

UNIVERSITY OF CALIFORNIA, SANTA BARBARA

INTERIM GUIDANCE TO INVESTIGATORS & ADMINISTRATORS INVOLVED IN HUMAN STEM CELL RESEARCH

I. PURPOSE

The UC Santa Barbara campus is issuing this interim guidance to investigators and administrators in response to federal and state legislation regarding human adult and embryonic stem cell research. Because of limitations on the use of federal funds for some stem cell research, investigators and administrators are advised to take extra care in managing space and equipment use and direct expenditures. As the campus gains experience with stem cell research, the guidance will be revised as necessary and eventually finalized.

II. BACKGROUND

President George W. Bush, on August 9, 2001, announced restrictions on the use of federal funding for human embryonic stem cell lines, unless all of the following criteria are met:

- The stem cells were derived from an embryo that was created for reproductive purposes and was no longer needed;
- Informed consent was obtained for the donation of the embryo and that donation did not involve financial inducement; and
- The derivation process was initiated prior to 9 p.m. EDT on August 9, 2001.

The National Institutes of Health (NIH) maintains the Human Embryonic Stem Cell Registry, which lists stem cell lines that meet these criteria and may be supported with federal funds. See the Registry website at <http://stemcells.nih.gov/research/registry>. Any cell line that is not explicitly listed in this registry is a “non-approved line.” UCSB has chosen to describe these cell lines as “non-registered” to avoid confusion related to other regulatory approval processes.

California Proposition 71, the California Stem Cell Research and Cures Initiative, was passed by voters in 2004 to stimulate research utilizing stem cell lines. This statewide ballot measure created the California Institute for Regenerative Medicine (CIRM) as a state agency to distribute \$3 billion in funding for stem cell research, research facilities and other research opportunities at California universities and research institutions. The Independent Citizens Oversight Committee (ICOC) is the 29-member governing board for the Institute. ICOC members are public officials, appointed on the basis of their experience earned in California's leading public universities, non-profit academic and

research institutions, patient advocacy groups and the biotechnology industry. See <http://www.cirm.ca.gov/>. The ICOC is in the process of developing additional regulations under the California Code of Regulations that apply to CIRM awards.

Also applicable is California's Health and Safety Code section 125300, which explicitly states that stem cell research, including research involving human embryonic stem cells (hESC), human embryonic germ cells (hEGC), and human adult stem cells (hASC), is permitted. Sections 125300 and 125119 require all research projects involving the derivation or use of hESC, hEGC, and hASC to be reviewed by an institutional review board (IRB). Research involving human embryonic stem cells may also be subject to review and approval by an Embryonic Stem Cell Research Oversight (ESCRO) Committee formed by UCSB.

III. DEFINITIONS

Derivatives - Derivatives are DNA, RNA, proteins, and any other products secreted by or extracted from human embryonic stem cells. They do not include data obtained from stem cell research, which are treated separately in the protocols. The federal funding prohibition applies both to the cell lines themselves and to their derivatives.

Equipment – Tangible personal property with an expected useful life of more than one year and an acquisition cost of \$5,000 or more.

Exempt Equipment– Items specifically identified in a federal award as UCSB property without further obligations to the government. This occurs infrequently.

Fair Market Value – The depreciated value of an equipment item at a specific date and time as determined by UCSB Materiel Management. Fair market value will change over time and should be reassessed at least annually.

Human Embryonic Stem Cells (hESCs) – Pluripotent cells that are self-replicating derived from human embryos and are capable of developing into cells and tissues of three primary germ layers. Although hESCs may be derived from embryos such stem cells are not themselves embryos.

Non-Registered Stem Cell Lines – Those cell lines that are not included in the Human Embryonic Stem Cell Registry maintained by the National Institutes of Health, <http://stemcells.nih.gov/research/registry>.

OMB Circular A-21 – Entitled “Principles for Determining Costs Applicable to Grants, Contracts and Other Agreements with Educational Institutions,” this is a guidance document from the Office of Management and Budget (OMB) to federal

agencies, which they then apply to award recipients. This Circular describes the process for determining what costs may be charged to federal awards and the method of calculating a Facilities and Administrative (or indirect cost) rate. See the full text at http://www.whitehouse.gov/omb/circulars/a021/a21_2004.html.

OMB Circular A-110 – Entitled “Uniform Administrative Requirements for Grants and Agreements With Institutions of Higher Education, Hospitals, and Other Non-Profit Organizations,” this document establishes award recipient standards for pre-award activities; post-award activities including management of fiscal, property, procurement, reporting and record retention systems, and termination; and after-the-award activities including close out responsibilities. See the full text at <http://www.whitehouse.gov/omb/circulars/a110/a110.html>.

Registered Stem Cell Lines – Those cell lines that are included in the Human Embryonic Stem Cell Registry maintained by the National Institutes of Health and available at the following website: <http://stemcells.nih.gov/research/registry>.

Stem Cells – Cells with the ability to divide for indefinite periods in culture and to give rise to specialized cells. All stem cells—regardless of their source—have three general properties: they are capable of dividing and renewing themselves for long periods; they are unspecialized; and they can give rise to specialized cell types, e.g., muscle, neuron, bone, or skin.

IV. GUIDANCE RELATED TO REQUIRED REVIEWS

A. REVIEW BY THE INSTITUTIONAL REVIEW BOARD

All human stem cell research to be conducted by our researchers is required under the California Health and Safety Code to be reviewed and approved, in advance, by an Institutional Review Board (IRB). The IRB must approve the use of adult and embryonic stem cells, whether available as commercial lines or derived by the researcher. Under UCSB’s Federalwide Assurance, the IRB’s review responsibilities extend to all activities involving university employees, space or other resources.

B. ADDITIONAL REVIEW BY THE EMBRYONIC STEM CELL OVERSIGHT COMMITTEE

Human embryonic stem cell research protocols also are evaluated by the campus Embryonic Stem Cell Oversight (ESCRO) committee for adherence to National Academy of Science and CIRM guidelines pertaining to local oversight of all issues related to derivation and research use of human embryonic stem cell lines. All stem cell lines must be derived in compliance with applicable requirements for informed consent and donor compensation policies.

Investigators initiate this review by completing a Stem Cell research application http://research.ucsb.edu/compliance/documents/Stem_Cell_Form.doc. Questions about applying for ESCRO review of stem cell research protocols may be directed to Norma Marquez at 893-4180.

V. GUIDANCE RELATED TO FISCAL MANAGEMENT

A. FINANCIAL MANAGEMENT FOR RESEARCH USING REGISTERED HUMAN EMBRYONIC AND ADULT STEM CELLS

Registered hESCs and adult stem cell lines are unrestricted and have no conditions imposed on the use of federal funds for these activities.

B. FINANCIAL MANAGEMENT FOR NON-REGISTERED hESC RESEARCH

The NIH and the Division of Cost Allocation of the U.S. Department of Health and Human Services confirm that institutions can comply with the federal stem cell funding policy by strictly adhering to the cost accounting principles from the OMB Circulars. This is consistent with the procedures currently used by the university to account for charges on individual federal grants and contracts. That is, charges to federal funds must be allowable, reasonable, allocable (directly attributable to the project in proportion to the benefit received), and the methodology for determining costs consistently applied. The NIH Stem Cell Frequently Asked Questions website (<http://stemcells.nih.gov/info/faqs.asp>) provides general and specific information regarding charges for registered and non-registered cell line research.

Principal Investigators have primary responsibility for programmatic and fiscal management of their research projects. As such, they must ensure that all members of the research teams utilizing non-registered hESC lines are informed of these Interim Guidelines and the restrictions on the use of federal funds for non-registered hESC research.

Allowable - Federal policy is clear with respect to human embryonic stem cell research:

- Federal funding (NIH, National Science Foundation, Department of Defense or any other federal agency) may not be used directly or indirectly for research on non-registered hESC lines.

Federal policy does not prohibit research with non-registered hESC lines, but the above limitation requires investigators to secure non-federal sources to

support the activities. Non-federal sources include awards (grants, contracts or gifts) from private sponsors and state agencies.

- Research on non-registered hESC lines must be performed with non-federal funding.

Because of the federal restriction, stem cell investigators and administrators should closely monitor research activities in order to prevent the shift of non-registered stem cell research costs to federal awards.

Allocation of Costs – Investigators and department administrators should continue to follow the cost principles described in OMB Circular A-21 and the Cost Accounting Standards. In addition, investigators and department administrators should develop an allocation methodology for expenses that are split between or among projects. Cost allocation can be based on actual usage, a percentage determined by the quantity of activities performed or the number of staff working on each project, or another reasonable method. In any case, the methodology must be documented in writing for audit purposes by the department and consistently applied to costs during the life of the project unless justified by documented changes.

1. Personnel Costs (Salaries and Fringe Benefits) – All personnel compensated for performing research on non-registered hESC lines must be paid from non-federal funds.

Confirmation of cost allocation is provided by the Principal Investigator or the direct supervisor of the individual regularly reviewing time sheets or expenditure ledgers and, for federally-supported projects, certifying quarterly effort reports (Personnel Activity Report) for personnel. This is especially important for personnel splitting time between research supported by federal awards and research involving non-registered hESCs.

Due to the nature of federal awards that support a major portion of salary and benefits, e.g., Mentored Scientist and Career Scientist, it may be difficult to document an allocation methodology separating federal training/research activities from non-registered research activities. To discuss the acceptability of an investigator's plan to separate costs, please contact your Officer in OR/Sponsored Projects.

2. Students (undergraduates, graduates, postdoctoral) – All employed students performing research on non-registered hESC lines must be paid from non-federal funds. Students who are supported by federal training grants or fellowships are not eligible to participate in projects involving non-registered hESC lines due to the impracticality of separating training and research activities. If the

situation arises, please obtain advice from your Officer in OR/Sponsored Projects.

3. Expendable Supplies – Excess supplies purchased, but unused, on federally funded projects may not be used for non-registered hESC research. New supplies purchased for the performance of research on non-registered hESC lines must be charged to non-federal funds.

It is recommended that a separate supply inventory be established for projects utilizing non-registered hESC lines. In situations where federally-supported hESC research and non-registered hESC research are conducted in close proximity, inventory purchased with federal funds should be clearly identified as unavailable for use in other projects. This may, but need not, include maintaining locked supply cabinets, usage logs, or color tags indicating availability or unavailability for non-registered hESC lines.

4. Equipment –Federal regulations in OMB Circular A-110 (Section C.34) and 45CFR §74.33 and §74.34 apply additional restrictions on the use of equipment. Note the equipment definition in Section II.

In some cases, use and disposition of equipment depends upon the Fair Market Value of the item. Determinations must be obtained in writing from the UCSB Equipment Manager, 805-893-7377. In the following section, the term “owned by” means “title held by.”

Equipment purchased solely for use in research on non-registered hESC lines must be charged to non-federal funds.

Equipment owned by UC may be used for non-registered hESC line research if the equipment was purchased solely with non-federal funds or if the title to the equipment belongs to UC. (Note: If previously funded by the federal government, the government must relinquish/transfer title to UC before use on non-registered lines.)

Equipment owned by the federal government may be used for non-registered hESC research only in the following circumstances:

- pursuant to approval of the appropriate federal agency; or
- UC purchases the equipment from the federal government and has documentation of such transaction, including title transfer.

Equipment purchased as a shared resource and funded by federal and non-federal sources may be used for non-registered hESC lines research, only if the use is thoroughly documented and does not exceed the non-federally-funded proportion of usage based upon the purchase share. The Principal Investigator or the supervisor of the research equipment is responsible for maintaining a log of equipment

utilization. This log should identify any use on projects involving non-registered cell lines and provide periodic cost analysis to ensure appropriate use.

5. Recharge Activities – Recharge activities are approved through Budget and Planning to provide services to other campus units at rates calculated to recover the costs associated with that service. Any project utilizing non-registered cell lines must pay for recharge services with non-federal funds.

For recharge activities established in whole or in part with federal funds, the proportionate use for non-registered stem cell research should not exceed the percentage of non-federal support in the purchase price. See also Allocation of Costs.

6. Subawards, Consultants, Travel and Other Expenses – Expenditures in these categories related to research on non-registered hESC lines must be charged to non-federal funds. Cost allocation should follow the above concepts and documentation methodologies.

C. FACILITIES MANAGEMENT

1. Shared Space - The National Institutes of Health acknowledge that research on registered hESC lines and non-registered hESC lines may occur in the same laboratory space or room provided that an effort is made to separate and identify costs with the appropriate funding source. However, in order to ensure adequate management systems exist based upon these Interim Guidelines, UCSB has determined that non-registered hESC research should be conducted in space that is separate from federally-funded projects. If it is necessary to co-locate federal projects and non-registered hESC research, investigators should submit a plan to the Vice Chancellor for Research through their respective dean outlining a plan to manage the projects in a manner that guarantees compliance with federal costing policy.
2. Federally-Supported Facilities – UCSB investigators performing research involving non-registered hESCs may not use facilities constructed or supported directly by the federal government.