CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Scientific and Medical Accountability Standards
Working Group
Draft Briefing Paper:
Use of Embryos Created for Reproductive Purposes with Paid Gametes[1]

Background Acceptably Derived Cell Lines

The CIRM MES regulations contain provisions governing the derivation and use of hESC lines. Section 100080 established performance criteria for "acceptably derived" cell lines. Section 100080(a)(2)(B) specifies that CIRM-funded researchers may not utilize hESC lines derived from embryos created with paid gametes.

§ 100080 Acceptable Research Materials

All covered stem cell lines used in CIRM-funded research must be "acceptably derived."

(a) To be "acceptably derived," the stem cell line must meet one of the following criteria:

(2) The stem cell line is derived from human gametes, embryos, somatic cells, or tissue under the following conditions:

(A) Donors of human gametes, embryos, somatic cells or tissue gave voluntary and informed consent; and
(B) Donors of human gametes, embryos, somatic cells or tissue did not receive valuable consideration. This provision does not prohibit reimbursement for permissible expenses as defined in California Code of Regulations, title 17, section 100020, subdivision (h), as determined by an IRB; and
(C) Donation of human gametes, embryos, somatic cells or tissue was overseen by an IRB (or, in the case of foreign sources, an IRB-equivalent); and
(D) Individuals who consented to donate stored human gametes, embryos, somatic cells or tissue were not reimbursed for the cost of storage prior to donation.

This provision has two operational impacts:

(1) CIRM grantees may not derive cell lines from IVF-embryos containing paid gametes, and

(2) CIRM grantees cannot use hESC lines derived from IVF-embryos containing paid gametes.

[1] The term "IVF-embryo" refers to embryos originally created for reproductive purposes (as opposed to embryos created exclusively for research).

Policy Context

Nationally, the CIRM policy deviates from other jurisdictions that have developed policies to advance stem cell research. This deviation has raised concerns over the ability of CIRM researchers to utilize materials derived under other jurisdictional policies or the National Academies Guidelines. Table 1 summarizes policies in states with stem cell research programs, the NAS guidelines and Canada's Institutes for Health Research.

Table 1: Summary of State and Jurisdictional Policies

State or Jurisdiction		Derivation: Can IVF-embryos containing paid gametes be used to derive new hESC?	Utilization: Can hESC lines derived from IVF-embryos containing paid gametes be used?
CA-CIRM		No	No
Canada CIHR		No	No
CT		Yes	Yes
MA		Yes	Yes
MD		Yes	Yes
NAS		Yes	Yes
NJ		Yes	Yes

Data compiled in collaboration with the Interstate Alliance for Stem Cell Research (IASCR)

Research Findings

At the February 28, 2008 SWG meeting, staff were requested to perform additional research to evaluate the scientific implications of this standards. The following activities have been or continue to be performed:

- e-mail surveys to funded institutions asking them to describe the impact of this standard on the availability of hESC. (May, 2008)
- Telephone and in-person interviews with researchers, research administrators and cell registry developers to discuss regulatory impact. (Ongoing)
- An analysis of cell line utilization in CIRM grants to determine if specific lines are not being utilized by CIRM grantees. (Ongoing)

Comments fell into three general categories (1) scientific concerns over access to materials, (2) administrative concerns over the ability to verify the payment status of established cell lines, and (3) social and ethical concerns related to excluding certain donors.

Scientific Concerns

There was a general sense of lost opportunity among the research community. However, it is not clear if there has been an impact on research activities. For example, one CIRM-

funded researcher indicated that the current regulations have not hindered his ability to access scientifically useful cell lines.

> *We, however, have lost significant opportunities for work with stored embryos that would have been supplied by very willing donors but the eggs used to create the embryos were supplied by women who were paid beyond the CIRM restrictions.*

Respondents indicated that it is difficult to evaluate impact at this time, but as research progresses there are issues to consider. For example, variability in embryo quality was cited.

> *It is true that paid donor oocytes represent about 12% of ART cycles [according to the CDC], but donor oocytes generally come from younger women and result in better reproductive outcomes. This may have implications for research because these embryos may be also results in successful derivation.*
>
> *It is difficult to anticipate the impact of (payment) restrictions on outside cell lines at the moment because no one knows what they might be missing. Up until now the NIH lines have been a safe bet that allows you to get the job done. It is ironic to think though that in the future we may need NIH funding to utilize lines not allowed by CIRM.*

One SCRO chairperson also indicated that there may be uses for surplus embryos other than stem cell line derivation, and the "quality" issue cited above may be important.

Administrative Concerns

Research administrators raised concerns about data limitations inherent to the field. This concern was echoed in discussion with stem cell registry developers who indicated that banks and registries have focused on ensuring proper consent for embryo donation. One administrator from a bank that accepts embryos (created outside the institution) from individuals interested in donation indicated that embryos containing paid gametes are typically rejected because they are not able to obtain adequate consent from the original gamete donors. Another administrator indicated that this is not a problem when embryos are created at the institutional IVF clinic because detailed consents are obtained.

Researchers and administrators indicated that much of the international focus has been dedicated to consent and oversight. This point was echoed in discussions with registry developers who indicated primary attention given to (1) embryo "source" and (2) consent. The embryo source is important because many jurisdictions limit hESC utilization to lines created from embryos originally created for reproductive purposes ("surplus" embryos). Source categories for registries include IVF-embryos, research embryos/SCNT, parthogenesis and iPS. Obtaining consent forms and information about the consent and oversight process has also been a priority. Less emphasis has been given to payment status of established lines.

> *When there is uncertainty regarding payments for embryos then they are not getting approved for new derivations. Remember we are still at a stage where we*

> *are dealing with a stock of embryos that were created years ago. These embryos predate the regulations and folks were not focused on this issue so there is uncertainty.*
>
> *The challenge is even greater for derived lines. There is a lot of derivation going on and this information is not readily available. In many instances researchers are defaulting to NIH or UK lines because the regulations say we can; not because we know they conform to exact specifications.*

Representatives from Europe indicated that payment tends to be more of a U.S. issue. For example, in Europe payments are less common, and when they occur they typically involve smaller sums. As a result, less attention has been give to this issue in public policy and registry development.

Social and Ethical Concerns

Researchers, administrators and patient representatives expressed concern that the regulations limit donation. One patient representative suggested potential donors value the opportunity to contribute to research.

> *The CIRM regulations covering such donations for stem cell research makes no ethical, practical, or logical sense since:*
> 1. *the stored embryos that were created from the eggs that were paid-for will be destroyed (just like any other stored embryos under such conditions), and*
> 2. *there was no undue influence, as defined by CA laws, in the creation of the embryos.*

Policy Questions

The current policy governing "acceptable research materials" raises a number questions policy questions. It may be helpful to consider these questions independently for policy evaluation purposes.

1. Should CIRM funded researchers be able to use "outside" hESC lines if they are derived from IVF-embryos created with paid gametes?
2. Should CIRM funded researchers be able to utilize hESC lines derived from IVF-embryos created with paid gametes under an "authorized authority"?
3. Should CIRM funded researchers be able to utilize IVF-embryos created with paid gametes to derive new lines?