

**HARVARD UNIVERSITY
HUMAN EMBRYONIC STEM CELL RESEARCH
COST-ALLOCATION PROTOCOLS**

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Harvard University Human Embryonic Stem Cell Research Cost-Allocation Protocols

Current federal policy does not prohibit institutions from undertaking research on human embryonic stem cells (hESC). Rather, it prohibits the use of federal funds for research on all but certain designated hESC lines. Thus, 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.

Harvard University is promulgating these protocols in accordance with federal hESC research restrictions, to clarify steps researchers and administrators can take to ensure that hESC research can proceed unimpeded. The protocols describe steps to take in managing resources used for hESC research, including (1) personnel time, (2) facilities, (3) equipment, (4) materials, supplies, durable goods, and purchased services, (5) derivatives from hESC research, and (6) data and other intellectual property associated with hESC lines.

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

For questions about these cost-allocation protocols, please review the Frequently Asked Questions at <http://provost.harvard.edu/>, or contact Judith Ryan, Director for Cost Analysis and Compliance in the Office for Sponsored Programs (OSP), at 617-495-1520 (judy_ryan@harvard.edu); Jay Taft (FAS) at 617-495-1632 (taft@fas.harvard.edu); Sarah Axelrod (HMS) at 617-432-3284 (sarah_axelrod@hms.harvard.edu); or Deborah Carmel (HSPH) at 617-432-0990 (dcarmel@sphofs.harvard.edu).

I. Background

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 pm EDT on August 9, 2001. The National Institutes of Health (NIH) has established a registry of the stem cell lines that satisfy these criteria ("registry lines"); research on these lines is therefore eligible for federal funding. Research on human embryonic stem cell lines not listed on the NIH registry ("non-registry lines") is ineligible for federal funding.

Although the August 9, 2001 policy bars the use of federal funds for ineligible hESC research, it does not prevent researchers from conducting such research with non-federal funds. To comply with the policy, researchers and institutions that receive federal funding 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 funding 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 (NIH FAQs), available at <http://stemcells.nih.gov/info/faqs.asp>.

II. 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 these activities. For example, Section J.3 of OMB Circular A-21 says that the costs of alcoholic beverages are unallowable. Thus, while a laboratory may celebrate a colleague’s accomplishment with a bottle of champagne, it is not appropriate to charge the cost of the alcohol to the federal government. The laboratory may, of course, be reimbursed for other allowable expenses incurred in connection with federally supported projects.

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. Examples of indirect costs include building depreciation and use allowances, maintenance expenses, library expenses, and student and departmental administration expenses.

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 ineligible hESC 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 hESC research does not differ in practice from the allocation process for allowable activities not associated with a federal agreement. Take, for example, a professor who spends 50% of his/her time on a federally sponsored grant, 25% on teaching and administrative duties, and 25% on ineligible hESC research. In that case, 50% of the professor’s time could be allocated to the federal grant, but 50% of his/her time could not be; it is irrelevant for allocation purposes

whether s/he spends his/her time outside of the federal grant work performing unallowable activities or simply activities that do not benefit the federally sponsored research.

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 ineligible hESC research are subject to this approach; the costs of ineligible hESC 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.

III. Definitions of Terms

The terms used in these protocols shall have the following meanings:

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

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

Covered Equipment: tangible personal property used in hESC research with an expected useful life of more than one year and an acquisition cost of \$5,000 or more.

Materials, Supplies, and Other Commodities: consumable goods and reusable items, including laboratory supplies and equipment, with an acquisition cost of less than \$5,000 and an expected useful life of one year or less.

Durable Goods: reusable items, including laboratory supplies and equipment, with an acquisition cost of less than \$5,000 and an expected useful life of more than one year.

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

Derivatives: DNA, RNA, proteins, and any other products secreted by or extracted from human embryonic stem cells.

Data: information and other intellectual property generated from research.

IV. Provost's Approval of hESC Research

A Principal Investigator (PI) must submit a written proposal to conduct hESC research to the Office of the Provost for review by the Stem Cell Research Committee. The Office of the Provost shall notify the School(s) and OSP that a proposal has been submitted. The Stem Cell Research Committee shall review the proposal and make a recommendation to the Provost. Notice of the Provost's decision shall be provided to the PI, the School(s), and OSP.

V. Application of Federal Cost Principles to Specific Resources

In addition to obtaining the approval of the Provost to conduct hESC research, the PI must obtain confirmation from the School(s) that the proposal conforms to the protocols set out below.

The following protocols apply to Personnel, Facilities, Covered Equipment, Materials, Supplies, Durable Goods, and Purchased Services, engaged in eligible or ineligible hESC research, regardless of funding source. The Schools are responsible for implementing the protocols for these specific resources, in consultation with OSP.

A. Personnel

Harvard Personnel may work on hESC research projects or activities only with prior approval. Approval is required whether or not the hESC research is eligible for federal funding, and whether or not the individual receives federal funding for any purpose. The following two steps must be completed before an individual commences work on hESC research:

1. The individual must have written approval from the School(s).
2. The individual must agree to follow all of Harvard's research policies and recordkeeping requirements, including the hESC Cost-Allocation Protocols.

The following protocols apply to the approval of Personnel to participate in hESC research, regardless of funding source:

- a. Responsibility for Seeking Approval. The PI retains primary responsibility for seeking approval for Personnel to engage in hESC research.
- b. Tracking Effort. Harvard's existing policies and procedures for tracking and confirming work effort on federally funded research, including pay-rate policies, will apply so that appropriate effort is devoted to commitments under federal grants, and so that other activities, including ineligible hESC research, are not supported by federal funds.
- c. Allowable Effort. The total effort commitment of an individual requesting approval to work on ineligible hESC research may not exceed 100%, taking into account the individual's existing commitments, any allowable adjustments thereto, and the individual's proposed hESC research commitment(s). The total allowable amount of committed effort for faculty members or others with

teaching and administrative responsibilities may be less than 100% in accordance with School policy. This rule is subject to a narrow exception for limited additional work on other projects, including ineligible hESC research (*see* subsection e, below).

- d. **Individuals Holding Multiple Appointments.** Many Harvard Personnel have appointments or relationships elsewhere, including with affiliated hospitals and other institutions. The process for approving Harvard Personnel to engage in hESC research will take into account other appointments, relationships, and commitments.
- e. **Additional Work.** Some Personnel who are 100% funded by outside sources, such as federal NRSA 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, including hESC research, must be approved in advance by the School(s), in consultation with OSP, and will follow existing policies regarding additional work effort.
- f. **Work Benefiting Multiple Research Goals.** Some activities may require further analysis to determine whether they may be supported in whole, part, or not at all by federal funds. Research activities on registry lines may be supported by federal funds to the extent permitted by the particular grant. Research activities on non-registry lines may not be supported by federal funds. Certain types of activities may benefit both types of research, for example, the development of a reagent that can be used on both registry lines and non-registry lines. The time spent performing activities designed to benefit research on registry lines and on non-registry lines should be allocated in proportion to the benefit each receives.
- g. **Approval of Changes in Effort Commitments.** The PI retains primary responsibility for seeking approval from his/her School when there is any anticipated change in hESC effort commitment. The School will review and approve any change requests, in consultation with OSP.

B. Facilities

Harvard Facilities may be used in conducting hESC research if they are approved for use in advance. NIH guidance specifically provides that an investigator receiving NIH funds may derive new hESC lines in a university-supported laboratory as long as (a) all direct costs of doing the derivation are allocated to a non-federal funding source, and (b) the university has in place a method of separating costs so that the appropriate F&A costs allocable to the derivation of new hESC lines are charged to non-federal accounts. *See* [NIH FAQs, Funding Questions no. 7.](#)

The following two steps must be completed before a Facility may be used to conduct hESC research:

1. The PI must have written confirmation from the School(s) that the Facility has been approved for use in the conduct of hESC research.

2. The PI must adhere to limitations, if there are any, contained in the written approval regarding the usage of Facilities and related recordkeeping.

The following protocols apply to the approval of Facilities in which hESC research may be conducted:

- a. Responsibility for Seeking Approval. The PI retains primary responsibility for seeking approval for Facilities to be used in the conduct of hESC research.
- b. Tracking Usage of Facilities. Harvard's existing policies and procedures for tracking and confirming the usage 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, and so that the costs of using Facilities for other activities, including ineligible hESC research, are not supported by federal funds.
- c. Limitations on the Usage of Facilities. Harvard Facilities may be used for ineligible hESC research, subject to approval and any appropriate limitations. 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 to other Harvard activities, including non-federally sponsored research.
- d. Use of Multiple Facilities. As part of the approval process, the PI must disclose all locations (whether or not they are Harvard Facilities) where his or her ineligible hESC research will be conducted.
- e. Approval of Changes in Usage of Facilities. Any anticipated change in space usage where ineligible hESC research is conducted, whether addition or deletion of existing space, or changes in time or percentage of ineligible hESC research or other usage, is also subject to these protocols. Changes must be reviewed and approved by the School(s), in consultation with OSP.

C. Covered Equipment

Covered Equipment owned by Harvard may be used to conduct ineligible hESC research with advance approval. According to the NIH's current interpretation, the acquisition of equipment used in the conduct of ineligible hESC research may not be federally supported. Federal regulations (45 CFR §§ 74.33 and 74.34; OMB Circular A-110, at C.34) contain additional rules that restrict the use of federally owned equipment or other equipment acquired with federal funds.

The following two steps must be completed before Covered Equipment may be used to conduct hESC research:

1. The PI must have written confirmation that the Covered Equipment has been approved for use in the conduct of hESC research.

2. The PI must agree to limitations, if any, contained in the written approval regarding the use of Covered Equipment and related recordkeeping. Limitations may involve, for example, limits on time or percentage limits on Covered Equipment capacity.

The following protocols apply to the approval of Covered Equipment to be used in hESC research:

- a. Responsibility for Seeking Approval. The PI retains primary responsibility for seeking approval for Covered Equipment, whether existing at Harvard or proposed for acquisition, to be used in the conduct of hESC research.
- b. Tracking Usage of Covered Equipment. Harvard'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, will apply 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 hESC research, are not supported by federal funds.
- c. Usage of Covered Equipment. The School(s), in consultation with OSP, will issue approval as follows:
 - (i) Covered Equipment Owned by Harvard. Covered Equipment owned by Harvard may be used in conducting ineligible hESC 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, including restrictions imposed by non-federal sponsors.
 - (ii) Covered Equipment Owned by the Federal Government. Covered Equipment owned by the federal government may be used in conducting ineligible hESC research only in the following circumstances:
 - Use of the Covered Equipment is permitted pursuant to the terms of the federal award(s) under which the Covered Equipment was obtained, the terms of an equipment rental agreement, or the approval of the appropriate federal agency; or
 - Harvard purchases the Covered Equipment from the federal government and has documentation of such transaction, including title transfer.
 - (iii) Covered Equipment Owned by Harvard but Purchased with Federal Support. Covered Equipment owned by Harvard but acquired, in whole or in part, with

federal funds may be used in conducting ineligible hESC research only in the following circumstances:

- The federal grant supporting the Covered Equipment purchase, or the discrete portion of a renewable federal grant supporting the Covered Equipment purchase, has been completed and Harvard retains title to the equipment without restriction, observing any preferences for federal usage; or
 - Use of the Covered Equipment for ineligible hESC research is permitted pursuant to the terms of the federal grant or the approval of the appropriate federal agency; or
 - Harvard purchases the Covered Equipment in full, without federal restriction, and has documentation of such transaction.
- d. Approval of Changes in Usage of Covered Equipment. Any anticipated changes in usage of Covered Equipment are also subject to these protocols. Changes must be reviewed and approved by the Schools, in consultation with OSP.

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

Materials, Supplies, Durable Goods, and Purchased Services owned or acquired by Harvard may be used in conducting ineligible hESC research.

To ensure that usage of these items is appropriate, researchers must do the following:

1. The PI must determine, for cost-allocation purposes, which Materials, Supplies, Durable Goods, and Purchased Services were purchased specifically to carry out ineligible hESC research.
2. The PI must agree to recordkeeping requirements for tracking the usage of general-purpose Materials, Supplies, Durable Goods, and Purchased Services, to ensure that the federal government is not charged for ineligible hESC research. The School, in consultation with OSP, is responsible for ensuring that these requirements are followed.

The following protocols apply to the usage of Materials, Supplies, and Purchased Services:

- a. Consumable Materials and Purchased Services.
 - (i) Specific Purchases. If Purchased Services—such as the services of consultants, laborers, or maintenance/repair technicians—or Materials are purchased specifically to carry out ineligible hESC research, neither the direct costs of those items nor the indirect costs associated with their acquisition may be charged to the federal government.

- (ii) Materials from a General Supply. 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 must track usage and apply a written plan for allocating costs among different projects. Note that the indirect cost must be allocated as well, so, for example, if an ineligible project consumes a half of the cost of \$100 worth of Materials initially purchased with federal funds, then the indirect cost for \$50 of the Materials must be deducted from the indirect cost that would otherwise be charged to the federally sponsored project.
- b. Durable Goods. Reusable materials having an expected life greater than one year, including equipment costing less than \$5,000, must be allocated among the projects for which they are used, under a reasonable allocation plan consistent with School policies.

E. Derivatives from hESC Research

NIH guidance indicates that research on Derivatives from non-registry lines, like research on the lines themselves, may not be supported by federal funds. See [NIH FAQs, Funding Questions no. 3](#). The term “Derivatives” does not refer to Data obtained from stem cell research, which is addressed in a separate section below.

To ensure compliance with the NIH’s instructions, as well as other federal cost principles, researchers must do the following:

1. The PI must determine and record the source of the human embryonic stem cells and human embryonic stem cell derivatives, whether s/he plans to conduct federally funded research on registry lines, non-federally funded research on registry lines, or non-federally funded research on non-registry lines, and the use to which the Derivatives will be put.
2. The PI for each project must determine if usage of Derivatives is allowable, as summarized in the following matrix, subject to the detailed requirements set out in these protocols. The matrix assumes that the subsequent usage is not prohibited by the funding terms.

| <u>Source of Derivatives</u> | <u>Subsequent Research</u> | | |
|--|---|---|---|
| | Federally-funded research on registry lines | Non-federally funded research on registry lines | Non-federally funded research on non-registry lines |
| Registry lines—derivation federally funded | Yes | Yes | Maybe, if not restricted (see below) |
| Registry lines—derivation non-federally funded | Yes | Yes | Yes |
| Non-registry lines—derivation non-federally funded | No | Yes | Yes |

The following protocols apply to the use of hESC Derivatives:

- a. Ascertaining the Origin of the Stem Cell Derivatives. Before using hESC Derivatives, the PI must ask the party providing the Derivatives whether the Derivatives originated from a registry line or a non-registry line.
- b. Derivatives from Federally Funded Research on Registry Lines. Derivatives created from federally funded research may be used for subsequent federally funded research. Derivatives from registry lines may be restricted for use in non-federally funded research; their use may be allowed if the costs of the Derivatives are not charged to the federal government, and provided that the federal grant does not prohibit use of the Derivatives for non-federally funded research. If the nature of the Derivatives is such that estimating their costs is infeasible, the Derivatives may be used where: (1) the Derivatives are not needed to carry out the federally funded project; (2) the School(s), in consultation with OSP, approves the use of Derivatives from federally funded research based on OSP's review of the terms of the federal grant; and (3) and the federal government is not charged for any cost associated with use of the Derivatives in non-federal research.
- c. Derivatives from Non-Federally Funded Research on Registry Lines. Derivatives from hESC research that would have been eligible for federal funding but that was undertaken with non-federal funds are usable in any subsequent project, without restriction, except to the extent that the non-federal sponsor(s) may impose conditions on the use of such Derivatives.
- d. Derivatives from Non-Federally Funded Research on Non-Registry Lines. Costs associated with research on Derivatives from non-registry lines (including Personnel and Covered Equipment) may not be charged to federal

sources, even if such research is undertaken in whole or part to benefit a federally funded project.

F. Data or Other Intellectual Property Obtained from hESC Research

Researchers may use Data obtained from either eligible or ineligible hESC research in subsequent hESC projects, whether the subsequent projects are federally or non-federally funded. However, the federal government may not be charged for generating Data from ineligible hESC research, or for analyzing or manipulating Data for subsequent use in ineligible hESC research. These hESC Cost-Allocation Protocols govern the determination as to whether resources engaged in the generation, analysis, or manipulation of Data from hESC research may be charged to the federal government. 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.

VI. Further Guidance and Questions

The protocols contained herein are subject to revision in light of changed circumstances.

Any questions about the hESC Research Cost-Allocation Protocols and their application to specific research projects should be referred directly to Judith Ryan, Director for Cost Analysis and Compliance in the Office for Sponsored Programs (OSP), at 617-495-1520 (judy_ryan@harvard.edu); Jay Taft (FAS) at 617-495-1632 (taft@fas.harvard.edu); Sarah Axelrod (HMS) at 617-432-3284 (sarah_axelrod@hms.harvard.edu); or Deborah Carmel (HSPH) at 617-432-0990 (dcarmel@sphofs.harvard.edu).

In order that Harvard personnel do not receive conflicting or incomplete information, inquiries to NIH or other federal agencies about the application of federal cost principles to hESC research must be made by OSP on behalf of the University.

August 8, 2006