Summary of Regulatory Issues

iPS Research

At this time the MES regulations require review and oversight of basic research involving somatic cell reprogramming and iPSC experiments. There may be emerging issues that deserve consideration or clarification.

Issues for consideration:

- Novel application of reprogrammed cells: Reprogrammed cells or hESCs may have unique developmental potential. Are there special considerations or conditions that should be placed on potential applications? Note the recently approved revisions to the MES regulations allow anonymous cells and tissue (e.g. unknown consent status) to be used in reprogramming experiments; are there "down-stream" considerations regarding the use of these cells – for example, transplantation to humans?

Payments to Gamete Donors

The issue of payment for gametes, particularly oocytes, is well described.[1] The CIRM regulations prohibit payments to donors of gametes, embryos and somatic cells for funded research. The prohibition extends to hESC lines derived in other jurisdictions.

> *All covered stem cell lines used in CIRM-funded research must be "acceptably derived." To be" acceptably derived," the stem cell line must have been derived under the following [condition]:Donors of gametes, embryos somatic cells or human tissue did not receive valuable consideration.* §100080(e)(2)

Approximately 12% of stored embryos, created for reproductive purposes (IVF), contain gametes from paid donors (paid-IVF-embryos).[2] Under CIRM rules grantees may not utilize paid-IVF-embryos to derive hESC lines. This regulation extends this prohibition to the use of hESC lines derived in other jurisdictions from paid-IVF-embryos. This restriction exceeds a number of state regulations and other guidelines – see attachment 1. As illustrated in attachment 1, the acceptability of hESC lines derived from paid-IVF-embryos remains a source of regulatory inconsistency. Further, terms such as "payment," "compensation," and reimbursement are subject to different interpretations.

Issues for consideration:

- Exclusion of cell lines for payment: Exclusion of paid-IVF-embryos from the research stream has been raised as a concern. Other jurisdictions including

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[1] Isasi, R. and B. Knoppers, *Monetary payments for the procurement of oocytes for stem cell research: In search of ethical and political consistency.* Stem Cell Research, 2007. **1**: p. 37-44. http://www.sciencedirect.com/science/journal/18735061

[2] see http://www.cdc.gov/ART/ART2005/section4.htm

Massachusetts and Connecticut had determined paid-IVF-embryos do are eligible for derivation research. Should all paid-IVF-embryo lines continue to ineligible for use in CIRM-funded research?

Egg Sharing Arrangements for Outside Lines

Egg sharing refers to arrangements where the oocyte donor receives services in exchange for providing (*sharing*) oocytes for research. Such arrangements have been approved by the HFEA to allow women access to IVF services. A critical question for CIRM is whether all stem cell lines derived under HFEA license can be used by grantees.

- Lines recognized by authorized authority: How should the regulations treat such lines if they are derived under the auspices of an established regulatory authority where there may be variance from regulations governing CIRM grantees?

Consent for Research Materials

Voluntary informed consent is fundamental to research ethics. Recognizing that embryonic stem cell research raises numerous moral and ethical concerns, the NAS Guidelines, CIRM regulations and other jurisdictional policies require consent from all gamete donors for use of a human blastocyst in research.

> *When donor gametes have been used in the IVF process, resulting blastocysts may not be used for research without consent of all gamete donors.* NAS Guidelines 2005

A portion of existing frozen embryos where created using gametes from anonymous donors. It is impossible to re-contact anonymous donors to obtain consent for hESC line derivation. Typically, under state laws "dispositional authority" for embryos created using donor gametes is maintained by the woman in the IVF process. CIRM is aware of hESC lines that have been derived from embryos created using gametes from anonymous donors. Such hESC do not conform to the CIRM regulations or the NAS guidelines, and they are, therefore, ineligible for use in funded research.

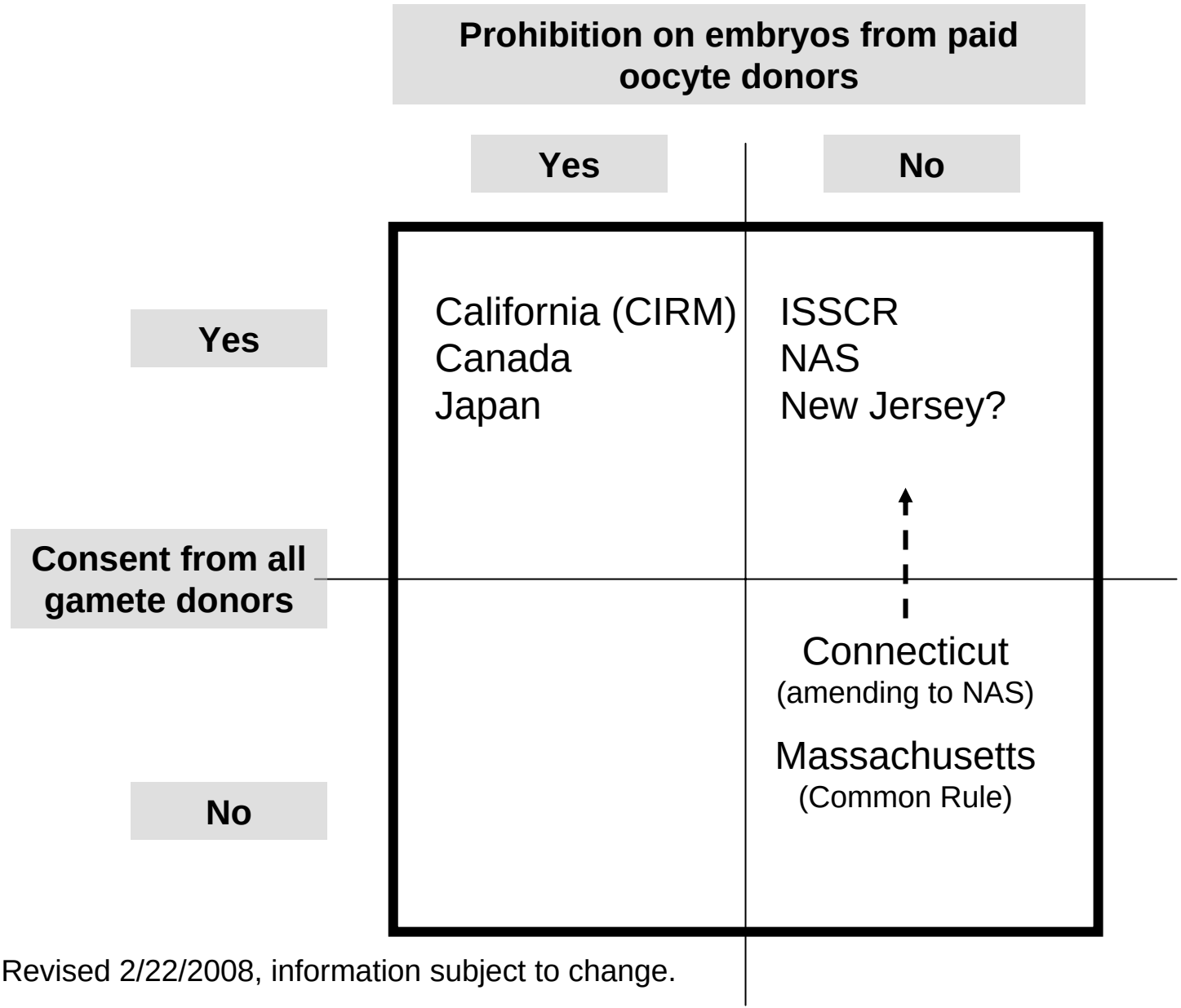
Issues for consideration:

- Exclusion of "historic" lines for consent: CIRM is aware of one clinical-grade commercial line that does not conform to the dual consent standard. One line in question was derived prior to the effective date of the CIRM regulations. Should Are "grandfathering" provisions be considered for scientifically significant materials developed prior to current regulatory requirements? What should be the process for making this determination?

Reporting Requirements

See correspondence and response to comment pertaining to this item.

Regulatory conditions for derivation of hESC from stored (frozen) embryos created for reproductive purposes, but no longer required by recipient.



Revised 2/22/2008, information subject to change.