ALBERT EINSTEIN COLLEGE OF MEDICINE
OF YESHIVA UNIVERSITY
MONTEFIORE MEDICAL CENTER

HUMAN STEM CELL RESEARCH

I. Applicability:
This policy applies to all research on gametes and blastocysts, including human embryonic stem cell research (hESC).

II. Policy:
- A. Montefiore Medical Center and the Albert Einstein College of Medicine believe that human pluripotent or totipotent stem cell research is essential to advancing the development of treatments for many human diseases. Montefiore and AECOM support the use of human embryos and hESCs (human embryonic stem cells) for legitimate research purposes. All research on embryos resulting from in vitro fertilization (IVF) or somatic cell nuclear transfer must be conduced in accordance with the requirements of this policy and applicable federal, state, and local laws, rules, and regulations.
- B. All research utilizing human embryonic stem cells requires review by the Embryonic Stem Cell Research Oversight Committee (ESCRO) (see Embryonic Stem Cell Research Oversight Committee below). The review will ensure that such use is ethical, scientifically sound, and necessary. Submission to both the ESCRO and the CCI/IRB is a requirement for all such research. Other forms of stem cell research using cells that have not been derived from gametes or blastocysts may be referred for ESCRO review on an individual basis as determined by the CCI/IRB.
- C. Researchers collaborating with another institution are required to obtain approval from the other institution's IRB, as well as the CCI/IRB, before the research can proceed.

III. CCI/IRB Approval
- A. In vitro research and laboratory animal research utilizing embryos or hESC lines where the source (donor) cannot be identified by the investigator does not constitute human subjects research and does not require CCI/IRB approval and monitoring. Such protocols must be submitted to the CCI/IRB to document the exempt status.
- B. Research involving embryos or hESC lines where the source (donor) may be identified by the investigator, including cell lines that retain links to identifiable information, is considered to be human subjects research that requires CCI/IRB review. Research involving embryos or hESC lines where there is interaction or intervention with a human subject, and/or information about such subject or tissue from such subject is obtained, is human subject research that requires CCI/IRB approval and monitoring.
- C. All use of embryos and/or hESCs, for transplantation into humans requires full CCI/IRB approval and monitoring.

IV. Informed Consent from the donor(s)
- A. Informed consent shall be required for any research use of gametes or blastocysts. Donors of both ova and sperm must give explicit consent. Blastocysts derived using anonymous donors cannot be utilized unless specific consent for research is obtained.

B. Preliminary consent for the research use of blastocysts derived from IVF is obtained at the same time consent is obtained for the freezing of extra blastocysts. This is at a later date from the original consent for the IVF procedure.
C. In cases in which the preliminary consent did not contain the requirements of this policy, additional, specific informed consent must be obtained at the time of donation for research use, even if prior indication of their intent to donate to research has been given. Donors should be informed that they retain the right to withdraw consent until the blastocysts are sent to the investigator for use in an experiment.
D. The informed consent document should, at a minimum, provide the following information:
    1. The gametes or blastocysts or will be used for research, including derivation of human embryonic stem cells (hESC) that may include research on human transplantation
    2. Donation is made without any restriction or direction regarding who may be the recipient of transplants of the cells derived, except in the case of autologous donation.
    3. Whether or not the identities of the donors will be readily ascertainable to those who derive or work with the resulting stem cell lines. If the identities of the donors are retained (even if coded), whether donors wish to be contacted in the future to receive information obtained through studies of the cell lines.
    4. Assurance that investigators and others involved in research projects will follow applicable and appropriate best practices for donation, procurement, culture, and storage of cells and tissues to ensure, in particular, the traceability of stem cells. (Traceable information, however, must be secured to ensure confidentiality.)
    5. Derived pluripotent and totipotent stem cells and/or cell lines might be kept for many years.
    6. The pluripotent and totipotent stem cells and/or cell lines might be used in research involving genetic manipulation of the cells or the mixing of human and non-human cells in animal models.
    7. The possibility that the results of study of the stem cells may have commercial potential and that the donor will not receive financial or any other benefits from any future commercial development.
    8. The research is not intended to provide direct medical benefit to the donor(s) except in the case of autologous donation.
    9. Embryos will be destroyed in the process of deriving hESC.
    10. Neither consenting nor refusing to donate blastocysts for research will affect the quality of any future care provided to potential donors.
    11. A statement of the risks involved to the donors.
    12. (In addition, donors can be offered the option of agreeing to some forms of stem cell research but not others.)

V. Embryo Procurement from Montefiore
A. With the exception of genetically abnormal embryos procured prior to cryopreservation following PGD, only cryopreserved embryos and not fresh embryos may be utilized for research.
B. All embryos must be created for implantation into either the donor/recipient or another recipient for the sole purpose of creating a pregnancy. No embryos are or may be created for research purposes. Embryos for research may be secured from

the Institute for Reproductive Medicine and Health only when no longer needed by the donors to create a pregnancy.

C. Embryos may not be purchased, and there may be no financial inducements for donation of the embryos.
D. Montefiore may charge the researchers reasonable costs of handling, transportation, processing, preservation, storage and quality control of embryos.
E. Privacy and confidentiality must be afforded to all donors.
F. Embryos from Montefiore may only be transferred for research pursuant to a protocol for embryo research banking that has been approved by Montefiore's IRB.
G. Embryos from Montefiore may only be transferred after execution of a material transfer agreement in a form acceptable to Montefiore's Office of Legal Affairs.
H. Researchers who obtain embryos from the Montefiore Institute for Reproductive Medicine and Health or any other site are prohibited from sharing the materials with others.

VI. Monetary Payments and Other Inducements

A. Monetary payment or other inducements to the donors of gametes or blastocysts for the use in research is prohibited.
B. Although selling of gametes and blastocysts is prohibited, their use for commercial purposes is permissible in some circumstances with CCI/IRB approval.
C. Through the informed consent process and documentation, the donors must be given the right to choose whether or not the cells can be used for unknown future research, including possible commercial purposes.

VII. Financial Support for Human Embryo and/or hESC Research

A. Except as set forth below, federal funds may not be used for: (i) the creation of a human embryo for research purposes, or (b) research in which a human embryo is destroyed, discarded, or knowingly subjected to greater than minimal risk, as determined by the CCI/IRB.
B. Research involving human pluripotent or totipotent stem cells derived from human embryos may be conducted with federal support. only if such cells are derived from cell lines meeting NIH criteria and listed on the NIH Human Embryonic Stem Cell Registry (see http://escr/nih.gov.)
C. Research involving the derivation of new human embryonic stem cell lines or the use of human embryonic stem cell lines that are not listed on the NIH Registry may not be conducted with federal support.
D. Research in accordance with this policy involving human embryos or hESC may be conducted with non-federal funding.
E. Current federal policy requires institutions to keep careful records so as to prevent federal funds from directly or indirectly supporting hESC research that is ineligible for federal support. Direct costs associated with a protocol approved by ESCRO and, if applicable, CCI/IRB must have in place a method of separating the costs of supporting the research so that any of the facilities and administrative (F & A) costs allocable to the ineligible research are excluded from the rates established and used to charge F & A costs to federally funded research. In addition, the principal investigator and the responsible departmental administrator must carefully and consistently allocate all costs of the ineligible research to a non-federal funding source.

VIII. Conflicts of Interest

A. The institutional Policy on Disclosing Conflicts of Interest shall apply to all research subject to ESCRO review.

EMBRYONIC STEM CELL RESEARCH OVERSIGHT COMMITTEE

To provide local oversight of all issues related to derivation and research use of human embryonic stem cells and to facilitate education of investigators involved in hESC stem cell research, AECOM/MMC has established an Embryonic Stem Cell Research Oversight Committee (ESCRO). The committee includes representatives of the public and persons with expertise in developmental biology, stem cell research, molecular biology, assisted reproduction, and ethical and legal issues in stem cell research. The committee does not substitute for the CCI/IRB review but rather provides an additional level of review and scrutiny warranted by the complex issues raised by stem cell research. ESCRO will also review human embryonic stem cell research using pre-existing anonymous cell lines that does not require monitoring by the CCI/IRB (Exempt Research).

I. ESCRO Policies and Procedures

1.0. Purpose

The purpose of the ESCRO Committee is to provide oversight of human embryonic stem cell research conducted at AECOM/MMC, in order to ensure that this research meets the highest scientific and ethical standards. The goals are achieved in collaboration with the CCI/IRB, other applicable compliance committees, and the participation of the research community.

2.0 Authority

AECOM/MMC policy requires the creation of an ESCRO to oversee hESC research. The policy is based on the recommendation of the National Academies of Science-Institute of Medicine Guidelines.

3.0 Function

The ESCRO reviews new protocols, modifications to currently approved research, and continuing research using hESCs or hESC lines and any proposed collection and use of germ cells designed to generate hESCs that are capable of differentiation along multiple cell lineages. Adult precursors that differentiate into cells of a single tissue type do not meet this criterion and would not be subject to ESCRO review.

4.0 Review

The ESCRO is one of several committees that may be required to review stem cell research. The other committees include but are not limited to the CCI/IRB, the Animal Research Committee (ARC), the Institutional Biosafety Committee (IBC), and other committees required by laws, regulations, or institutional policy.

4.1 Review Procedures

The ESCRO will assess protocols according to the ESCRO Review Standard Operating Procedures.

4.2 Scope of review and responsibilities

4.2.1 All issues related to derivation, use, procurement, and disposal of hESCs.

4.2.2 Scientific merit, including whether the cells are well-characterized and screened for safety

4.2.3 Ensure that the conditions under which cells are maintained and stored meet current scientific standards

4.2.4 For research that does not involve human subjects as defined by Federal regulations or State law, ensure that the cells were obtained ethically and with informed consent as required by law or policy

4.2.5 Compliance with relevant regulations and guidelines

4.2.6 Consultation and collaboration with the CCI/IRB and other relevant compliance committees

4.2.7 Maintain registry of hESCs and lines derived or obtained by investigators

4.2.8 Maintain registry of hESC research

4.2.9 Adverse Events

4.2.10 Monitoring

4.2.11 Suspension and Termination

4.2.12 Maintenance of records

4.2.13 Education

4.3 Approval

The ESCRO has the authority to approve, require modifications in a protocol in order to approve, or disapprove submitted research. The ESCRO will notify investigators in writing in a timely fashion of its decision. An ESCRO decision to require modifications or disapprove a submission will include a written statement to the investigator of the reasons for its decision and give the investigator an opportunity to respond in writing and, if requested, in-person.

4.4 Modifications to Approved Protocols

All modifications to approved protocols must be submitted prospectively to the ESCRO. No modifications may be implemented without prospective review and approval by the ESCRO and other applicable committees.

4.5 Continuing Review

The ESCRO will review on-going research at a minimum of once every year.

4.6 Appeals

Appeals of ESCRO decisions must return to the ESCRO for additional review. Investigators may request to present responses to ESCRO decisions during a convened meeting. Appeals must be in

writing and submitted directly to the ESCRO prior to an investigator's personal presentation to the ESCRO.

4.7 Exceptions to Full Committee Review

The ESCRO Chair or other qualified member of the committee has the authority to review (1) new protocols that involve in vitro research and utilize embryos or hESC lines where the source (donors) cannot be identified by the investigator (designated exempt research) and (2) modifications to currently approved protocols when the proposed changes are minor and do not modify the scientific design of the protocol, such as changes in investigators, replacement of equivalent proven laboratory techniques, laboratory relocation, etc.

4.7.1 Limits to Review Decisions

The ESCRO member conducting the review has the authority (1) to determine Exempt Status or (2) to approve or recommend modifications to the submission in order to achieve approval. The review may not be used to disapprove the submission, which requires a convened meeting of the ESCRO.

4.7.2 Reporting to the ESCRO

The ESCRO will be provided with a short description of all Exempt protocols and modifications of approved protocols.

4.8 Monitoring

The ESCRO has the authority to observe, monitor, and, audit research under its jurisdiction. ESCRO may appoint a third party for this purpose.

4.9 Adverse Events

Adverse events may occur with human subjects, employees, or cellular material. Any adverse events that occur with human subjects that by CCI/IRB policy require reporting to the CCI/IRB must also be reported to the ESCRO.

4.9.1 Required Reporting of Events with Employees

Any adverse events to employees that would be reported to the IBC/Environmental, Health, and Safety, must also be reported to the ESCRO.

4.9.2 Required Reporting of Adverse Laboratory Events

The investigator is responsible for documenting and reporting to the ESCRO laboratory events such as, but not limited to, the inability to expand cells due to contamination. Such reports should include the reason for the contamination, the disposition of the cells, and any corrective action.

4.10 Collaboration with the CCI/IRB

The ESCRO will collaborate with the CCI/IRB in order to ensure approved research meets the highest scientific and ethical standards. ESCRO approvals will be contingent upon CCI/IRB

approval of proposed research. ESCRO review will occur prior to CCI/IRB review and serve to inform the CCI/IRB review. ESCRO members are available to attend CCI/IRB meetings to discuss proposed research, as requested by the CCI/IRB. The CCI/IRB and ESCRO will freely exchange information in order to facilitate and coordinate the review of proposed research.

4.11 Suspension and Termination of ESCRO Approval

The ESCRO has the authority to suspend or terminate its approval of research that is not being conducted in accordance with the ESCRO's requirements, regulatory agency requirements, or that has been associated with unexpected serious harm to subjects, or others. Suspension or termination will be promptly reported to other applicable AECOM/MMC compliance committees, and the chair of the investigator's department.

5.0 Structure

The ESCRO shall consist of a minimum of seven members, including the Chair, appointed by the Dean or Executive Dean of AECOM and the President or designee of Montefiore. A majority of the voting members must have expertise in relevant scientific and/or medical fields, including molecular biology, developmental biology, stem cell research, assisted reproduction, legal issues and ethical issues re hESC research, as well as a non-scientific member who is not affiliated with AECOM or MMC.
There may be alternates and non-voting members.

5.1 Consultants

The ESCRO 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. These individuals may not vote with the ESCRO.

5.2 Ad Hoc Committees

The ESCRO may, as necessary, create standing ad hoc subcommittees, composed of members of the parent Committee and, as appropriate, consultants with relevant expertise to perform specific functions within the ESCRO's jurisdiction. Subcommittee members may serve as a voting member on more than one subcommittee.

5.3 Membership Terms

Members shall be appointed by the Dean or Executive Dean to serve for overlapping terms of five years and may be reappointed.

5.4 Support

Management and support services will be provided by the CCI/IRB Office.

6.0 Meetings

Meetings shall be held as often as necessary to provide timely review of submitted research. Meetings shall be conducted, and records of the proceedings kept, as indicated in other sections of this policy.

6.1 Quorum

The ESCRO may only review and act upon proposed research during a convened meeting with a majority of the members present. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.

6.2 Conflict of Interest

No member may participate in the ESCRO's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the ESCRO. Members with a conflict of interest must be recused from the discussion and the vote of the protocol except to answer questions of the Committee about the proposed research.

7.0 ESCRO Meeting Documentation

The ESCRO shall maintain documentation sufficient to meet the requirements of this policy.

7.1 Research and Cell Registries

The ESCRO will maintain an auditable database of:

a. hESC research conducted by CCI/IRB investigators
b. hESCs and cell lines derived or obtained by CCI/IRB investigators

7.2 Meeting Documentation

The ESCRO will maintain minutes of the meetings and relevant correspondence with investigators, including approvals and disapprovals. The Minutes shall be in sufficient detail to show:

1. attendance at the meetings;
2. actions taken by the ESCRO;
3. the vote on these actions, including the number of members recused, voting for, voting against, and abstaining;
4. the basis for requiring changes in or disapproving research; and
5. a written summary of the discussion of controversial issues and their resolution.

7.3 Documentation Maintenance

The ESCRO will maintain copies of reviewed proposals, reports of adverse events, progress reports, continuing review applications, correspondence with investigators, CCI/IRB and other applicable compliance committee approvals, and a list of ESCRO members.

7.4 Documentation Retention

The ESCRO will maintain related records for at least 10 years, and records relating to research that is conducted shall be retained for at least 10 years after completion of the research.