

# **Human Embryonic Stem Cell and covered Human Pluripotent Stem Cell Research Operating Procedures**

*Tutorial for NYULMC  
Researchers*

# About this tutorial

## Tutorial Topics

- Impact of federal and state funding issues on administration of hESC research
- Human Embryonic Stem Cell and covered Human Pluripotent Stem Cell Research Operating Procedures for:
  - human subjects
  - material transfer agreements
  - accounting
  - effort allocation and certification
  - facilities
  - equipment
  - expendable materials and supplies
  - derivatives
  - research data and intellectual property
- **Intended Audience** This tutorial is intended for NYULMC personnel, including faculty, staff, postdoctoral scholars, and students, as well as visiting scholars and other researchers, who will be working on research projects involving human embryonic stem cells and certain categories of work involving human pluripotent stem cells (hPSC)
- **Required Training** All personnel must complete this tutorial satisfactorily as a prerequisite to beginning research associated with human embryonic stem cells and certain categories of hPSC. It is the PI's responsibility to ensure that personnel complete the appropriate tutorial(s).
- **Grant/Award Setup** The PI must coordinate with Research Finance or Sponsored Programs Administration to identify or establish an account/award for funding the research.
- **Committee Approvals** All appropriate oversight committee approvals, e.g., IRB, IACUC, IBC, or RSC, and ESCRO, must be received before the hESC or hPSC research may be initiated.

\*Tutorial was based on the Tri-Institutional Tutorial for Human Embryonic & covered Human Pluripotent Stem Cell Researchers at Memorial Sloan-Kettering Cancer Center, The Rockefeller University and Will Cornell Medical College

# Terms & Acronyms

Frequently used terms & acronyms throughout this tutorial and the ESCRO Committee's policy:

**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 totipotent.

**Blastocyst** means a pre-implantation human embryo of about 150 to 250 cells produced by 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.

# Terms & Acronyms

**“ESCRO Committee”** means NYULMC’s Embryonic Stem Cell Research Oversight Committee, established by the Senior Vice President and Vice Dean for Science of NYULMC.

**“ESCRO registration”** means the registration of hPSC research as described in Section V(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 to develop into cells and tissues of the three primary germ layers (endoderm, ectoderm and mesoderm). These human embryos include those generated by fertilization, parthenogenic activation or somatic cell nuclear transfer.

**“hESC line”** means a stem cell line consisting of hESCs.

**“hESC research”** means research involving either the use or the creation of hESCs.

**“iPSC(s)”** means hPSCs 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.

# Terms & Acronyms

**“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 research”** means research involving hESC(s), human embryonic germ cells, hPSC(s), and/or human adult stem cells.

**“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).

An **“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.

# Terms & Acronyms

**“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.

An **“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).

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

# Terms & Acronyms

“**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 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).

# The Dickey Amendment & Derivation of hESC Lines

- The Dickey Amendment bans federal funding for any research in which embryos are destroyed, discarded or knowingly subjected to risk of injury.
- Research to derive new stem cells from human embryos may not be done with federal funds.
- Derivation of new hESC lines from embryos created either for reproductive purposes or research may be done with non-federal funds.



# Federal Directive Impacts Federal Funding for hESC Research

- Executive Order 13505: *Removing Barriers to Responsible Scientific Research Involving Human Stem Cells* issued March 9, 2009.
- [The NIH Guidelines for Human Stem Cell Research](#) issued July 7, 2009, implement Executive Order 13505 as it pertains to extramural NIH-funded stem cell research and establish policy and procedures under which the NIH will fund research involving human stem cells.
- Under these NIH Guidelines, the NIH established a [new Registry listing hESCs eligible for use in NIH funded research](#).
  - Federally funded hESC research may be conducted using hESC lines that are on the NIH Registry or for which assurance and documentation of compliance with the NIH criteria for appropriate provenance has been accepted by the NIH. Once accepted, the NIH will add the line to the Registry.
  - To be eligible for use in NIH funded research, the hESC line must have been derived from a donated embryo that was originally created for reproductive purposes and was subsequently determined no longer to be required for reproductive purposes.
- Under these NIH Guidelines, hESC lines are characterized as:
  - **Registry hESC Lines**  
Federal funds may be used ONLY for research using Registry hESC lines.
  - **Non-Registry hESC Lines**  
Federal funds may not be used directly or indirectly for research using non-Registry hESC lines (or their derivatives).
- Non-Registry hESC Research Can Proceed with Private Funds  
Although the NIH Guidelines bar the use of federal funds for research on non-Registry hESC lines, they do not prevent investigators from conducting such research with non-federal funds.

# New York State Regulations and Guidelines for State-funded hESC/hPSC Research

- Monies from the NYS Empire State Stem Cell Trust Fund may be used to support derivation of hESC from embryos generated either for reproductive or research purposes as well as research using hESC and other human pluripotent stem cells.
- New York State law specifically prohibits use of Fund monies for research involving human reproductive cloning.
- NYS requires ESCRO review for any state-funded research involving:
  - human embryonic stem cells
  - human totipotent or pluripotent cells and cell lines
  - human neural and gonadal progenitor stem cells
  - other human somatic tissues for stem cell research (excluding cells that remain restricted in potential and are not known to possess totipotent or pluripotent potential)

# NAS Guidelines for Research With Human Embryonic Stem Cells

- In April 2005, the [National Academy of Sciences released a set of guidelines for the conduct of hESC research](#). In the absence of federal regulations, the NAS Guidelines play an important advisory role for hESC research by providing recommendations for ensuring that hESC research is conducted in an ethically appropriate manner. hESC researchers are strongly encouraged to review the full set of [NAS Guidelines](#) and the Amendments to the Guidelines issued in [2007](#), [2008](#) and [2010](#).
  - The NAS Guidelines cover
    - Blastocysts made for reproductive purposes and later donated for research
    - Blastocysts made specifically for research using IVF
    - Somatic cell nuclear transfer (NT) into oocytes
    - The transplantation of hPSC into animals at any stage of development or maturity
    - The use of hPSC in in vitro experiments designed or expected to yield oocytes or sperm.
- The ESCRO Committee's policies and procedures for the conduct of hESC and hPSC research are informed and guided by the NAS Guidelines. While the NAS Guidelines are not regulations or laws, they should generally be followed.
- [NYU Langone Medical Center has established an Embryonic Stem Cell Regulatory Oversight Committee \(ESCRO\)](#) and has charged the ESCRO with responsibility for oversight, review and approval of all hESC research, both Registry and non-Registry, and all covered hPSC research to be conducted at the three institutions, regardless of funding source.
- The ESCRO Committee may move away from the NAS Guidelines if and as situations arise that justify a different course.

# NAS Guidelines on Use of Existing hESC

## Recommendations of particular interest for researchers using existing hESC lines include:

- The provenance of hESC should be documented. The ESCRO Committee requires, at a minimum, assurance that the embryos used in derivation of the hESC line were obtained with proper consent.
- Institutions should maintain an inventory listing hESC researchers and descriptions of their hESC research.
- All protocols involving the combination of hESC with nonhuman embryos, fetuses or adult animals must be reviewed by the IACUC for review of animal welfare issues and by the ESCRO Committee for consideration of the consequences of human contributions to the resulting chimeras.
- If there is a possibility that hESC or differentiated hESC derivatives transplanted into adult animals could contribute in a major organized way to the brain of the recipient animal, scientific justification for the experiments must be strong and proof of principle using nonhuman (preferably primate) cells is desirable.
- Experiments in which hESC, their derivatives or other pluripotent cells are introduced into nonhuman fetuses and allowed to develop into adult chimeras require careful consideration because of the issue of human cell contribution to the resulting animal. Consideration of any major functional contribution to the brain should be a main focus of review.
- Introduction of hESC into nonhuman mammalian blastocysts should be considered only under circumstances in which no other experiment can provide the information needed.
- Research use of existing de-identified hESC does not require IRB review unless the research involves introduction of the hESC or their derivatives into patients or the possibility that the identity of the donors of the blastocysts, gametes, or somatic cells is readily ascertainable or might become known to the investigator.

# NAS Guidelines on Deriving new hESC

## Recommendations of particular interest for researchers deriving hESC research include:

- An IRB should review the process for obtaining consent to donate gametes, blastocysts or somatic cells to be used to generate new hESC.
- The scientific rationale for the need to generate new hESC lines must be presented and the basis for the numbers of embryos needed should be justified.
- Researchers should demonstrate appropriate expertise or training in derivation or culture of either human or nonhuman hESC before permission to derive new hESC lines is given.
- When nuclear transfer is proposed as the means to generate new hESC, the protocol must provide strong scientific rationale for this approach.
- Blastocysts may not be used for research without consent of all gamete donors.
- The process of making embryos for infertility treatment should be free of the influence of investigators who propose to derive or use the hESC in research.
- No payments may be made for donating blastocysts for research purposes.
- No cash or in kind payments should be provided to oocyte, sperm or somatic cell donors. Reimbursement for direct expenses incurred by an oocyte donor as a result of the procedure to donate should be allowed.
- Consent for blastocyst donation should be made at the time of donation.
- The consent form used for donation of embryos or gametes should, at a minimum, inform the potential donors that the embryos will be used to derive hESC for research and will be destroyed in the process, that the resulting hESC may be kept for many years, and may be used in human transplantation, in research involving genetic manipulation or may be mixed with human or non-human cells in animal models, and that the donors may not direct or restrict use of resulting hESC, will not receive financial or other benefits from commercial development resulting from the hESC, and will not receive direct medical benefit from the research. For a full description of the recommendations for the informed consent, see NAS Recommendation #18.
- Investigators must document how they will characterize, validate, store and distribute any new hESC line and how they will maintain the confidentiality of any coded or identifiable information associated with the hESC line.

# NAS Guidelines on Use of hPSC

## Recommendations of particular interest for researchers using human pluripotent stem cells include:

- The provenance of hPSC should be documented. The ESCRO Committee requires, at a minimum, assurance that the materials from which the hPSC were derived were obtained with proper consent.
- All protocols involving the transplantation of hPSC into animals at any stage of development or maturity must be reviewed by the IACUC for review of animal welfare issues and by the ESCRO Committee for consideration of the consequences of human contributions to the resulting chimeras.
- If there is a possibility that the hPSC transplanted into the animals could contribute in a major organized way to the brain of the recipient animal, scientific justification for the experiments must be strong and proof of principle using nonhuman (preferably primate) cells is desirable.
- Experiments in which hPSC are introduced into nonhuman fetuses and allowed to develop into adult chimeras require careful consideration because of the issue of human cell contribution to the resulting animal. Consideration of any major functional contribution to the brain should be a main focus of review.
- Introduction of hPSC into nonhuman mammalian blastocysts should be considered only under circumstances in which no other experiment can provide the information needed.
- Research use of existing de-identified hPSC does not require IRB review unless the research involves introduction of the hPSC into patients or the possibility that the identity of the donors of the blastocysts, gametes, or somatic cells from which the hPSC were derived is readily ascertainable or might become known to the investigator.

# Prohibited Research

**Under the current ESCRO Committee operating guidelines for hESC and covered hPSC research and consistent with NAS Guidelines, the following research will not be permitted:**

- Research involving in vitro culture of any intact human embryo, regardless of derivation method, for longer than 14 days or until formation of the primitive streak begins, whichever occurs first.
- Research in which hESC or hPSC are introduced into non-human primate embryos.
- Research in which embryonic stem cells obtained from any species, including hESC, are introduced into human embryos.
- The transfer of hESC research products, including embryos created by in vitro fertilization (IVF) or somatic cell nuclear transfer (SCNT), of hPSC into a human uterus.
- The transfer of human embryos into the uterus of a non-human species.
- Research involving the breeding of any animal into which hESC or hPSC have been introduced such that they could contribute to the germ line.
- Research that involves transplantation of hPSC cells into human blastocysts.

# Oversight for hESC and covered hPSC Research

- Research with hESC or covered hPSC research conducted at NYULMC must be reviewed by appropriate administrative offices and approved by the ESCRO Committee.
- The administrative review is conducted to assist the PI with compliance with institutional and regulatory requirements related to the conduct of hESC and covered hPSC research.
- The ESCRO review and approval are a requirement for the conduct of hESC and covered hPSC research to ensure that the research is ethically appropriate, as recommended by the NAS Guidelines.
- hESC and covered hPSC research may require review and approval by other institutional oversight committees, e.g., IRB, IBC, IACUC, and/or RSC, depending on the specific protocol. These reviews need to be completed **prior** to the review by the ESCRO Committee .
- NYULMC ESCRO Committee must maintain records of the hESC lines used and stored at the institutions, general descriptions of hESC and covered hPSC research conducted, documentation of training completed by hESC and covered hPSC researchers, and evidence of ESCRO review for all hESC and covered hPSC research.



# ESCRO's Review of Proposals: Criteria

- Information provided by the PI on the NYULMC ESCRO application form should be complete and written in lay language.
- Relevant NAS Guidelines
- NYULMC Human Embryonic Stem Cell Policy
- Assurance that other oversight committee reviews have been completed as appropriate.

# ESCRO Policy & Approval

**The ESCRO Committee's approval process is designed:**

- to allow hESC and covered hPSC research to proceed unimpeded,
- to ensure compliance with ESCRO's policies and procedures, and regulatory requirements,
- to ensure federal funds are not used to support non-Registry hESC research directly or indirectly,
- to ensure all faculty, staff, postdoctoral scholars, and students as well as visiting scholars and other researchers involved in hESC and covered hPSC research are appropriately trained on the hESC and covered hPSC operating procedures.

# Responsibilities of Research Personnel

- Complete this Tutorial (required for all hESC and covered hPSC protocols) and the training on the Use of Human Subjects, as appropriate.
- Initiate IRB review for research on any hESC and covered hPSC that meets the OHRP definition as human subjects research.
- Initiate IBC review for research involving recombinant DNA work, if applicable
- Initiate IACUC review for research involving laboratory animals, if applicable
- Initiate RSC review for research involving radioactive materials, if applicable
- Complete and submit the ESCRO Application for research on all hESC and covered hPSC .
- Complete and submit a Material Transfer Agreement Form, as appropriate, for each hESC line or hPSC line requested, if applicable
- Comply with NYULMC policy's for reporting and managing financial conflicts of interest.
- Establish or identify an appropriate sponsor/award # for each research protocol.
- Submit a short [annual progress report](#) to the ESCRO Committee for all approved protocols.

# Expedited Review

PIs may seek expedited review/registration only for certain categories of research involving hESC, hPSC, human multipotent stem cell and/or human somatic cells derived from hESC or hPSC.

To qualify for expedited review, proposed work must:

- ☐ Involve the use of existing, de-identified hESC and/or hPSC and/or human multipotent stem cell lines or human somatic cell lines derived from hESC and/or hPSC only.
- ☐ Use only cell lines that meet the NYULMC criteria for acceptability with regard to provenance.
- ☐ Involve only *in vitro* use of the hESC, hPSC, human multipotent stem cell or human somatic cell lines.
- ☐ Not be intended or expected to generate gametes (oocytes or sperm).
- ☐ Have all other applicable committee approvals, e.g., IRB, IACUC, IBC, RSC.
- ☐ Involve only personnel who have completed this training.

# NYULMC hESC Inventory

- NYULMC maintains an inventory of hESC that are used or stored at NYULMC
- The ESCRO Committee has determined that if an existing hESC line meets the following criteria, it should be considered allowable for use. Note that proposed use of an allowed hESC still must be reviewed by the ESCRO Committee.
  - The line is on the [NIH hESC Registry](#).
  - The line was generated prior to the issuance of the NAS Guidelines in April 2005 and assurance that the embryos used to generate the line were donated with proper consent is documented.
  - If the line was generated after the issuance of the NAS Guidelines, donation of the embryo and gametes and derivation of the hESC must be in accordance with NAS Guidelines

# Human Subjects Research

**Follow the NYULMC's established policies for Institutional Review Board (IRB) approval.**

Proper consent for the donation of gametes, somatic cells, and/or embryos must be obtained using a consent form approved by an IRB.

hESC research involving identifiable embryos or identifiable hESC or hPSC must be reviewed by an IRB. If there is the possibility that the identity of the donors of the blastocysts, gametes, or somatic cells is easily ascertainable or might become known to the investigator, the research must be reviewed by an IRB. This work cannot be approved under an [Expedited Application](#).

Research involving introduction of hESC or hPSC or their derivatives into patients must be reviewed by an IRB.

The protocol must be approved by an IRB **prior** to review by the ESCRO Committee.

# Special Considerations in hESC or hPSC Research

- Whenever practicable, the attending physician responsible for infertility treatment and the investigator deriving or proposing to use hESC or hPSC should not be the same person.
- Donation of embryos for research requires consent from both the gamete and the embryo donors.
- Donors should be informed that they have the right to withdraw consent until the blastocysts are actually used in cell line derivation.
- hESC or blastocysts, human or otherwise, or hPSC may not be introduced into a human uterus.

# Conflict of Interest

- Follow NYULMC's procedure for reporting and managing any financial conflict of interest related to the proposed hESC or covered hPSC research.
- Any conflict of interest should be reported to the [Conflict of Interest Management Unit](#) **prior** to ESCRO review of the protocol.



# Accounting

Researchers must establish or identify the appropriate grant/award for each project utilizing non-Registry human embryonic stem cells. This information will be recorded in the ESCRO application.



# Effort Allocation and Certification

**Follow NYULMC's established policies for:**

- Tracking, allocating and confirming effort on sponsored projects for all personnel to ensure that effort devoted to non-Registry hESC research is not paid with federal funds,
- Proper allocation of salaries and benefits when an individual is working with multiple sources of support.

**IMPORTANT Salary must be allocated and charged to gift and institutional accounts consistent with effort set forth on the projects.**

# About Post Docs & Students

- **Follow NYULMC's policy and application processes for gaining approval in advance for additional work involving hESC research for postdoctoral fellows and students funded 100% by federal sources.**
- Postdoctoral fellows and students who are funded by federal institutional training grants or fellowships, such as National Research Service Awards (NRSA) are required to pursue their research training full time under the terms of the award. For efforts beyond their federal commitments, trainees are required to verify the allowability with their respective grant offices.
- Such arrangements must be approved in advance by [SPA](#). They will conduct a review of the funding terms of the award. Approval will be granted on a case-by-case basis

# Separation of hESC Research

- Facilities that are **fully** federally funded and materials purchased with federal funds **cannot be used** for non-Registry hESC research.
- [Following federal guidance](#), it is not required that non-Registry hESC research be performed in physically separate space or facilities. NYULMC follows accepted federal guidelines so that federal funds are not spent on non-Registry hESC research.
- To help ensure that these guidelines are followed, the PI must list any space that will be used for non-Registry hESC research on the application form.

# Location for Non-Registry hESC Research

## When research on non-Registry hESC will be conducted

- Use the ESCRO application form to list each lab, room, and office.
  - This will alert the Research Finance or the Sponsored Programs Administration Office to research the funding of each facility for any federal contribution.
- Update and re-submit the application form **before** any project location changes.

# Equipment for hESC research

Depending upon the source of funding used to purchase the equipment, use of the equipment for non-Registry hESC research may not be allowed.

Please list whether existing or new equipment will be used in non-Registry hESC research and where it is located.

**Equipment owned by  
the federal government**

**DO NOT USE  
ON  
NON-REGISTRY  
hESC**

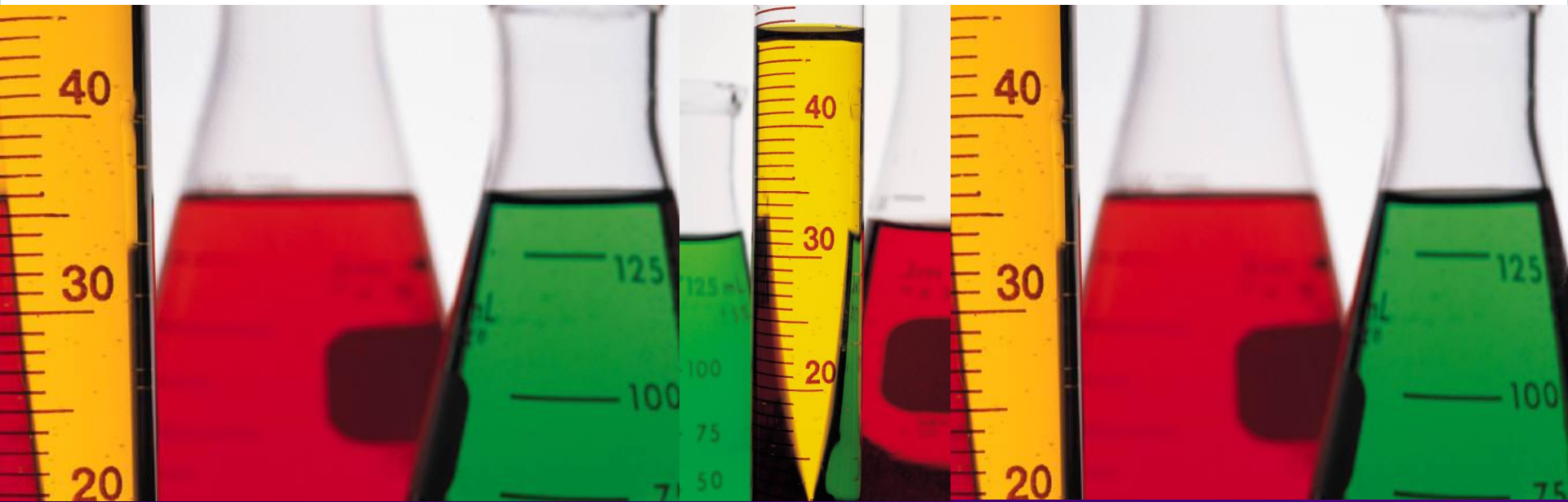
**Equipment owned by your  
institution**

**MAY BE USED  
FOR  
NON-REGISTRY  
hESC**

Consult with Research Finance or SPA Office for approval for use of equipment for non-Registry hESC research. If you are unsure whether an item constitutes “equipment” or whether it may be used in support of non-Registry hESC research, consult the following slide.

# Expendable Materials and Supplies

- Expendable materials and supplies in your current inventory that were purchased with federal funds may not be used for non-Registry hESC research.
- New expendable materials and supplies for non-Registry hESC research must be purchased with non-federal funds (e.g., gifts, department or institutional research funds).



# Allocation Methodology for Materials and Supplies

- To avoid risk of charging materials and supplies for non-Registry hESC to federal projects, purchase supplies for non-Registry hESC research separate from all other research where practical.
- If you must purchase expendable materials and supplies that benefit multiple projects, including non-Registry hESC research, use a reasonable allocation methodology to accurately assign costs to the projects. This allocation methodology must be documented. When making such purchases to support non-Registry hESC research, make sure costs are not allocated to federal projects.

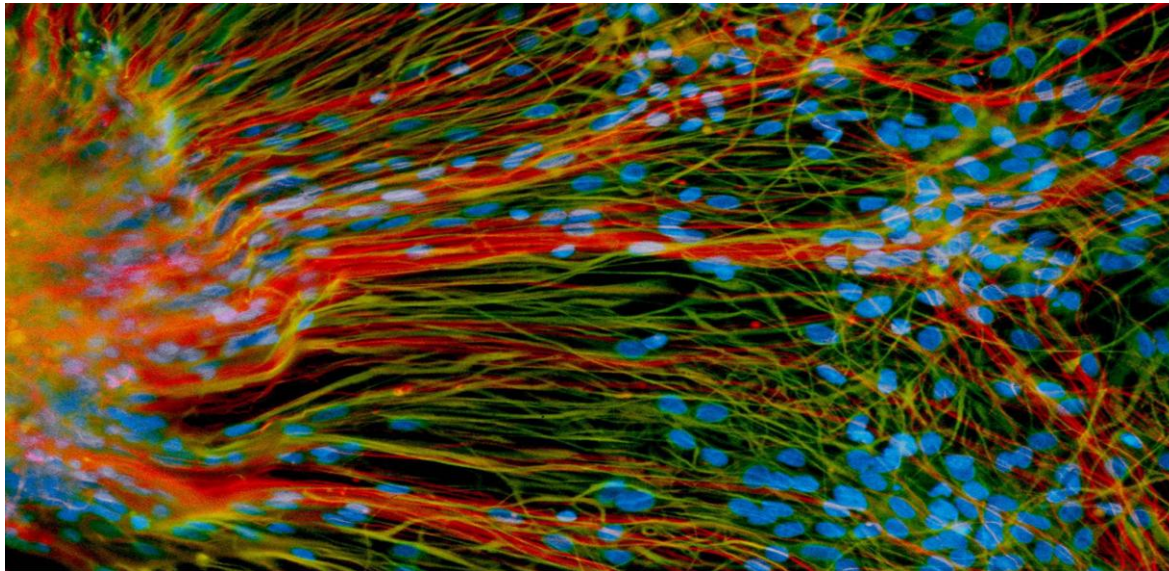


# Site Visits May Be Conducted Periodically

- Laboratories where non-Registry hESC research is performed may be periodically visited by administration officials to ensure that only approved equipment and materials are used to support non-Registry hESC research.

# Derivatives from hESC Research

- Research using derivatives from non-Registry hESC lines **cannot** be supported by federal funds. Please follow the same procedures for ensuring that federal funds are not used for work with derivatives from non-Registry hESC lines as you would for work with non-Registry hESC.
- Proposed work involving derivatives of hESC does **not** require review and approval by the ESCRO Committee unless it falls into the category of covered hPSC research or unless ESCRO review is required as a condition of the funding agency. Review by other oversight committees may be required based on the specific protocol.



**Caption:** Derived from human embryonic stem cells, in the lab of UW-Madison stem cell researcher Su-Chun Zhang, 11/01

# Using hESC Derivatives in Subsequent Research

Derivatives	Subsequent Research involving:		
	<u>Federally-funded</u> research on Registry lines	<u>Non-federally funded</u> research on Registry lines	<u>Non-federally funded</u> research on non-Registry lines
Made from Registry hESC using <u>federal funds</u>	Yes	Yes	Needs case-by-case review
Made from Registry lines using <u>non-federal funds</u>	Yes	Yes	Yes
Made from Non-Registry lines using <u>non-federal funds</u>	No	Yes	Yes

The information presented in this matrix is based on the assumption that the subsequent use is not prohibited by the funding terms of the award.

# Use of Derivatives from Federally-Funded Research in non-Registry hESC Research

- If you want to use derivatives from hESC that were created using federal funds for subsequent research involving non-Registry hESC, you need to verify that there are no restrictions prohibiting such work.
- Derivatives made during federally-funded research may be used in the conduct of non-Registry hESC research when:
  - the derivatives are not needed to complete the period of grant support from which they resulted,
  - the period of federally-funded grant support from which the derivatives resulted has been completed or the data regarding those derivatives has been published, and
  - the award's terms and conditions do not prohibit the use of such derivatives.

# Data & Intellectual Property

Researchers may use data or information obtained from either Registry or non-Registry hESC research in subsequent hESC projects if:

1. the data have been published or
2. permission to use the data has been granted by the original researcher whether the subsequent projects are federally or non-federally funded.

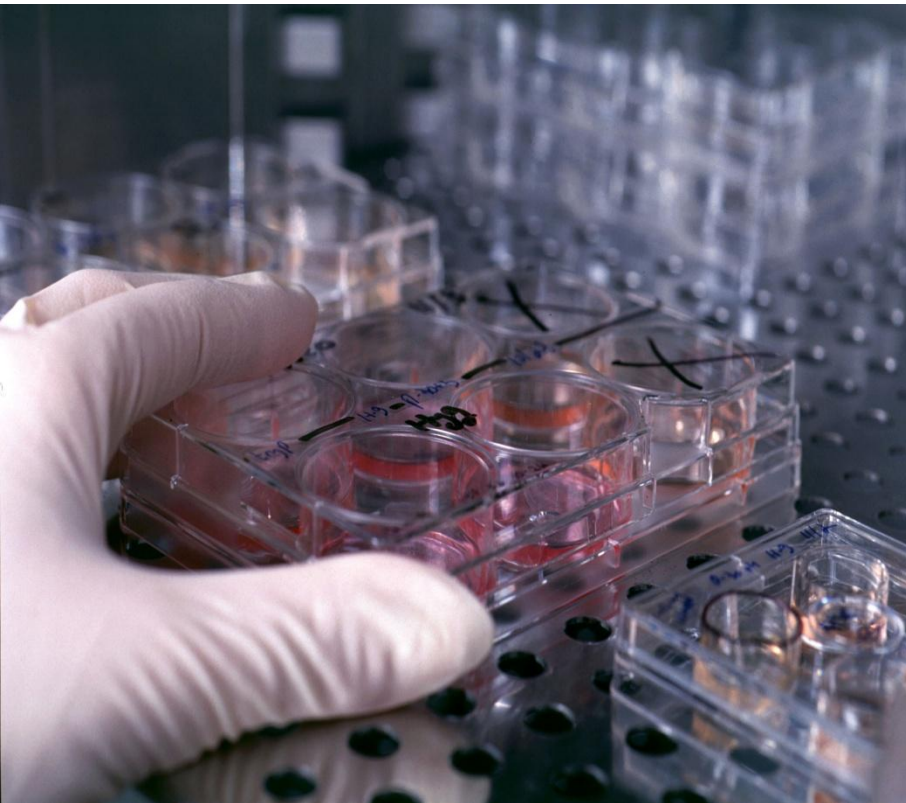
However, the federal government may not be charged for generating data from non-Registry hESC research, or for analyzing or manipulating data for subsequent use in non-Registry hESC research.

## Constraints On Data Usage

Data and information usage is subject to the usual considerations of third-party intellectual rights as well as any specific grant or contract conditions on data usage imposed by suppliers or sponsors of the data including other research institutions and federal funding agencies.

# Starting the Project

## Administrative and Compliance Requirements for Initiating Work with hESC:



1. This tutorial have been completed by all personnel involved in hESC or covered hPSC research.
1. The ESCRO and other appropriate oversight committees have approved the protocol.

# Continuing Compliance

- Abide by the hESC and covered hPSC Research Operating Procedures and all relevant institutional policies.
- Notify the ESCRO Committee of any significant protocol deviation within 30 days of its occurrence, and of any changes in location, equipment or personnel in advance of the change.
- Notify the ESCRO Committee of any adverse events or unforeseen incidents related to your protocol that was reported to an IRB, IACUC, IBC, and/or relevant agency and the committee's or agency's response to the report and any actions required within 30 days of the response.
- File a short [annual progress report](#) on the resultant research and any protocol changes for ESCRO review by the anniversary date of the initial approval.

# Further Guidance

**The procedures are subject to revision in light of changed circumstances including further guidance from federal officials, the NAS or the ESCRO Committee, and will be updated on a continuing basis as needed.**

**You may be asked to complete supplemental training if such changes occur.**