Summary of Major Modifications to National Academies (NA) Guidelines Recommended by the Standards Working Group

Scope of Chapter:

To be consistent with CA law, the regulatory scope of the Interim Regulations is limited to *CIRM grantees* and *all research funded by CIRM*. Subsequent sections (e.g. 100002 and 100003) describe *research eligible for CIRM funding*.

Approved Cell Lines:

Section 100002(b), was added to identify existing cell lines available for use in CIRM-funded research.

> (a) hES cell lines approved by the National Institutes of Health, deposited in the United Kingdom Stem Cell Bank, or derived by, or approved for use by, a licensee of the Human Fertilisation and Embryology Authority shall be deemed to have complied with the requirements for informed consent and donor compensation and therefore do not require documentation by the ESCRO committee or equivalent body designated by the investigator's institution. hES cell lines derived under equivalent standards to the United Kingdom Stem Cell Bank or such other benchmark organizations, as recommended by the Standards Working Group and approved by the Independent Citizens' Oversight Committee would also qualify for exception for documentation for informed consent and donor compensation. The equivalency could be determined by the ESCRO committee or the Standards Working Group or a committee established by the Standards Working Group and approved by the Independent Citizens' Oversight Committee.

ESCRO Committees:

Language was added to Section 100006(a) to allow two or more research institutions to form a joint ESCRO committee. The NA Guidelines required each institution to create an ESCRO committee. The joint ESCRO committee is intended to provide flexibility. As in the NA guidelines, the "primary activity of the ESCRO Committee will be to assure that inappropriate research is not conducted and the controversial research is well justified and subject to appropriate additional oversight". Stanford and other institutions have relied on that guidance to structure their ESCRO bodies as providing oversight rather than necessarily performing all functions within the ESCRO or ESCRO entity. I think that this is what is intended in the CIRM Guidelines, but a statement in this summary similar to the NA clarification would be very helpful to the community.

The ESCRO committee registry requirements are described in greater detail using language that was originally included in the NA Guidelines for storage (e.g. Banking) of cells. This language is intended to reduce ambiguity by identifying who is responsible for what requirements.

(6) Maintain, at a minimum, a registry of stem cell lines, including information regarding all of the following, unless the requirement for documentation has been waived pursuant to subdivision (b) of section 100002: (1) whether the cells were obtained ethically and with informed consent in a manner consistent with Section 100007; (2) whether they are well-characterized and screened for safety; (3) the conditions under which they are maintained and stored.

Procurement of Gametes, Blastocysts or Cells for hES Generation

One inadvertent change was made in Section 100007(f)(2) on consent. This change results in a significant deviation in intent from the NA Guidelines. In the NA Guidelines, it is optional to allow donors to consent to some forms of hESC research but not others, in the Guidelines Recommended by SWG, it is mandatory. A recommendation for restoring the intent of the NA Guidelines is offered by the President (see cover memo).

(2) The consent process shall ascertain whether donors have objections to any specific forms of research to ensure that their wishes are honored, and donors shall be offered the option of agreeing to some forms of hES cell research but not others.

Prohibited Activities:

In Section 100008(e), the time limit for use of intact embryos is set at 12 days after cell division begins as specified in Proposition 71, rather than 14 days as specified in the NA Guidelines.

Sharing & Banking of Cell Lines:

Section 100009, contains new language to encourage participation in central repositories for human embryonic stem cell lines. Section 100009(a), indicates CIRM's intent of making materials available through one or more central banks. CIRM itself will likely establish a stem cell bank and require investigators to deposit lines in this bank.

(a) Institutions engaged in CIRM-Funded hES derivation or research shall be encouraged at present and possibly mandated in the future to create or participate in central repositories for hES cell lines, including through partnerships or augmentation of existing quality research cell lines repositories, and shall adhere to high ethical, legal, and scientific standards consistent with Section 100009(a) and Section 100007.

Section 100009(b), indicates that cell lines derived or modified with CIRM-funding are required to be placed in a cell bank. The SWG felt very strongly about the principle of making cell lines available, but recognized that specific requirements might be better given grants policy or guidance documents.

(b) Cell lines derived or modified in any way with CIRM-funds are required to be shared through a well recognized stem cell bank that will make the lines widely available to investigators. Cell lines derived or modified in any way with CIRM-funds are required to be deposited in a bank in a timely manner.

Section 100009(c), all additional banking requirements in the NA Guidelines are "encouraged" but not "required."