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NIH EXECUTIVE SECRETARIAT

Dear Harold:

In my January 22nd letter to you I provided an outline of NBAC's plans for completing our report on research involving human stem cells, and our hope to provide the President (and others) with the benefit of any conclusions we might come to along the way. Given your own interest in NBAC's work, I wanted to share with you some of the commission's thinking at this point, even though no specific conclusions have been reached. This thinking is preliminary and is based on our most recent meeting (March 2-3), and reflects my views.

We seem to be coming to general agreement that federal funding for research involving the derivation and use of human embryonic stem (hES) cells should be permitted for at least the following categories of research: research using hES cells obtained from fetal tissue, and research using hES cells obtained from embryos in excess of those needed from infertility treatments. The commission is less close to agreement on the appropriateness of using federal funds to use (or derive) hES cells from embryos intentionally produced for research purposes (for example from somatic cell nuclear transfer), but I am confident that we will have something to say about this.

I am also enclosing a working draft, "Points to Consider," for your information. I had asked NBAC staff to prepare this document for two reasons: first, it may provide a useful summary of many of the ethical issues that might arise in research involving hES cells; second, it could, eventually, be included in our report as a suggestion for use (or adoption) by others. The commission has taken no position on this document at this time, but you may find it useful as you continue your thinking on how NIH will consider ethical issues. I recognize that this document reflects the model utilized by the Recombinant DNA Advisory Committee, but we took no position on whether it should be used by any particular group in that way.

We remain on target for completing our report by June, and I hope you will continue to follow our deliberations. I would be pleased to provide any clarification on any of these points.

Sincerely,

Harold T. Shapiro
Chair

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NBAC STAFF DRAFT

Points To Consider In Evaluating Basic Research Involving Human Stem Cells

The following *Points to Consider* are presented not to prejudge the question whether human stem cell research should be conducted using federal funds. Rather, this document describes some of the ethical, clinical, scientific, and legal issues that could be considered when designing and/or reviewing studies that involve access to and use of human stem cells. These *Points to Consider* are only relevant for designing and evaluating studies where the role of the individual(s) who provide gametes, fetal tissue or embryos is limited to providing these materials for research that is intended to develop generalizable new knowledge. *These Points to Consider do not apply to situations in which an individual would be the recipient of a stem cell-based therapy, nor do they apply to studies involving human/animal hybrids.*

I. Scientific and Research Design Considerations

Several issues arise when designing research involving human stem cells, consideration of which would help ensure that research is well-designed, important, feasible, and timely. These issues are of particular significance given the nature of the materials.

- A. The Source From Which The Human Stem Cells Will Be Obtained
 - 1. From existing cell lines (such as neuronal or hematopoietic stem cells)
 - 2. From aborted fetal tissue (following spontaneous or induced abortion or surgical termination of ectopic pregnancy)
 - 3. From stored/spare embryos obtained from infertility treatment
 - 4. From embryos produced for research purposes (including somatic cell nuclear transfer)
- B. Previous Research Involving Animals
- C. Alternatives To Using Human Stem Cells
- D. Future Plans And Conservation Of Gametes, Fetal Tissue, and Embryos
 - 1. Will stem cells be produced and stored for later use?
 - 2. If a particular protocol is being proposed using stored embryos, does it use only the number of embryos necessary?
 - 3. What plans exist in the event that additional stem cells are needed?
- E. The Research Setting
 - 1. Are the investigators scientifically qualified to carry out the proposed research?
 - 2. Is the research environment (including facilities) appropriate for the conduct of research involving stem cells?

II. Identification of Providers and Donors, Recruitment Practices, and Compensation

Several issues in identifying individuals (or couples) who may be asked to consider providing gametes, fetal tissue, or embryos for research involving human stem cells, consideration of these issues could help to ensure that no inappropriate burden, inducement or exploitation would occur.

- A. Identification And Recruitment Practices
 - 1. Are potential donors or providers identified through advertisements to the general public? Are they identified through direct solicitation? Do they self-select?
 - 2. Is the selection of such individuals equitable and fair?

3. Are these individuals vulnerable to undue influence, coercion or exploitation? Does the recruitment method raise concerns about undue influence or coercion of the prospective donors? embryos?
4. Are the potential donors capable of giving an informed consent?
5. In which circumstances is it appropriate to identify and recruit an individual as well as his or her partner?

B. Compensation And Reimbursement

1. Will any financial compensation be paid to individuals (or couples) who provide source material ?
2. Does the compensation exceed the costs already being incurred (for example, the cost of embryo storage)? Will this fact be disclosed?
3. Does the compensation reimburse the individual (or couple) for specific services (e.g., gametes, infertility services)?
4. When is the offer of compensation made relative to individual's (or couple's) decision to make available the materials from which stem cells will be derived?

III. Informed Consent

Several issues arise in the process of informed consent (including the content of consent forms); considering these issues would help to ensure that ensure prospective donors or providers of source materials would receive timely, relevant and appropriate information to make informed and voluntary choices

A. General Considerations For Individuals (or Couples) Who Provide Gametes, Fetal Tissues or Embryos

1. Who will obtain informed consent? Will a clinician and researcher be available to answer questions?
2. Is it appropriate for others to participate in the consent process (e.g., partner or family member)?
3. Will psychological support mechanisms be in place when needed?
4. Are the purposes of stem cell research (in general) fully described?
5. If a specific research protocol is being contemplated with stem cells obtained, is the protocol fully described?
6. What are the possible risks to the woman (or partner) from the procedure to obtain stem cells, and how will these be minimized?
7. Will the consent form clearly disclose that stem cell research is not intended to benefit them directly?
8. Is it clear that decisions to consent to or refuse the procedures to obtain stem cells will not enhance the quality of care they will receive?
9. Will individuals be informed that no medical or genetic information about the gametes, fetal tissue, embryos, or stem cells derived from these sources will be provided?
10. What measures will be taken to protect the privacy and confidentiality of individuals who provide gametes, fetal tissue or embryos?
11. Is the source of funding for research (public, private, public/private, philanthropic) disclosed?
12. What known commercial benefits, if any, are expected to arise for the investigators seeking to obtain human stem cells?

B. Issues Specific To Consenting To The Use of Fetal Tissue

1. Is there a description of what is usually done with fetal tissue at the institution at which individuals are undergoing termination of pregnancy? Is this information available in written form and provided to the individuals?
2. Is there a description that the decision to permit research will entail that research may begin immediately.

C. Issues Specific To Consenting To The Use of Embryos Obtained From Infertility Treatments

1. Is there a description of what is usually done with spare embryos at the institution at which individuals are undergoing infertility treatment? Is this information available in written form and provided to the individuals?
2. Will information be made available about whether the spare embryo was viable and normal or non-viable and abnormal?
3. Is there a description of options available (e.g., permit material to be used in research, cryopreserve, discard, donate to another couple for infertility treatment)?
4. Is it clear that the embryos used in research will not, under any circumstances, be transferred to any woman's uterus?
5. Is it clear that the research will result in the destruction of the embryo? Is the method described?

D. Issues Specific To Consenting To The Use of Gametes¹

1. Will individuals be informed whether embryos will be produced with the gametes (e.g., using *in vitro* fertilization, or somatic cell nuclear transfer?)
2. Is there a description of what is usually done at this institution with gametes not used for research?
3. Is there a description of options available (e.g., permit materials to be used in research, cryopreserve, discard, donate to another couple for fertilization and transfer)?
4. Is it clear that the embryos produced for research purposes (whether by IVF or somatic cell nuclear transfer) will not, under any circumstances, be transferred to any woman's uterus?

IV. Review Issues

Several issues arise in the review and oversight of research involving human stem cells; consideration of these issues will provide assurance that, regardless of the source of funding, appropriate compliance with applicable regulations, guidelines and other standards will occur. These considerations would supplement, not replace, applicable federal and state regulations.

A. Applicability of Relevant Regulations

1. What current guidelines, regulations, rule, or policies apply to the conduct of this research?
2. What mechanisms are in place to assure compliance with these regulations?

B. Applicability of Professional Practice Standards

C. IRB Review

D. Submission of Research Findings for Publication

E. Other Responsibilities of Investigators and Collaborating Clinicians

¹ Note: For persons who provide sperm anonymously, the details of the consent form and the specificity of the informed consent process may vary—EMM 2/15/99