TOPIC:

Human Stem Cell Research: 2009 NIH Guidelines

INTRODUCTION:

On July 6, 2009, the National Institutes of Health ("NIH") issued final "Guidelines for Human Stem Cell Research" ("Guidelines") __. The Guidelines implement President Obama's March 9, 2009 Executive Order 13505, "Removing Barriers to Responsible Scientific Research Involving Human Stem Cells __" as it relates to NIH-funded research. Executive Order 13505 permits the Secretary of Health and Human Services, through the Director of NIH, to "support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem cell research, to the extent permitted by law." It revoked prior restrictions put in place by former President George W. Bush, who limited federal funding for research involving human embryonic stem cells ("hESCs") to certain existing hESC lines.

The Guidelines took effect on July 7, 2009. On July 30, 2009, President Obama instructed other federal agencies and departments that support and conduct stem cell research to adopt NIH's Guidelines "to the fullest extent practicable in light of legal authorities and obligations __." He also gave such agencies and departments 90 days to submit to the Office of Management and Budget any proposed changes to existing guidance, policies, and procedures pertaining to stem cell research. In light of that directive, although this Note addresses NIH-funded research, other federal agencies can be expected to implement similar standards and processes for hESC research the agencies fund.

DISCUSSION:

Underlying Principles

The Guidelines are based on two core principles: (1) hESC research offers the possibility of better comprehending "human health and illness" and identifying "new ways to prevent and/or treat illness"; and (2) voluntary informed consent should be obtained from individuals who donate embryos for research purposes.

Basic Outline

The Guidelines answer several key questions regarding NIH-funded hESC research. Such questions include:

(1) From what sources may hESCs involved in NIH-funded research be derived?

(2) What types of hESC research are ineligible for NIH funding?

(3) How will NIH determine whether hESCs are eligible for use in NIH-funded research? What process will institutions need to follow to show that particular hESC lines satisfy the new NIH criteria?

(4) What is NIH's funding policy for research using hESCs derived from embryos donated before the Guidelines took effect, which may not always satisfy the new eligibility criteria?

(5) What is NIH's funding policy for research involving hESCs derived from embryos donated outside the United States, where hESC requirements may not mirror those adopted by NIH?

Basic Eligibility Criteria for NIH Funding

Subject to specified conditions, the Guidelines generally permit NIH funding of research that involves the use of NIH-registered hESCs __ and "certain uses of induced pluripotent stem cells." The various conditions imposed by NIH are discussed below.

The Guidelines identify several categories of stem cell research that are ineligible for NIH funding, even if the stem cells to be used would otherwise satisfy the Guidelines. For instance, the Guidelines make clear that NIH will not support research involving hESCs or human induced pluripotent stem cells that are "introduced into non-human primate blastocysts." Nor will NIH fund research that involves the "breeding of animals where the introduction of hESCs . . . or human induced pluripotent stem cells may contribute to the germ line." In addition, NIH rejected calls from organizations such as the Association of American Universities ("AAU") to expand the sources from which eligible hESCs may be derived __. Specifically, the Guidelines provide that NIH funding will not be available for research involving hESCs derived from sources such as therapeutic cloning (also referred to as somatic cell nuclear transfer ("SCNT")), parthenogenesis, or embryos created for research. In the preamble to the Guidelines, NIH explains that it declined to allow funding for research using hESC lines or pluripotent cells derived from these types of additional sources because such research raises "complex ethical and scientific issues" on which there is no public consensus.

The Guidelines further note that annual appropriations legislation prohibits "NIH funding of the derivation of stem cells from human embryos." Known as the Dickey-Wicker Amendment, the appropriations rider to which the Guidelines refer bans the use of federal funds for the creation of human embryos for research purposes or for research in which human embryos are "destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed" for federally-funded research on fetuses in utero __. Although there is some support among members of Congress to eliminate the limitations imposed by the Dickey-Wicker Amendment, such limitations remain in place to date.

Eligibility Processes and Conditions

Stem cells derived from embryos donated in the United States on or after July 7, 2009

The Guidelines describe two processes by which an institution can establish NIH funding eligibility for research that involves hESCs derived from embryos donated on or after July 7, 2009, the date on which the Guidelines took effect. The institution may either:

(1) Propose to use hESCs from the newly-created NIH Human Embryonic Stem Cell Registry ("Registry") __, which lists hESC lines that are approved for use in NIH-funded research and is updated as hESCs are reviewed and found eligible ("Option 1"); or

(2) Assure NIH that the hESCs proposed for use satisfy certain specified conditions, and submit supporting information ("Option 2"). NIH will make a determination as to eligibility and eligible lines will be added to the Registry.

If the institution determines to proceed under Option 2, it must assure NIH that the hESCs were derived from human embryos in accordance with seven criteria and provide certain supporting documentation such as consent forms and written policies for review by NIH. The seven criteria:

(1) Purpose of embryos' creation: The embryos were created through in vitro fertilization for reproductive purposes and "were no longer needed for this purpose."

Stem cells derived from embryos donated in the United States before July 7, 2009

Stem cell lines derived from embryos donated in the United States before July 7, 2009 also must satisfy the new eligibility requirements. The stem cell lines previously approved for NIH-funded research by the Bush administration are not exempt from the new requirements – that is, they are not "grandfathered."

An institution can use the two processes described above to establish NIH funding eligibility for research that involves hESCs derived from embryos donated in the United States before July 7, 2009. In addition, the Guidelines also create a third process, whereby hESC lines created prior to issuance of NIH's Guidelines that do not satisfy the specific informed-consent and other procedural requirements of Option 2 may nonetheless be considered and, where appropriate, approved by NIH for NIH funding. Institutions may submit, to a Working Group of the Advisory Committee to the NIH Director, materials such as consent forms and written policies. The submitted materials must show that the hESCs were derived from human embryos that (a) were created for reproductive purposes using in vitro fertilization, (b) were no longer needed for reproductive purposes, and (c) were donated for research purposes with the voluntary written consent of the donor.

In evaluating hESCs' eligibility for use in NIH-funded research, the Working Group will consider the principles espoused in Option 2. It will also consider whether, as part of oral or written informed consent communications, donor(s) were (1) "informed of other available options pertaining to the use of the embryos"; (2) "offered any inducements for the donation of the embryos"; and (3) "informed about what would happen to the embryos after the donation for research." In appropriate cases, it may also consider federal regulatory principles applicable to human subjects research (45 C.F.R. Part 46, Subpart A or the "Common Rule"); however, basic research on deidentified hESCs typically does not trigger applicability of the Common Rule. The Working Group recommends to the Advisory Committee whether hESCs should be found eligible. The Advisory Committee in turn makes its own recommendations to the Director of NIH, who renders final eligibility determinations.

Stem cells derived from embryos donated outside the United States

The Guidelines permit use of hESCs derived from embryos donated outside the United States either before, on, or after the effective date of the Guidelines. Institutions that seek NIH funding for research involving hESCs derived from embryos donated outside the United States generally must adhere to the processes and criteria described above for embryos donated before, on, or after July 7, 2009. NIH recognizes, however, that foreign governments "may not or cannot change their national donation requirements to precisely comply with the NIH Guidelines" and views "ethically derived foreign hESCs" as "an important scientific asset" for the United States. Accordingly, the Guidelines provide an alternate approval mechanism for foreign hESCs. Under that mechanism, institutions planning to use foreign hESCs in NIH-funded research may submit an assurance (and supporting documentation) that "the alternative procedural standards of the foreign country where the embryo was donated provide protections at least equivalent" to those set forth in Option 2. The Working Group will review the submission and make a recommendation to the Advisory Committee regarding whether the foreign country's procedures are equivalent to those of NIH. The Director of NIH renders final decisions on foreign procedural equivalence.

Assurance Prior to Use of NIH Funds

The Guidelines advise that, prior to expending NIH funds, a funding recipient will be required to assure NIH that hESCs involved in the funded project appear on the NIH Registry. Such assurances should be provided "when endorsing applications and progress reports submitted to NIH for projects using hESCs." In addition, NIH clarified in a July 15, 2009 Notice that use of grant funds for hESC research will not be approved, and no new uses of hESCs may be initiated in ongoing funded studies, until the hESC line(s) to be used is approved through the new NIH process and listed in the Registry __. For hESC lines that an institution proposes for addition to the Registry, the institution is required to submit an assurance providing that the donation of the embryo from which the cell line was derived met the eligibility requirements of the Guidelines.

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FN4. The Guidelines define hESCs as “cells that are derived from the inner cell mass of blastocyst stage human embryos, are capable of dividing without differentiating for a prolonged period in culture, and are known to develop into cells and tissues of the three primary germ layers.”

FN5. See, e.g.

Government Guidance:

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