

May 24, 2006

**COLUMBIA UNIVERSITY  
HUMAN EMBRYO AND HUMAN EMBRYONIC STEM CELL RESEARCH  
SPECIAL OPERATING PROCEDURES\***

**I. INTRODUCTION**

Current federal regulations severely constrain federal support for research involving human embryos and human embryonic stem cells (“hESC”). While federal funds may not be used, directly or indirectly, to support research involving human embryos or hESC lines other than certain designated lines, federal policy does not prohibit the use of human embryos or such non-designated cell lines in research funded from non-federal sources, and University investigators may engage in such research.

The University has adopted an Institutional Policy on the Conduct of Research with Human Embryos and Human Embryonic Stem Cells (the “Embryonic Research Policy”), dated May 24, 2006, and has formed a University Human Embryo and Stem Cell Research Committee (the “Embryonic Research Committee”) to review and approve all human embryo and hESC research at the University. The University is promulgating these Special Operating Procedures (these “Procedures”) in accordance with human embryo and hESC research restrictions, to clarify how researchers and administrators can ensure that human embryo and hESC research will proceed unimpeded. These Procedures describe steps to take in managing resources used for human embryo and hESC research, including (1) personnel time, (2) facilities, (3) equipment, (4) expendable materials and supplies, (5) derivatives from human embryo and hESC research and (6) data and other intellectual property associated with human embryos and hESC.

These Procedures are intended to address only those issues presented by current federal human embryo and hESC research policy. They supplement, but do not replace, the University’s other research and personnel policies.

**II. CERTAIN DEFINITIONS**

**Covered Equipment:** tangible personal property used in Embryonic Research with an expected useful life of more than one year and an acquisition cost of \$2,000 or more.

**Data:** information and other intellectual property generated from research.

**Derivatives:** DNA, RNA, proteins and any other products secreted by or extracted from Human Embryos or hESC.

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\*These Procedures were originally issued as the Columbia University Human Embryonic Stem Cell Research Special Operating Procedures on December 21, 2005.

**Durable Goods:** reusable items, including laboratory supplies and equipment, with an acquisition cost of less than \$2,000 and an expected useful life of more than one year.

**Eligible Embryonic Research:** research involving Registry hESC.

**Embryonic Research:** Eligible Embryonic Research and Ineligible Embryonic Research.

**Facilities:** laboratory space, offices and other locations owned or operated by the University and used in the conduct of research.

**Human Embryo:** any organism, prior to implantation, that is derived by fertilization, parthenogenesis, cloning or any other means from one or more human gametes or human diploid cells.

**Ineligible Embryonic Research:** research involving Human Embryos or Non-Registry hESC.

**Materials and Supplies:** consumable goods and reusable items, including laboratory supplies and equipment, with an acquisition cost of less than \$2,000 and an expected useful life of one year or less.

**Non-Registry hESC:** hESC lines not listed on the Registry.

**Personnel:** all individuals who are or expect to be engaged in work on Embryonic Research, regardless of funding source, including faculty, post-doctoral fellows, research associates, students and technicians.

**Purchased Services:** professional contract services, such as the services of consultants, laborers or maintenance and repair technicians.

**Registry:** the NIH Human Embryonic Stem Cell Registry.  
<http://stemcells.nih.gov/research/registry/>

**Registry hESC:** hESC lines listed on the Registry.

### III. BACKGROUND

Since 1996, annual appropriations legislation has included a ban on the federal funding of Human Embryo research. The most recent version of the restriction can be found in the Consolidated Appropriations Act, 2006, P.L. 109-149, Division F, Title V, Section 509 (December 30, 2005).

On August 9, 2001, President Bush announced that federal funds may not be used for research using hESC lines unless (1) the stem cells were derived from an embryo that

was created for reproductive purposes and was no longer needed; (2) informed consent was obtained for the donation of the embryo, and the donation did not involve financial inducements; and (3) the process of derivation was begun prior to 9 p.m. EDT on August 9, 2001. The National Institutes of Health (“NIH”) has established the Registry, which lists the hESC lines that satisfy these criteria; research on these lines is therefore eligible for federal support. All other hESC research is ineligible for federal support.

Although the August 9, 2001 policy bars the use of federal funds for Ineligible hESC Research, researchers may conduct such research with non-federal funds. To comply with the policy, researchers and institutions that receive federal support must keep account of the expenses associated with Ineligible hESC Research to ensure that no federal funds are used, directly or indirectly, to support such research. According to NIH instructions, institutions will satisfy that requirement if they treat the costs of Ineligible hESC Research as “unallowable” costs under federal research policy and follow applicable federal cost principles such as OMB Circular A-21, which describe how to keep budget and accounting records so as to prevent federal funds from subsidizing unallowable activities. See NIH, Stem Cell Information, Frequently Asked Questions, (<http://stemcells.nih.gov/info/faqs.asp>) (“NIH FAQ’s”). For purposes of these Procedures, the University has voluntarily agreed to apply the same restrictions to research involving Human Embryos.

#### **IV. GENERAL PRINCIPLES**

The cost principles set out in OMB Circular A-21 do not forbid institutions that receive federal support from engaging in “unallowable” activities. They forbid only the use of federal funds to pay for such activities.

According to OMB Circular A-21, institutions can avoid shifting the costs of unallowable activities to the federal government if they (1) do not impose the direct costs of such activities on the federal government and (2) do not request reimbursement from the federal government for the indirect costs--what the Circular refers to as “facilities and administrative” (“F&A”) costs associated with unallowable activities. F&A costs are “costs that are incurred for common or joint objectives and, therefore, cannot be identified readily and specifically with particular sponsored projects, and instructional activity, or any other institutional activity.” See OMB Circular A-21, at B.4.

A further discussion of direct costs and indirect costs is included in Annex A.

#### **V. EMBRYONIC RESEARCH COMMITTEE APPROVAL**

The Embryonic Research Policy requires that each investigator at the University who wishes to engage in any research involving Human Embryos or hESC, whether Eligible hESC Research or Ineligible hESC Research, obtain the prior approval of the Embryonic Research Committee and, in connection with such approval, that the principal investigator (the “PI”) submit certain information to the Committee for its review.

The Embryonic Research Committee has determined that such information should include a Embryonic Research Tracking Form (a “Tracking Form”), a copy of which is attached hereto as Annex B. The Tracking Form must be completed for all Embryonic Research, regardless of funding source, at the time a proposal is submitted to the Embryonic Research Committee and prior to any change in the location of a project.

The Tracking Form will be forwarded to the Office of the Controller, which will assist the Embryonic Research Committee in its determination of the applicability of these Procedures to the proposal submitted for review. The Embryonic Research Committee will establish the terms under which the project may be undertaken and will so notify the PI. The PI in turn must agree to comply with all of the University’s research policies and record keeping requirements, including these Procedures.

## **VI. APPLICATION OF SPECIAL OPERATING PROCEDURES**

### **A. Personnel**

University Personnel may work on Embryonic Research projects with the prior approval of the Embryonic Research Committee.

The following Procedures apply to the approval of Personnel to participate in Embryonic Research:

1. The University’s existing policies and procedures for tracking, allocating and confirming work effort on federally funded research will apply so that appropriate effort is devoted to commitments under federal grants and so that other activities, including Ineligible Embryonic Research, are not supported by federal funds.

2. As with all projects, the total effort commitment of an individual’s existing and proposed Embryonic Research commitments may not exceed 100%.

3. The effort attributable to Ineligible Embryonic Research, as well as the effort spent on other projects, should be tracked in accordance with the University’s regular processes.

4. Some Personnel who are 100% funded by outside sources, such as National Research Service Award recipients, are permitted under the terms of their funding to engage in limited or part-time work beyond their existing commitments. Any such additional work involving Embryonic Research must be approved in advance by the Embryonic Research Committee.

## **B. Facilities**

University Facilities may be used in conducting Embryonic Research if they are identified in the Tracking Form and approved for such use in advance by the Embryonic Research Committee.

The following Procedures apply to the approval of Facilities in which Embryonic Research may be conducted:

1. The University's existing policies and procedures for tracking and confirming the use of Facilities for federally funded research, and the direct and indirect costs associated with that usage, will apply so that only allowable costs are charged to federal grants.

2. University Facilities may be used for Ineligible Embryonic Research, subject to approval and any appropriate limitations. Some limitations may arise where the Facilities have been constructed, outfitted or renovated in whole or in part with federal funds. Other limitations may involve, for example, limits on time, allocation of space or percentage use and will take into account the Facilities' other commitments, if any, to federally sponsored projects and other University activities.

3. As part of the approval process, the PI must disclose all locations (whether or not they are University Facilities) where Ineligible Embryonic Research will be conducted.

4. Any anticipated change in space usage where Ineligible Embryonic Research is conducted, whether an addition to or a deletion of existing space, is also subject to these Procedures. Changes must be reviewed and approved by the Embryonic Research Committee.

## **C. Covered Equipment**

Covered Equipment owned by the University may be used to conduct Ineligible Embryonic Research if it is approved for such use in advance by the Embryonic Research Committee.

The following Procedures apply to the approval of Covered Equipment to be used in Embryonic Research:

1. The University's existing policies and procedures for tracking and confirming the acquisition and usage of Covered Equipment for federally funded research, and the direct and indirect costs associated with acquiring and using Covered Equipment, must be strictly observed so that only allowable costs are charged to federal grants, and so that the costs of acquiring or using Covered Equipment for other activities, including Ineligible Embryonic Research, are not supported by federal funds.

2. Covered Equipment may be used for Ineligible Embryonic Research, subject to approval and any appropriate limitations. Limitations may apply where the Covered Equipment has been purchased with federal funds. Other limitations may involve, for example, limits on time or percentage limits on Covered Equipment capacity or different rates charged for use of such Equipment.

3. The Embryonic Research Committee will issue approvals as follows:

a. **Covered Equipment owned by the University.** Covered Equipment owned by the University may be used in conducting Ineligible Embryonic Research if the following conditions are satisfied:

- Acquisition of the Covered Equipment was not supported by federal funds, and
- Use of the Covered Equipment is not subject to any other restrictions imposed by non-federal sponsors.

b. **Covered Equipment owned by the University but purchased with Federal Support.** Covered Equipment acquired, in whole or part, with federal funds, even though the University holds title to it, may in general not be used in conducting Ineligible Embryonic Research, except in the following circumstances:

- The Covered Equipment has been purchased under an NIH sponsored agreement and has been designated by NIH as “Exempt Property”, as to which the University has no further obligation to the federal government; or
- Use of the Covered Equipment for Ineligible Embryonic Research is permitted pursuant to the terms of the federal grant or the approval of the appropriate federal agency; or
- The University has purchased the Covered Equipment from the federal government in full, without further federal restriction, and has documentation of such transaction.

c. **Covered Equipment owned by the Federal Government.** Covered Equipment owned by the federal government may in general not be used in conducting Ineligible Embryonic Research, and such use will be approved by the Embryonic Research Committee only in special circumstances with express federal approval. However, as indicated in paragraph (b) above, if the University purchases the Covered Equipment from the federal government in full, without further federal restriction, and has documentation of such transaction, the Embryonic Research Committee will generally approve the use of such Covered Equipment in Ineligible Embryonic Research.

3. Any anticipated changes in usage of Covered Equipment are also subject to these Procedures. Changes must be reviewed and approved by the Embryonic Research Committee.

#### **D. Materials, Supplies, Durable Goods and Purchased Services**

Materials, Supplies, Durable Goods and Purchased Services owned or acquired by the University may be used in conducting Ineligible Embryonic Research.

The following procedures apply to the usage of Materials, Supplies, Durable Goods and Purchased Services:

1. The PI must determine, for cost allocation purposes, which Materials, Supplies, Durable Goods and Purchased Services were specifically purchased to carry out Ineligible Embryonic Research. Neither the direct costs of those items nor the indirect costs associated with their acquisition may be charged to the federal government.

2. Materials withdrawn from general supply should be charged at their actual net cost “under any recognized method of pricing inventory withdrawals, consistently applied.” See OMB Circular A-21, at J.31. Transportation charges may be included. The PI should track usage for allocating costs among different projects.

3. Durable Goods must be allocated among projects for which they are used, under a reasonable allocation plan consistent with University policies.

#### **E. Derivatives from Embryonic Research**

Research on Derivatives from Human Embryos or Non-Registry hESC may not be supported by federal funds. See NIH FAQ’s Funding Questions no.3. The term “Derivatives” does not refer to Data obtained from Embryonic Research, which is addressed in Section G below.

The following Procedures apply to the use of Derivatives from Embryonic Research:

1. The PI for each project must determine and record the source of the Derivatives on the Tracking Form, whether s/he plans to conduct Eligible Embryonic Research or Ineligible Embryonic Research, and the use to which the Derivatives will be put. Before using Derivatives, the PI must ask the party providing the Derivatives whether the Derivatives originated from Human Embryos or Non-Registry hESC.

2. The PI must determine if usage of Derivatives is allowable, as summarized in the following matrix, subject to the detailed requirements set out in these Procedures. The matrix assumes that the subsequent usage is not prohibited by the funding terms.

Source of Derivatives	Subsequent Research		
	Federally funded Research on Registry hESC	Non-federally funded research on Registry hESC	Non-federally funded research on Non-Registry hESC /Human Embryos
Registry hESC – Derivation federally funded	Yes (a)	Yes (a)	Subject to review (a)
Registry hESC – Derivation non-federally funded	Yes (b)	Yes (b)	Yes (b)
Non-Registry hESC /Human Embryos – Derivation non-federally funded	No (c)	Yes (c)	Yes (c)

**a. Derivatives from Federally Funded Research on Registry hESC.**

Derivatives created from federally funded Eligible Embryonic Research may be used for (i) subsequent federally funded or non-federally funded Eligible Embryonic Research and (ii) subsequent non-federally funded Ineligible Embryonic Research only with the prior approval of the Embryonic Research Committee.

**b. Derivatives from Non-Federally Funded Research on Registry hESC.**

Derivatives created from non-federally funded Embryonic Research may be used for subsequent federally or non-federally funded Eligible Embryonic Research.

**c. Derivatives from Non-Federally Funded Research on Non-Registry hESC/Human Embryos.** Derivatives created from non-federally funded Ineligible Embryonic Research may **not** be used for subsequent federally funded Eligible Embryonic Research, but may be used for subsequent non-federally funded Eligible Embryonic Research or Ineligible Embryonic Research.

**F. Derivatives from Federally Funded Research other than Embryonic Research.** Derivatives created from federally funded research other than Embryonic Research include but are not limited to antibodies, plasmids and other vectors. Such derivatives may be used in the conduct of Ineligible Embryonic Research when (1) the derivatives are not needed to carry out the segment of the Research in which they were derived, (2) the segment is completed or the data regarding such derivatives have been published, and (3) the award’s terms and conditions do not prohibit the use of such derivatives.

**G. Data or Other Intellectual Property obtained from Embryonic Research**

Data obtained from either Eligible Embryonic Research or Ineligible Embryonic Research may be used in subsequent hESC research, whether the subsequent



projects are federally or non-federally funded. However, the federal government may not be charged for generating Data from Ineligible Embryonic Research, or for analyzing or manipulating Data for subsequent use in Ineligible Embryonic Research. Any use of Data is subject to the usual consideration of third-party intellectual property rights, as well as any specific grant or contract constraints on Data usage imposed by the suppliers or sponsors of the Data, including other research institutions and federal funding agencies.

## **VII. Further Guidance and Questions**

These Procedures are subject to revision in light of changed circumstances or further guidance from federal officials.

In order that University Personnel do not receive conflicting or incomplete information, inquiries to NIH or other federal agencies about the application of federal cost principles to Embryonic Research must be made only by the Executive Vice President for Research or the Associate Controller or their designees.

Any questions about these procedures and their application to specific research projects should be referred directly to David Hirsh, Executive Vice President for Research, at 212-854-1696 ([dih1@columbia.edu](mailto:dih1@columbia.edu)) or Richard Ruttenberg, Associate Controller, Restricted Funds, at 212-854-1050 ([rr40@columbia.edu](mailto:rr40@columbia.edu)).

## DIRECT AND INDIRECT COSTS

### A. Direct Costs

To determine whether the direct costs of resources such as personnel, equipment and other materials can be borne by the federal government, the recipient institution must determine that the costs are allowable, reasonable and allocable to work conducted under federally sponsored agreements, and must exclude unallowable costs.

Although the direct costs of unallowable activities may not be charged to the federal government, the government will pay its share of resources that are used for both federal and non-federal purposes. OMB Circular A-21 states that “a cost is allocable to a particular cost objective (i.e., a specific function, sponsored agreement, department, or the like) if the goods and services involved are chargeable or assignable to such cost objective in accordance with relative benefits received or other equitable relationship.” See OMB Circular A-21, at C.4.A. For example, if personnel time or general-purpose laboratory materials are being used for both federally sponsored research and unallowable research, the federal government will pay the cost of that proportion of the resource being used for federally sponsored research.

The process of determining the direct costs of resources used for Ineligible Embryonic Research does not differ in practice from the allocation process for allowable activities not associated with a federal agreement.

### B. Indirect Costs

In general, indirect or F&A costs may be allocated to the federal government by applying a government-approved F&A rate, as negotiated by the recipient institution, to the direct costs of individual federally funded projects. This approach assumes that there is an established relationship between the direct costs of research projects and the F&A costs – represented by the F&A rate – and that it is therefore possible to identify the F&A costs associated with a particular project by applying the predetermined rate to the total amount of direct costs associated with the project. The NIH guidance indicates that the indirect costs of research with Non-Registry hESC are subject to this approach; the costs of such research may be included in the regular F&A cost allocation base, and associated indirect costs may be allocated pursuant to ordinary allocation principles. The NIH FAQs state that compliance with these methodologies “will prevent the shifting of unallowable stem cell research costs to federally sponsored programs.” See NIH FAQs, Funding Questions No.4. The same methodologies will apply to research with Human Embryos.

**Annex B**

**Human Embryo/Human Embryonic Stem Cell Research Tracking Form**

This Form must be completed for all research that involves the use of human embryos or human embryonic stem cells (“hESC”) regardless of funding source when a proposal is submitted for the approval of the Embryonic Research Committee and prior to any change in project location.

PI Name: \_\_\_\_\_ Date: \_\_\_\_\_

Dept: \_\_\_\_\_

Phone: \_\_\_\_\_ Email Address: \_\_\_\_\_

Funding Sources: \_\_\_\_\_

Project Title: \_\_\_\_\_

**Type of Research  
(check all that apply)**

- Registry hESC**  
Those included on the National Institutes of Health Human Embryonic Stem Cell Registry <http://escr.nih.gov>  
  
Cell Line Number: \_\_\_\_\_
- Non-Registry hESC**  
Those excluded from the National Institutes of Health Human Embryonic Stem Cell Registry <http://escr.nih.gov>  
  
Origin and Designation of Cell Line: \_\_\_\_\_
- Human Embryos**  
  
Origin of Embryos: \_\_\_\_\_

**Project Location**

(include laboratory, shared equipment rooms(s), office space and any other space where a portion of the research is performed.)

- On-Campus**  
**Building** \_\_\_\_\_ **Room** \_\_\_\_\_ **Purpose** \_\_\_\_\_  
  
**Building** \_\_\_\_\_ **Room** \_\_\_\_\_ **Purpose** \_\_\_\_\_  
  
**Building** \_\_\_\_\_ **Room** \_\_\_\_\_ **Purpose** \_\_\_\_\_
- Off Campus**  
**Address** \_\_\_\_\_ **Purpose** \_\_\_\_\_
- Address** \_\_\_\_\_ **Purpose** \_\_\_\_\_

**For Human Embryo and Non-Registered hESC Only**

**Equipment/Core Facilities**

Will equipment with an acquisition cost of \$2,000 or more and an expected useful life of more than one year be used on this research project? Yes  No

If yes, which equipment? \_\_\_\_\_

Will all such equipment reside in the project location(s) listed above? Yes  No

If not, where will equipment reside? \_\_\_\_\_

Will core facilities be used? Yes  No

If yes, which of the following core facilities?

- Bioinformatics (ICRC)
- Cell and Tissue Kinetic Core Facility (VC)
- Confocal Microscopy (P&S)
- DNA Analysis and Sequencing (ICRC)
- Flow Cytometry/(ICRC)/Fluorescence Activated Cell Sorter (ICRC)
- Gene Expression Profiling (ICRC)
- Molecular Biology/Molecular Genetics (DERC)
- Proteomics (P&S)
- Transgenic Mouse Facility (HHSC)
- Transgenic Mouse Facility (ICRC)
- Other \_\_\_\_\_  
(specify facility and location)