable) in accordance with regulatory and institutional requirements, unless waived by the IRB;

8.8 Delegating responsibilities to qualified study team members that are commensurate with their training and qualification;

8.9 Maintaining documentation for each study in compliance with federal and institutional policy;

8.10 Retaining research records after study completion in compliance with federal and institutional policy.

Exceptions to this requirement may be granted on a case-by-case basis by the Dean's Office at Einstein and/or the Office of Legal Affairs at MMC.

Note: The PI may not be a resident, fellow, postdoctoral, or other trainee. Adjunct and Visiting faculty may serve as a co-PI but not as PI.

The PI must understand the responsibilities associated with conducting all covered research. PIs and co-investigators must comply with applicable federal regulations, state and local laws, institutional policies, and the determinations of the ESCRO. PIs are responsible for training staff and for conducting the research at Einstein/MMC.

I. Committee Meetings

1. The minutes of the ESCRO Committee meetings shall include but not be limited to the following items: record of attendance, declared conflicts of interest, protocols reviewed (including controverted issues), documentation of approval intervals (if applicable), and ESCRO Committee votes. ESCRO Committee meetings may be held by teleconference by which all parties can hear and be heard by persons present.
   1.1 Documentation shall include enumeration of the number of ESCRO Committee members voting for and against the actions taken by the ESCRO Committee and the number of members abstaining from the vote (e.g., 5-for, 1-against, 1-abstain), including the name(s) of any voting member(s) who abstained from the vote due to conflict-of-interest or other considerations.
   1.2 The minutes will be circulated by email after the meeting for review and approval.

J. ESCRO Committee Composition

1. Number & Qualifications

The ESCRO Committee shall comprise at least five (5) voting members, including the Chair, who shall collectively have adequate scientific, medical, and ethical training and experience to promote the appropriate review of research activities pertaining to Covered Research conducted by Einstein/MMC faculty, staff or students, giving due consideration to issues of diversity consistent with applicable law and policy, to include Einstein's Equal Opportunity and Affirmative Action Policy Statement, Einstein's Affirmative Action Program, and Einstein's Diversity and Inclusion Strategic Plan for Excellence.. Of the voting members present at the meeting, one member must be a scientist with relevant expertise and one member must be an ethicist.

2. Alternate Members

The ESCRO Committee may include standing alternate voting members to serve in the absence of regular voting members. Each alternate voting member shall have expertise similar to that of the regular voting member for whom s/he is serving as a replacement. The alternate voting member shall assume all of the responsibilities of the voting member for whom s/he is serving as a replacement. Alternate voting members may attend ESCRO Committee meetings without serving as replacements for a regular voting member; however, in this capacity, alternate members may not vote. If the Chair is absent or recused due

to a conflict of interest, a senior and experienced ESCRO Committee member may be designated to serve as meeting Chair.

3. Consultants

The ESCRO Committee may, at its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the ESCRO Committee. These individuals may not vote with the ESCRO Committee. Consultants shall be asked, at the time they are contacted to review a research study, if they have a conflict of interest with the study on which they are being asked to consult.

K. ESCRO Committee Appointments and Terms

1. Appointment of Chair

The Chair of the ESCRO Committee shall be appointed by and report to the Executive Dean.

2. Appointment of Members

The ESCRO Committee Chair in conjunction with the Director of OHRA shall recommend potential members of the ESCRO Committee to the Executive Dean.

3. Terms of the Members

There are no set term periods for appointments. Appointment may be evaluated periodically and automatically renewed.

L. Management and Responsibilities of the ESCRO Committee

1. General Management

The ESCRO Committee shall be managed as determined by the Executive Dean. The Executive Dean shall ensure that adequate facilities, equipment, and resources are available to support the ESCRO Committee. The Executive Dean shall be responsible for providing an appropriate level of administrative support to the Chair of the ESCRO Committee and the ESCRO Committee members. Management on a day-to-day basis shall be carried out under the direction of the Director of the Office of Human Research Affairs.

2. Overall Responsibilities

The ESCRO Committee shall be responsible for:

2.1 Providing oversight over all issues related to derivation of hES cell lines and all issues related to the use of hES cell lines and/or SCNT in research at Einstein or MMC;
2.2 Review and approve the scientific merit of research protocols;
2.3 Review compliance of all Einstein/MMC hES cell research with all relevant regulations and guidelines;
2.4 Providing consultation to researchers working with all types of HuSCs;
2.5 Maintaining a database of research protocols reviewed;

2.6 Maintaining a registry of all hESC lines that are imported into or maintained at, Einstein or MMC;
2.7 Maintaining a registry of investigators who are conducting hES cell research;
2.8 Auditing ESCRO approved research, and suspending or terminating ESCRO Committee approval of research determined not to be conducted in compliance with applicable federal and state regulations and/or institutional policies;
2.9 Reviewing, on a routine basis, current ESCRO Committee policies, and assuring appropriate revisions to these policies as new, applicable federal and/or state regulations are implemented; and
2.10 Facilitating education of investigators involved in hES cell research.

3. Responsibilities of the Executive Chair and Chair
   3.1 Executive Chair Responsibilities
      3.1.1. In consultation with senior ESCRO Committee members, periodically evaluate committee members and the chairs.
      3.1.2. In consultation with the ESCRO Administrators, periodically evaluate the composition of the ESCRO Committee to maintain appropriate expertise and compliance with applicable regulations, laws, and institutional policies.
      3.1.3. Review reports of research noncompliance. Identify and obtain additional expertise (either on IRB staff or externally) for proper interpretation. Determine appropriate actions, assessment of corrective action plans, and the need for additional follow-up.
      3.1.4. The Executive Chair is a voting member of the ESCRO Committee.
      3.1.5. The Executive Chair has all of the responsibilities of the IRB Chair, as outlined below
   3.2 ESCRO Committee Chair Responsibilities:
      3.2.1 Conducting committee meetings and ensuring the committee complies with all federal regulations.
      3.2.2 Advise on reviewer assignments.
      3.2.3 Serve as a scientific resource to the research community.
      3.2.4 Ensure all regulatory determinations are made for each study during the full board meeting.
      3.2.5 Review, correct, and confirm full board minutes.
      3.2.6 The Chair is a voting member of the ESCRO Committee

4. Responsibilities of the Members

ESCRO Committee members shall

   4.1 Review and evaluate proposed research in a manner that is consistent with the Policies and Procedures of the ESCRO Committee; and
   4.2 Attend convened meetings, participate in deliberations, and vote. Members are expected to attend all meetings and membership may be revoked if a member is unable to attend a sufficient number of meetings.

5. Resignation or Termination of Chairs and Members
    A. Chair

The Executive Dean shall have the authority to terminate the appointment of the ESCRO Committee Chair.

B. Members

ESCRO Committee members may be dismissed by the Executive Dean due to a failure of the Committee member to attend a sufficient number of meetings and/or otherwise actively participate in ESCRO Committee functions.

Resignation of ESCRO Committee membership shall be submitted, in writing, to the Chair of the ESCRO Committee or the Director of the Office of Human Research Affairs.

M. Support for the ESCRO Committee

1. ESCRO Committee Protocol Files and Record Retention

ESCRO Committee staff under the direction of the Office of Human Research Affairs shall maintain records of research submitted for ESCRO Committee review, including records relating to the provenance of all stem cell lines used in research, consent of gamete donors, applicable ethical and research standards, and reports of adverse or unexpected outcomes that pose a threat to the health or safety of any individual or raise new ethical issues. The files shall be maintained for at least six years following the termination of ESCRO Committee approved research and to the extent they are required to be maintained by applicable law or policy, including Einstein's Record Retention Policy.

ESCRO Committee staff shall also maintain ESCRO Committee meeting minutes, a roster of all current ESCRO Committee members, biographical sketches of current ESCRO Committee members, and a record of inquiries submitted to the ESCRO Committee.

2. Database of Submitted Research Protocols and Registry of Human Embryonic Stem Cell Lines

ESCRO Committee staff shall maintain a secure computer database of research submissions.

ESCRO Committee staff shall maintain a registry of all hESC lines maintained at or imported into the institution.

3. Review of Submitted Materials

Applications submitted for ESCRO Committee review shall be screened by ESCRO Committee staff to verify that the submission is complete, and complete applications shall be assigned to a meeting of the ESCRO Committee in as timely a manner as practicable.

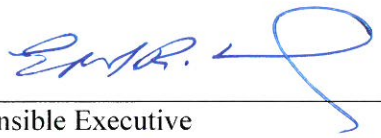
V. Effective Date

Effective as of: April 8, 2021

VI. Policy Management and Responsibilities

Einstein's Office of Human Research Affairs is the Responsible Office under this Policy. The Executive Dean is the Responsible Executive for this Policy. The OHRA Director is the Responsible Officer for the management of this Policy.

VII. Approved (or Revised)



Responsible Executive

April 19, 2021

Date