

APPENDIX A-2
Empire State Stem Cell Board
Contract Policy Statements and Conditions
Rev. approved 4/08

A. Ethical Considerations

The Empire State Stem Cell Board (ESSCB) stipulates that each awarded grant contract satisfy the following requirements:

In accepting an award from the New York State Department of Health for support from the Empire State Stem Cell Fund, the contracting organization shall ensure that each project investigator agrees to conform strictly to the codes of practice, regulations and laws governing ethical conduct of scientific research in his/her own laboratory/institution. He/she shall be solely responsible for any violation of these standards. If experimental procedures conducted pursuant to this project are performed in another state or country, either directly by the Principal Investigator (PI) and any co-investigators, or in collaboration with other persons, the PI and contracting organization shall ensure that such research complies with New York State laws and regulations that would be applicable to such research if performed in New York State. Representatives of the contracting organization will inform NYSTEM program administrators of any and all instances of actual or potential lapses in scientific integrity by any project participant as soon as this information becomes known to the contracting entity. The contracting organization is fully responsible for investigation of these instances.

B. Human Subjects Research

Human subjects research is essential to the continued advancement of scientific knowledge concerning stem cell biology. In carrying out such research, the rights and welfare of all individual research participants are of critical importance. Furthermore, additional safeguards must protect especially vulnerable research subjects, including minors, mentally disabled adults who lack capacity to provide informed consent to research participation, and prisoners.

Accordingly, no research study shall be approved for funding recommendation by ESSCB unless it is demonstrated that all the following requirements are satisfied:

- The research study will comply with New York State Public Health Law (PHL) Article 24-A, Sections 2440 to 2446, unless the research is subject to, and in compliance with, policies and regulations promulgated by any agency of the federal government for the protection of human subjects.
- The research study will comply with 45 CFR Part 46 (unless exempt from the requirements of this Part) and, if applicable, 21 CFR Parts 50 and 56; 21 CFR 312; 21CFR 361; 21 CRF 812.
- The research study will comply with all other applicable federal and New York State laws, regulations and guidelines.
- The research study has been approved by an Institutional Review Board (IRB).

- If applicable, the applicant organization's IRB has received, reviewed, and accepted written approval from an authorized representative of each site where the study will take place.
- The IRB has determined that the investigator will immediately withdraw a subject from the research study if continued participation would be detrimental to the subject's well-being.
- The IRB will communicate to NYSTEM program administrators (i) any unanticipated problems involving risks to subjects, (ii) any serious or continuing noncompliance with IRB policy or requirements; and (iii) any suspension or termination of IRB approval of the research study.

Vulnerable Populations

Under Article 24-A of the New York State Public Health Law, research which has no prospect of providing direct benefit and posing more than minimal risk to research participants is prohibited for research participants who are minors, mentally disabled adults who lack capacity to provide informed consent to research participation, or prisoners. No research study in which any research participant is a minor, a mentally disabled adult who lacks capacity to provide informed consent to research participation or a prisoner shall be approved by ESSCB unless it is demonstrated to the Board, and the Board determines, that **all** the following requirements, in addition to the requirements set forth above, are satisfied:

- The IRB has determined that the research study constitutes either: research with a prospect of direct benefit to research participants; or research with no prospect of direct benefit to research participants that presents minimal risk.
- If the research involves one or more mentally disabled adult, each investigator must use IRB approved methodologies and procedures for initial capacity assessment of those individuals, including: procedures for notice to a prospective subject that his/her capacity to consent to research is under consideration; notice to a prospective subject of a determination that he/she lacks the capacity to consent to research; and the opportunity for a prospective subject to contest such a determination of incapacity through a second opinion and a judicial proceeding prior to enrollment in the research.
- The IRB has determined that, prior to involving in a research study a minor, a mentally disabled adult who lacks the capacity to provide informed consent to research participation, or a prisoner, each investigator will obtain such individual's assent to research participation.¹

The Department of Health reserves the right to revise or expand requirements applicable to human subjects research as part of negotiation of any contract arising from this request for applications.

¹ A minor's objection need not be honored if an independent physician determines that the research intervention or procedure holds out a prospect of direct benefit that is important to the health or well-being of the minor, and is available only within the context of the research.

C. Animal Use

ESSCB requires that all individuals and institutions that conduct research using animals supported by the Empire State Stem Cell Fund adhere to all federal, state and local laws pertaining to humane care and use of animals for research purposes. Research applications submitted to the Board for consideration must have been reviewed and approved by an Institutional Animal Care and Use Committee (IACUC) whose guidelines are in compliance with the U.S. Public Health Service's *Policy on Humane Care and Use of Laboratory Animals*, and *Guide for the Care and Use of Laboratory Animals*, as well as any other federal, state and local laws or regulations (e.g., the federal Animal Welfare Act and its implementing regulations; and PHL Article 5, Title I, Sections 504 and 505-a).

D. Tissue

ESSCB will support research using human tissue and require that such research adhere to all federal, state and local laws and regulations pertaining to use of such tissue, including, but not limited to, 42 USC Section 289g et seq.; Public Health Law Article 5, Title V, sections 570 to 581; Article 24-A, sections 2440 to 2446; Article 43, sections 4301 to 4309; Article 43-B, sections 4360 to 4366; and 10 NYCRR Part 52.

E. Human Embryonic Stem Cell Research

1. *Scope.* The following types of research ("Human Stem Cell Research" or "HSC Research") are subject to the requirements of this section.

Research involving:

- a) human embryonic stem cells;
 - b) human totipotent or pluripotent cells;
 - c) human pluripotent stem cell lines;
 - d) human neural and gonadal progenitor stem cells; or
 - e) other human somatic tissues for stem cell research (excluding cells that remain restricted in tissue potential and are not known to possess totipotent or pluripotent potential).
2. *National Academy of Science (NAS) and International Society of Stem Cell Research (ISSCR) Guidelines.* HSC Research must comply with either NAS or ISSCR Guidelines to the extent applicable, and must also comply with any additional or conflicting requirements of this Contract.

3. *Embryonic Stem Cell Research Oversight (ESCRO) Committees.*
- a) HSC Research must be approved by an Embryonic Stem Cell Research Oversight (ESCRO) Committee that meets the standards set forth in the NAS or ISSCR Guidelines and in paragraph (d) below. However, research permissible without ESCRO Committee review under Category 1 of the ISSCR Guidelines or Section 1.2 (a) of the NAS Guidelines shall not require ESCRO review if notification is provided to the ESCRO Committee.¹
 - b) The ESCRO Committee shall be responsible for the initial and ongoing review and oversight of the research at the institution where the research is being conducted.
 - c) The ESCRO Committee shall ensure that research complies with either NAS or ISSCR Guidelines to the extent such Guidelines are applicable, and also complies with any additional or conflicting requirements of this Contract.
 - d) The ESCRO Committee shall create and follow written policies that include the following standards:
 - i) Committee Membership: The membership of the ESCRO Committee responsible for oversight for the contracting institution should have sufficient diversity among its members, including consideration of race, gender and background, and should be sensitive to such issues as community attitudes, to promote respect for its advice and counsel. The ESCRO Committee should be composed of qualified persons of both sexes. The members present at a meeting in which research funded under this contract is approved by the ESCRO Committee must include at least one scientist with relevant expertise and one ethicist. The purpose of diverse membership on the ESCRO Committee is to ensure that different perspectives are given a voice; the ESCRO Committee should encourage different perspectives and voices in its discussion of protocols and in its minutes.

² Category 1 of the ISSCR Guidelines (section 10.1) provides: "Experiments that are permissible after review under existing mandates and by existing local committees, and are determined to be exempt from full SCRO review. These will include experiments with pre-existing human embryonic stem cell lines that are confined to cell culture or involve routine and standard research practice, such as assays of teratoma formation in immune-deficient mice. We recommend that all institutions pursuing such research establish a mechanism capable of determining that a) these projects can be adequately reviewed by committees with jurisdiction over research on human tissues, animals, biosafety, radiation, etc. and b) that full review by a SCRO mechanism or body is not required. This mechanism should include a determination that the provenance of the human embryonic stem cell lines to be used has been scrutinized and deemed acceptable according to the principles outlined in this document, and that such research is in compliance with scientific, legal and ethical norms."

Section 1.2(a) of the NAS Guidelines provides: "Purely in vitro hES cell research that uses previously derived hES cell lines is permissible provided that the ESCRO committee or equivalent body designated by the investigator's institution (see Section 2.0) receives documentation of the provenance of the cell lines including (i) documentation of the use of an acceptable informed consent process that was approved by an Institutional Review Board (IRB) or foreign equivalent for their derivation (consistent with Section 3.6); and (ii) documentation of compliance with any additional required review by an Institutional Animal Care and Use Committee (IACUC), Institutional Biosafety Committee (IBC), or other institutionally mandated review."

- ii) Conflict of Interest Policies: The policies shall address conflicts of interest in a manner that is in alignment with other institutional conflict of interest policies, including, but not limited to, those governing the activities of the IRB. Such policies shall preclude a member from participating in the initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the ESCRO Committee.
- iii) Recordkeeping: The policies shall address recordkeeping requirements for the activities of the ESCRO Committee and for research reviewed by the Committee that are in alignment with the policies developed by the institution's IRB in accordance with the requirements of 45 CFR Part 46 and guidance issued by the Office for Human Research Protections. In addition, the ESCRO Committee shall develop and adhere to policies for maintaining records relating to the provenance of all stem cell lines used in funded research, consent of gamete donors, applicable ethical 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. Records relating to the activities and review of the ESCRO Committee and to the research conducted shall be retained for at least six years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the Department of Health at reasonable times and in a reasonable manner.

- 4. *Consent to Donation*: Consent to donate gametes or embryos to research must be obtained prior to donation. With respect to obtaining re-consent from gamete or embryo donors immediately prior to donation to research, the ESCRO Committee should apply the standards set forth in ISSCR Guidelines 11.2, but may choose to use the stricter NAS Guidelines.
- 5. *Payment*: The ESCRO Committee should review information, where available, regarding the payment of donors who produced gametes originally for reproductive purposes to ensure compliance with the ISSCR Guidelines 11.5(a). Where no such information is reasonably available, the ESCRO Committee need not ensure that payment history complies with either NAS or ISSCR Guidelines.

F. Publication and Intellectual Property Rights

- 1. It is ESSCB's intent that the results of research it supports through its sponsorship be disseminated and made easily available to the research community and the lay public. Manuscript submission for publication of research funded by the Fund shall not be delayed by investigators or their research institutions for more than 60 days after the manuscript is completed. Research results are to be submitted promptly for publication in internationally recognized scientific journals. Publication should not be delayed for commercial or other reasons beyond the editorial period needed to ensure scientific accuracy and presentation.

- a. All publications reporting research supported by NYSTEM funds published in peer reviewed journals must be deposited in the National Institutes of Health National Library of Medicine's PubMed Central (PMC). NYSTEM encourages investigators to sign copyright agreements that specifically allow the published manuscript to be deposited for public posting on PMC. As investigators are encouraged to publish NYSTEM-funded research findings as "open access" publications, contract funds may be used to cover costs required for such "open access" publication.
 - b. An electronic copy of each such publication must be filed with the progress report pursuant to the contract.
 - c. Within 60 days of publication, the investigator must submit to NYSTEM program administrators a 500 word abstract of the publication suitable for the general public, highlighting the research findings. A full literature citation and a brief biographical sketch of the NYSTEM-funded Principal Investigator must also be submitted. This information will be made available to the public through the NYSTEM website.
 - d. Support by the Empire State Stem Cell Fund shall be acknowledged in all publications, presentations and products of research in a form consistent with the publication's guidelines, e.g.,: "supported by the Empire State Stem Cell Fund through New York State Department of Health Contract # <<>>. Opinions expressed here are solely those of the author and do not necessarily reflect those of the Empire State Stem Cell Board, the New York State Department of Health, or the State of New York."
2. It is ESSCB's intent that the resources, materials and methods created through its sponsorship be disseminated and made easily available to the research community. All such materials described in invention disclosures, publications, or other public forums shall be made available to requesting investigators. The contractor may collect reasonable costs for provision of such resources and may require execution of appropriate material transfer agreements, licenses, or confidentiality agreements (see paragraph #4, below).
3. With regard to ESSCB funded research, where the grantee organization has not made reasonable efforts to protect the property interests or because the grantee has failed to share the research developments, the State shall retain march-in rights. The State shall have the right to a perpetual royalty-free, non-exclusive and irrevocable right to reproduce, publish or otherwise use, and to authorize others to use, for research and governmental purposes only, any published or otherwise reproducible material, device, invention, technique, material, or methodology developed under or in the course of performing this funded research, dealing with any aspect of the research activity, or of the results and accomplishments attained from the research.
4. The contractor must have written agreements with researchers requiring prompt disclosure of inventions made in the performance of ESSCB-funded research. Within 60 days of such disclosure the contractor shall notify NYSTEM of the invention disclosure. The contractor shall notify NYSTEM upon the filing of any patent application in the progress report pursuant to the contract. The contractor shall provide NYSTEM with advance written notice of any assignment or transfer of intellectual property rights generated as a result of research supported by the Fund. Any such assignment or transfer must acknowledge, and be subject to the rights retained by the State pursuant to the above paragraph #2.

Assignment and ownership allocation of intellectual and industrial property rights generated from research supported by the Fund is to be determined by the parties concerned (researchers, and their research organizations or institutions), consistent with organizational policies. Prior to execution of a negotiated contract, appropriate arrangements (existing or proposed) regarding intellectual and industrial property rights must be made by the contracting organization and communicated to NYSTEM program administrators. Such arrangements may include: provisions about dissemination of information such as disclosure and methods of publication, and provisions regarding ownership and exploitation of the results arising from the research supported by the Fund. However, to protect the State's interests and to streamline invention reporting procedures, contracts between the New York State Department of Health and the contracting institution will, except to the extent inconsistent with this paragraph, incorporate the provisions of 37 CFR 401.14 with the following modifications throughout: *Federal or Government* will refer to New York State, and *agency* will refer to the Department of Health.

5. Contractor agrees, pursuant to the provisions of the New York State Administrative Procedure Act relating to access to data, added by Chapter 647 of the Laws of 1999, and Chapter 229 of the Laws of 2000, to provide the Department with the study, any data supporting that study, and the identity of the principal person or persons who performed such study. If such study is used as the basis for the promulgation, amendment, or repeal of a rule, regulation, or guideline used in enforcement of a statute, rule, or regulation, the study, any data supporting that study, and the identity of the principal person or persons who performed the study shall be subject to disclosure in accordance with the law.

G. Reporting Requirements

Scientific/Technical and Financial Reports shall be submitted as provided in Appendix C.

H. Equipment

Equipment may not be purchased within ninety (90) days of contract termination.

Upon satisfactory completion of the contract, as determined by the State Department of Health, all equipment purchased hereunder may be retained by the contractor.

I. Other Information

1. Documents submitted to the Department of Health on behalf of NYSTEM will not be returned to the applicant.
2. Appendix B (Budget) may be reviewed and revised each year, depending on research progress and the availability of funds.
3. The New York State Department of Health may require reimbursement of all or a part of the award if ineligible expenses have been incurred or inaccurate accounting statements have been submitted.

4. Neither the Department of Health nor the State of New York will assume any responsibility for any damage or injuries caused or resulting from research conducted with the financial support of the Fund.
5. Recipient entities accept auditing of their contract expenditures by an appointed representative of NYSTEM at any reasonable time.
6. Assurances and Certifications. The New York State ESSCB has adopted the following federal regulatory mechanisms to ensure responsible administration of its awards and to preserve the integrity of the research enterprise it supports. By signing this Grant Contract, the authorized representative of the organization certifies that, in addition to all applicable state and local statutes and regulations, the applicant organization will comply with applicable federal regulations and statutes, including but not limited to:
 - a. *Vertebrate Animals:*
 - Animal Welfare Act as amended (7 USC 2131 et sec.), if applicable, and other federal statutes and regulations relating to animal care and use.
 - b. *Research Misconduct:*
 - 42 CFR Part 50, Subpart A, "Responsibilities for PHS awardees and applicant institutions for dealing with and reporting possible misconduct in science."
 - 42 CFR 94, "Public Health Service standards for the protection of research misconduct whistleblowers" (effective on the date set forth in the final rule).
 - Each covered institution must certify that it will comply with the above policies and the requirements of the Final Rule.
 - A copy of the institution's Annual Report on Possible Research Misconduct (Form 6349), routinely sent to all PHS awardees by the Office of Research Integrity, shall be forwarded to NYSTEM program administrators.
 - c. *Conflict of Interest*
 - 42 CFR 50, Subpart F, "Responsibility of applicants for promoting objectivity in research for which PHS funding is sought."
7. The Department of Health reserves the right to revise or expand the requirements applicable to research conduct, as well as legal and administrative oversight.