December 19, 2005

To: SWG

Fr: CIRM

Re: Update on Public Comments on Draft CIRM Regulations

Since our posting of the 12/1/05 CIRM Draft Medical and Ethical Standards (MES) Regulations, we have received a considerable number of comments from research institutions that will be affected. Comments have been received in writing and at a workshop attended by institutions performing or intending to perform stem cell research in California. This memo attempts to summarize comments related to thematic areas. Solid bullets (•) identify points that emerged in discussion. Hollow bullets (○) with blue text identify staff responses.

Regulatory Need: There were a number of comments aimed at ensuring that the CIRM MES Regulation do not make CIRM-funded research overly burdensome. The major theme was that CIRM regulation should complement existing oversight mechanisms.

- There is a long history of effective institutional oversight of research.
- New rules and regulations should target issues not adequately addressed by existing rules and regulations.
- For regulated institutions CIRM MES Regulations should tell us *what else* we need to do by identifying the *true ethically problematic* issues.

- *CIRM MES Regulations are focused on unique issues related to gamete and blastocyst donation which are not addressed in current research regulations.*
- *CIRM may also be funding private sector research which may not be regulated by many of the same rules governing academic intuitions.*

Scope of Regulations: Expanding the scope of the regulation from embryonic to human stem cells raised concerns.

- Embryonic stem cells are comparatively easy to define; adult stem cells require a precise definition.
- Definition should not unintentionally regulate routine research utilizing anonymous human tissue.
- Researchers want clear guidance on how to handle stored tissue samples.

- *By focusing on human stem cell lines derived from human subjects or through the procurement of gametes and blastocysts one may omit stored tissues from the scope of regulation.*

ESCRO/IRB: There is a range of views regarding the need for scientific and ethical review and the role of the ESCRO committee. Major topics included (1) membership (2) the issue of scientific merit, (3) ESCRO/IRB authority, (4) flexibility and (5) compliance, assurance and monitoring.

- CIRM should state *lay member* rather than *not affiliated with institution*.
- CIRM will review and fund proposals based on scientific merit, so doesn't a decision to fund imply high scientific merit?
- NA Guidelines ask the ESCRO to provide special scrutiny for research in which the identity of the donors is readily ascertainable to the researchers.
- The ESCRO and IRB will have overlapping authority to review ethical consideration.
    - In contrast to the previous point some commentators indicated that multiple reviews can be helpful. They described experiences where additional reviews have resulted in improvements in research protocols.
    - An existing ESCRO member also pointed out that ESCROs will have a much less intensive work load than an IRB providing the ability to focus on the stem cell research issues.
- Why doesn't CIRM indicate what needs to be reviewed and let the institutions sort out the details?
- What does adequate ESCRO *notification* entail?
- There is not a specific monitoring function for the ESCRO, *we can only have so much trust*.

- *CIRM may require ESCRO scientific review and approval as a condition of applying for a CIRM grant.*
- *The National Academies report provides a compelling rationale for an added level of review and oversight. The (ESCRO) committee will not substitute for an Institutional Review Board but rather will provide an additional level of review and scrutiny warranted by the complex issues raised by hES cell research.*
- *The draft regulations already have a high degree of flexibility; for purposes of ensuring accountability (particularly in a regulatory context) some responsibilities are best specified as who is responsible for what.*
- *CIRM will require reporting in its Grants Administration Policy to facilitate monitoring and institutions are free to develop internal procedures and policies to ensure compliance.*

Informed Consent: Three issues: (1) waiting period; (2) informed consent by someone separate from the researcher; (3) flexible vs. prescriptive standards; (4) objections to specific studies; and (5) evaluation of comprehension received multiple comments.

- Having a waiting period between consent and the procedure seem overly paternalistic.
- Who would be the appropriate person to provide 3rd party consent? It will be difficult to separate from the research team for issues such as expertise in a specific clinical procedure and the associated risks.

- Informed consent requirements may be a challenge for IVF clinicians who do research.
- Consent issues may be one area where a prescriptive approach is useful. Institutions need examples to strive for consistency.
- There are real practical problems to allowing donors to object to specific types of research; one can't predict future types of research; consent should be for an irrevocable donation.
- Evaluation of comprehension is an "interesting" idea but potential to open a big "can of worms."

Other Specific Comments:

- Objecting to specific types of research could present very practical problems and even result in discrimination; donation should be open ended and irrevocable.
- Putting limits on who can donate (for example only parents) is one approach for reducing potential ethical problems.