

IASCR Notes from Discussion of the Draft NIH Guidelines

On May 5-6, the Interstate Alliance on Stem Cell Research convened to consider the NIH draft Guidelines on Human Stem Cell Research. The meeting included discussions with NIH staff on the Guidelines and the process for their development. Following the meeting with NIH staff, the IASCR participants engaged in discussion to consider issues related to the draft Guidelines. This meeting summary describes the primary policy issues identified by the IASCR membership.

The IASCR is a voluntary body whose mission is to advance ethically and scientifically worthy stem cell research by fostering effective interstate collaboration and by promoting efficient and responsible use of public funds. The IASCR was established to facilitate coordination among states that wish to advance stem cell research. IASCR emphasis has been on the evaluation and development of policy mechanism to support the sharing of data, resources, and cell lines across state borders to ensure the efficient development of research programs.

Throughout the discussion, IASCR participants commended the prompt response to President Obama's Executive Order 13505 and indicated their desire to work with the NIH to support ethically responsible and scientifically worthy stem cell research. The IASCR participants also recognized the extraordinary effort of NIH staff to perform outreach to stakeholders and the public on this important health policy issue. This effort was evidenced by NIH participation in the IASCR meeting.

In the subsequent discussion among the IASCR participants, a number of issues emerged, and they are summarized below to advance our common organizational goals of supporting ethically and scientifically worthy stem cell research.

- **IASCR member states funding hESC research apply independent oversight to ensure ethically responsible and scientifically worthy research.**

Federal law (the Common Rule) provides a regulatory framework for protecting research participants. The Common Rule requires institutional review boards (IRBs) to review and approve the process for obtaining voluntary informed consent from individuals participating in research – including the donation of cells and tissues.

States funding hESC research have applied oversight through expert review bodies, following principles of the Common Rule, to the donation of embryos and other research materials for hESC research. The Common Rule supports ethically responsible and scientifically worthy research by:

- Requiring independent oversight such as through IRBs which have extensive experience reviewing informed consent in the context of human tissue research;
- Ensuring a process for voluntary informed consent including the review of consent procedures performed outside the United States;
- Requiring no undue inducements to donors.

Simply reiterating the informed consent elements of the Common Rule and acknowledging that existing independent oversight mechanisms such as IRBs are sufficient in the NIH Guidelines, rather than setting new and unique requirements, would support ethically responsible oversight. As a reminder, informed consent as mandated by the Common Rule includes:

- A statement that the study involves research
 - An explanation of the purposes of the research
 - The expected duration of the subject's participation
 - A description of the procedures to be followed
 - Identification of any procedures which are experimental
 - A description of any reasonably foreseeable risks or discomforts to the subject
 - A description of any benefits to the subject or to others which may reasonably be expected from the research
 - A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
 - A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
 - For research involving more than minimal risk, an explanation as to whether any compensation is offered, and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained
 - An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
 - A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits, to which the subject is otherwise entitled
- **Many established hESC lines have been derived under published federal agency guidance that, if extended voluntarily to all derivations of hESCs, fulfills the core standard of responsible and scientifically worthy research in the draft NIH guidelines.**

There has been published federal agency guidance (via OHRP) on stem cells since 2002. This guidance says that it applies to federally funded work, plus other research when institutions voluntarily agree to follow the Common Rule "across the

board." The guidance says that when there's an interaction with subjects or identifiable information is used, the Common Rule applies.

State grantees and other derivers that voluntarily followed the 2002 federal agency stem cell guidance, and voluntarily extended it to all embryo donations and all derivation work, should be recognized as having performed responsible stem cell research, and resulting lines can be used with federal funds. The guidance may be found here:

<http://www.hhs.gov/ohrp/humansubjects/guidance/stemcell.pdf>

Research institutions have taken the initiative to apply this heightened standard even when not mandated by law. NIH or Federal policy should not later change the terms which would also have the unintended consequence of wasting embryos that patients specifically donated with consent to research.

- **Acknowledging the established system of independent oversight, which states have mandated and other entities have followed voluntarily, could address concerns over the availability of hESC lines and blastocysts donated for research.**

IASCR members have expressed concerns that some lines may be rendered ineligible on purely technical grounds if the detailed conditions and consent criteria in the draft NIH Guidelines are applied retroactively. Such an outcome would be unfortunate given many older lines were derived according to the higher federal standards for human subjects protection described above. An analogous situation exists for some donated blastocysts. Nationwide there are a number of tissue banks that routinely collect blastocysts for research. These tissue banks are an important source of material for hESC derivation. Tissue banks adhere to detailed procedures for consenting donors and complying with state and national laws. These blastocyst should not be disqualified on purely technical grounds. Donors hope to contribute to humanity by supporting scientific discovery and medical research.

States have applied the established system of IRB oversight in a manner that enables a determination that hESC lines and blastocysts have been procured in accordance with the higher federal standards. To support the common mission of advancing ethically responsible science, NIH should consider recognizing that when the established system of robust independent oversight (such as through an IRB) has been used, that should enable the use of responsibly derived and scientifically worthy materials. As indicated above the Common Rule already incorporates the major consent elements proposed in the draft NIH Guidelines. Recognizing the IRB oversight approach in the NIH Guidelines could allow use of materials procured according to the higher federal standards, including:

- Eligible lines approved for research use between 2001-2008;
- Eligible lines derived in the United States;

- Eligible lines derived outside the United States;
- Eligible donated blastocysts currently stored in tissue banks.
- **Parthenogenic cell lines may be derived and utilized in member states provided they meet standards for ethical derivation.**

Established parthenogenic cell lines represent an important scientific resource due to their unique genetic constitution and method of derivation. Research involving the comparison of embryo derived lines, induced pluripotent lines from somatic cells, and parthenogenic lines may be particularly informative for understanding a range of issues related to mechanisms of reprogramming and differentiation. In addition, the unique immunologic profile of parthenogenic lines may be particularly important in the development of cell products for clinical transplantation.

- **Registering hESC lines determined to be compliant with national and state guidelines or regulations.**

Member states have adopted regulations or executed legally binding contracts requiring research institutions to determine that hESC lines utilized in sponsored research conform to specific consent and robust independent oversight requirements. Consistent with the proposed draft NIH guidelines, states require institutions to assure hESC lines comply with these requirements.

Institutions have reported that the continued evaluation of hESC provenance represented the major resource commitment for oversight committees. It was common for multiple institutions to be evaluating the same lines resulting in a duplication of labor.

To support more efficient use of research funds, consistency and better certainty among NIH grantees, NIH should consider supporting initiatives designed to determine the provenance of established lines. The compliance status of lines could then be made available to funded researchers through a registry or database. Some IASCR member states are actively evaluating such an approach. Registration efforts could be enhanced by a coordinated national effort.