

Empire State Stem Cell Board
Ethics Committee Meeting Minutes
June 27, 2008

The Empire State Stem Cell Board Ethics Committee held a meeting on Friday, June 27, 2008, at the Department of Health offices, 90 Church Street, New York, New York. Commissioner Richard F. Daines, M.D., presided as Chairperson.

Ethics Committee Members Present:

Dr. Richard F. Daines, Chairperson
Fr. Thomas Berg
Ms. Brooke Ellison
Dr. Samuel Gorovitz
Dr. Robert Klitzman
Dr. Vivian Lee
Rev. H. Hugh Maynard-Reid
Rev. Monsignor William Smith
Dr. Daniel Sulmasy
Mr. Robert Swidler

Funding Committee Members Present:

Mr. Kenneth Adams
Dr. Bradford Berk
Dr. Hilda Hutcherson

Department of Health Staff Present:

Dr. David Anders
Ms. Bonnie Brautigam
Ms. Judy Doeschate
Mr. Michael Heeran
Ms. Sharon Johnson
Ms. Marti McHugh
Ms. Amy Nickson
Dr. Tia Powell
Dr. Lawrence Sturman
Ms. Mary Szesnat
Ms. Linda Tripoli
Dr. Ann Willey

Observers Present:

Dr. Michelle Cissell
Mr. Ed Ellison
Ms. Jean Ellison
Ms. Barbara Meara
Dr. Glenn Monastersky
Ms. Kelly Ryan

Opening Remarks and Introductions

Chairman Daines called the meeting to order and welcomed Board members, staff and the public. He noted that although the Ethics Committee would be meeting initially, all members of the Board had been invited to attend the Ethics Committee meeting since the full Board would be meeting later in the day.

Dr. Daines advised members that this would be the last meeting that Dr. Tia Powell would be attending since she accepted a position as director of the new Center for Bioethics at Albert Einstein College of Medicine and Montefiore Medical Center. Dr. Daines thanked Dr. Powell for her service to the Board, as well as to the Task Force on Life and the Law.

Dr. Daines then asked Committee members and staff to briefly introduce themselves.

Approval of Minutes for the May 13, 2008, Ethics Committee Meeting

Dr. Daines directed Committee members to the draft minutes for the May 13, 2008, meeting of the Ethics Committee that were included in their agenda books. Dr. Klitzman moved to approve the minutes and Rev. Maynard-Reid seconded the motion. The motion passed unanimously.

Rev. Monsignor William B. Smith arrived, and Dr. Daines welcomed him to the Board. He advised members that Monsignor Smith is Professor of Moral Theology at St. Joseph's Seminary in Dunwoodie, Yonkers and has been appointed to the Ethics Committee.

Presentation: Oocyte Donation Risks

Dr. Daines reminded members that at the April meeting, Ethics Committee members requested more information on the gamete donation process, the risks of oocyte donation, and related issues. Dr. Daines then turned the floor over to Dr. Powell to introduce Dr. Catherine Racowsky who would be presenting information to the Board on these topics.

Dr. Powell advised members that Dr. Racowsky served on the Institute of Medicine's Committee on Assessing the Medical Risks of Human Oocyte Donation for Stem Cell Research (IOM Committee) that developed the report by the same name that was distributed to Board members in May. Dr. Racowsky is also Director of the Assisted Reproductive Technology Lab at Brigham and Women's Hospital in Boston and an Associate Professor of reproductive biology at Harvard Medical School. Dr. Racowsky presented information on the risks of ovarian stimulation, surgical risks, psychological risks, cancer risks, and risks to future fertility.

Dr. Racowsky first provided a brief overview of ovarian physiology and ovarian stimulation for oocyte harvesting. She noted that in order to increase the number of eggs that can be retrieved from a single donor, the donor normally takes a regimen of follicle stimulating hormone (FSH) shots. The donor is carefully monitored, and mature eggs are retrieved using a long retrieval needle connected to tubing which is inserted through the vagina wall and into the ovary. She noted this procedure is usually performed with anesthesia.

Dr. Racowsky noted that the most prominent risk of ovarian stimulation is ovarian hyperstimulation syndrome (OHSS), which is caused by the patient or donor responding over-exuberantly to the hormone regimen. Its symptoms include increased ovarian size and increased permeability of the blood capillaries, leading to an accumulation of fluid in the abdomen. This tends to lead to electrolyte disturbances and rapid weight gain. In severe forms of OHSS, there can be breathing difficulties; hemoconcentration, or an increased concentration of red blood cells; kidney; and liver problems. She noted that OHSS is classified as mild, moderate, or severe and that about 20 percent of women experience mild OHSS. Mild OHSS causes some discomfort and is routinely managed on an out-patient basis. Moderate OHSS, which results in major discomfort, fluid build-up, and often nausea and vomiting, occurs in about three to six percent of the cases and requires hospitalization because of the need to monitor the patient closely. Severe cases of OHSS occur in one-tenth to three-tenths of a percent of all cases and may include kidney failure and respiratory problems requiring hospital admission. Dr. Racowsky emphasized that the data she was providing was based upon in vitro fertilization (IVF) patients and not egg donors, because there is much more history and data for individuals undergoing IVF procedures. She noted that this is a critical distinction because the resulting pregnancy can add to the risk of developing the side effects.

Dr. Racowsky then discussed the potential risks associated with the surgery and anesthesia. She noted that Dr. Mark Sauer had found that there were serious risks from anesthesia in about two of 1,000 egg donors. She also noted that the use of proper aseptic techniques and consideration of the patient's previous medical history made the risks from anesthesia and the surgery very low. She observed that the complications for IVF patients tend to be four times as great as for egg donors. She also advised members that there is no data to suggest that egg retrieval surgery poses any risk to a woman's future fertility.

Dr. Racowsky noted that there can also be psychological risks for donors and potential donors. The risks may include issues associated with the screening process

which could reveal some previously unknown psychological or medical condition that disqualifies a woman from donating. During the donation process itself, some women report mood swings and irritability caused by the fertility drugs, pain caused by the injection, and anxiety from anticipation of the surgical procedure. She noted that these issues usually disappear after the procedure is complete. For women who donate for reproductive purposes, there can also be concerns about the potential offspring and regrets in the future.

Dr. Racowsky also addressed the potential cancer risks associated with the procedure because of the concern that the use of the fertility drugs may lead to an increased risk of hormone-dependent cancers such as breast, ovarian, and uterine (endometrial) cancers. She provided information from several studies and noted the limitations of the studies, including their focus on infertility patients who have an increased prevalence of these types of cancer, the low incidence of cancer, and the lack of long-term historical data due to the relative recent use of IVF procedures. Dr. Racowsky advised members that the evidence to date does not support a relationship between fertility drugs and an increased prevalence of breast or ovarian cancer. However, there is a suggestion that infertility drug use increases the risk of uterine cancer. She noted nulliparity, i.e. a woman never having carried a pregnancy, is also an increased risk factor for uterine cancer. She also noted that studies show that women who have taken fertility drugs or who have had ovarian stimulation do not impact a woman's long-term fertility.

Dr. Racowsky concluded that with appropriate selection and careful monitoring of stimulation, OHSS should be preventable in all or almost all egg donors; that the anesthetic and surgery risks are very low; that there are potential psychological risks that can be addressed in most cases with appropriate counseling; and that most cancer studies are reassuring in not showing a strong association between fertility drug use and cancer rates, although some have shown increased risk with greater drug use or when patients have been followed over a longer period of time. She recommended the Board consider setting up a national registry for egg donors and long-term follow-up, possibly including the type and quality of drugs used and the number of donation cycles per donor, so that the available information on risks can be clarified.

In response to questions from Board members, Dr. Racowsky stated that advertising is a typical way of recruiting donors and that some people have family members or friends who suffer from diseases that would benefit from stem cell research which may make them want to donate. She advised members that the American Society for Reproductive Medicine (ASRM) currently suggests that compensation for IVF egg donors around \$5,000 is acceptable; that anything above \$5,000 needs to be justified; and that compensation of \$10,000 and above is considered inappropriate. She also stated that she thought egg donors should be compensated, but noted that how that is done is very tricky in light of the potential for undue inducement.

Dr. Sulmasy provided some rough calculations suggesting that if somatic cell nuclear transfer were used to treat a disease, such as diabetes, it would require the retrieval of so many eggs that it would result in very large numbers of women

experiencing OHSS, and significant numbers dying. Dr. Racowsky acknowledged that there are genuine risks on a larger scale, but thought that the risks could be mitigated in the right hands. Dr. Berk noted that harvesting very large numbers of eggs for common diseases is not likely to be a cost effective approach and that most people in the stem cell field anticipate that therapeutic cell lines would be used on an “off-the-shelf” approach that would not require harvesting eggs from hundreds of thousands of women.

In response to other questions she acknowledged that the number of individuals who were diagnosed with cancer in the studies was very low (less than one percent), and that there appeared to be an increased association with cancer in the longer term studies. Dr. Racowsky endorsed the idea of the Board using some of its funds to study these issues further and to help develop a donor registry. Members also questioned when it would be appropriate to advise donors or potential donors of the results of additional testing (such as genetic markers for cancer or Alzheimer’s) and what the limits of such testing should be. Dr. Racowsky suggested the consent should provide donors with the opportunity to not be given the information even if something is discovered later.

Informed Consent for Gamete Donors

Dr. Daines noted that Dr. Racowsky’s presentation was a lead-in to the next discussion on the issue of informed consent and noted that the issue is not unique to the Board or to stem cell research. He stated that the New York State Task Force on Life and the Law (Task Force) issued a report in 1988 on the procurement and distribution of organs and tissues in New York State which led to the adoption of Public Health Law 43-B and the creation of the Department of Health’s tissue bank licensure program. The Task Force issued another report on assisted reproductive technologies in 1998 that also addressed the issue of gamete donation. This led to the development of an informative booklet aimed at potential egg donors entitled, “Thinking of Becoming an Egg Donor?” which is relevant to some of the issues being discussed by the Board. He then turned the floor over to Dr. Willey, Director of Planning and Policy in Wadsworth Center, to provide a brief overview of the Department’s tissue bank licensure program and relevant regulations.

New York State Tissue Bank Statute and Regulations

Dr. Willey noted that Public Health Law Article 43-B and associated relevant regulations were included in the agenda book under Tab 3. She provided Board members with a brief overview of Public Health Law Article 43-B which establishes the Department’s authority to license and oversee tissue donation, procurement, banking, and distribution, including the donation and use of reproductive tissue and gametes. She noted that this statute also creates the New York State Transplant Council and gives that body authority over the development of regulations governing the licensure and operation of tissue banks.

Dr. Willey briefly highlighted some of the regulations contained in 10 N.Y.C.R.R. Part 52 which implements Article 43-B, including Subpart 52-1 (definitions); Subparts 52-2 and 52-3 (requirements for tissue bank licensure); and specific sections of Subpart 52-8 that govern gamete banks, including section 52-8.4 (selection criteria for donors), section 52-8.8 (informed consent requirements), and section 52-8.9 (record-keeping requirements). She noted that reproductive tissue banks have certain staffing requirements, including a need for a medical director and medical advisory committee that are responsible for overseeing the selection, screening, and education of potential donors. She also noted that facilities procuring or distributing tissue for research purposes must be licensed and comply with the provisions of Subpart 52-11 (nontransplant banks). Dr. Willey noted that any recommendations concerning informed consent or other requirements for the procurement and use of stem cells should be developed within the context of existing regulations and requirements.

Committee Discussion of Standards on Informed Consent

Dr. Daines thanked Dr. Willey and then turned the floor over to Dr. Powell to lead the discussion on informed consent.

Dr. Powell asked members for their thoughts or any concerns they had regarding the informed consent process. Several members stated they thought the International Society for Stem Cell Research (ISSCR) templates included in the agenda books were a good tool to start with, but identified some issues with the forms that they may want to address. It was noted that it is not clear how much information is given to potential donors regarding the types or results of tests performed or the types of research being conducted. Many of the blanks in the form regarding specific risks and information about the nature of the study may be completed thoroughly or may be handled superficially. In some cases the language used would not be clear to the average reader. Members also questioned whether the notice regarding potential significant genetic findings and the reporting of results was appropriate or adequate.

Some members suggested some specific edits to the ISSCR forms. Dr. Gorovitz suggested that the phrase “you have the right to agree or to refuse to” could be looked at as implying the person is being resistant or uncooperative and recommended changing it to “right to agree or right to decline.” Fr. Berg suggested that perhaps using the phrase “you are free” to do this or not do this would make it even clearer that it is a choice. Mr. Swidler stated he thought the forms understated the benefits of stem cell research and its potential. He noted there are other specific edits he might recommend, but suggested that the Committee should clarify what it is contemplating with the forms before making specific edits.

Dr. Powell noted the Committee should consider whether it wants to develop a model form or templates and how they envision that being handled. Dr. Klitzman favored the idea of developing template consent forms to assist institutions in developing policies and processes, but maintaining flexibility for each institution to adapt the forms for their own uses. He suggested also looking into other alternatives for informing

donors of risks, such as the Board contracting with an entity to develop informational DVDs, pamphlets, or decisional aids. Dr. Lee recommended that the Committee should decide first whether it wants to provide guidelines for informed consent and then let that discussion inform any subsequent development of documents. She also recommended the Committee should look at how other fields have addressed similar issues. Dr. Daines recommended the Committee should be clear about what they are proposing and distinguish between developing guidelines or guidance on principles for consent versus templates and backup media presentations. Mr. Swidler favored developing both guidance or guidelines and a template that would make it easier for researchers to meet the requirements. Dr. Klitzman expressed an interest in seeing examples of forms that are being used elsewhere, such as in California or at Harvard.

Dr. Powell ended by asking members to send any suggested edits or ideas to Ms. Roxland so she could put together revised documents for the Committee that incorporate their suggestions. She advised members that Ms. Roxland would also look at other available tissue donation documents to help the Committee come up with recommended templates while they continue to sharpen their ideas about a recommendation.

Adjourn and Break

Dr. Daines noted the Ethics Committee would be taking a break for lunch and that the full Board would reconvene at 12:30 P.M. Dr. Daines then asked for a motion to adjourn the meeting of Ethics Committee. Dr. Gorovitz so moved. Dr. Sulmasy seconded the motion. The motion passed unanimously.

Approved: September 4, 2008