

Empire State Stem Cell Board
Ethics Committee Meeting
Minutes
February 22, 2008

The Empire State Stem Cell Board Ethics Committee held a meeting on Friday, February 22, 2008 at the Department of Health's Offices at 90 Church Street in New York City. Commissioner Richard F. Daines, M.D., presided as Chairperson.

Ethics Committee Members Present:

Dr. Richard F. Daines, Chairperson
Fr. Thomas Vincent Berg
Dr. Samuel Gorovitz
Dr. David Hohn
Dr. Robert Klitzman
Rev. H. Hugh Maynard-Reid
Dr. Daniel Sulmasy
Mr. Robert Swidler

Ethics Committee Member Participating via Teleconference:

Ms. Brooke Ellison

Ethics Committee Nominee Present:

Ms. Nancy Dubler

Funding Committee Member Present:

Dr. Michael Stocker

Department of Health Staff Present:

Dr. David Anders
Ms. Bonnie Brautigam
Mr. Thomas Conway
Ms. Judy Doeschate
Ms. Rose Firestein
Ms. Lalitha Iyer
Ms. Amy Nickson
Dr. Tia Powell
Dr. Lawrence Sturman
Ms. Mary Szesnat
Ms. Ester Baker Warshaver
Dr. Ann Willey

Observers Present:

Dr. Michelle Cissell
Ms. Arana Hankin
Ms. Crystal Mainiero
Dr. Glenn Monastersky
Ms. Kelly Ryan
Ms. Sherry Spalliero
Ms. Jo Wierderhorn

Opening Remarks and Introductions

Chairman Daines called the meeting of the Ethics Committee to order and welcomed Board members, staff and the public. Dr. Daines introduced Ms. Nancy Dubler, who has been nominated by New York State Assembly Speaker Silver to serve on the Ethics Committee and had been asked to participate in the discussions of the Ethics Committee.

Dr. Daines reported that Dr. Rudolf Jaenisch, a pioneering stem cell investigator, had accepted Wadsworth Center's invitation to deliver the 2008 Brown-Hazen Award Lectures on April 3rd and 4th in Albany. Dr. Daines encouraged everyone to attend the lectures.

Dr. Daines also advised Committee members that Governor Spitzer has included second-year funding of \$50 million in his budget for the 2008-2009 fiscal year, as well as the balance of unspent funds from the \$100 million first year appropriation. Dr. Daines then asked Committee members and staff to briefly introduce themselves.

Approval of Minutes for the January 17, 2008 Ethics Committee Meeting

Dr. Daines directed Committee members to the draft minutes for the January 17, 2008 meeting of the Ethics Committee under tab 1 of the agenda book and asked for a motion to approve the minutes. Dr. Klitzman so moved; Dr. Gorovitz seconded the motion. Fr. Berg suggested the first paragraph on page 3 of the minutes be revised to reflect that the restrictions contained in the Ethics Committee's fourth recommendation would have only applied to the first round of grants. With that change noted, the motion passed unanimously.

Survey: ESCRO Committee Policies and Practices in New York State

Dr. Daines noted that at its last meeting, Committee members had expressed an interest in learning more about Embryonic Stem Cell Research Oversight (ESCRO) committees currently operating in New York State. He turned the floor over to Dr. Powell to provide the results of a survey conducted by staff.

Dr. Powell noted there were only a few ESCRO committees up and operating in New York State and many remain in the start-up phase. She advised members that the composition of ESCRO committees are generally based on the National Academies' Guidelines on Human Embryonic Stem Cell Research (NAS Guidelines). However, some committees lacked community members. The survey also revealed that all committees have women, while not all have minorities.

Dr. Powell advised members that the management and records of ESCRO committees are generally patterned after that of Institutional Review Boards (IRBs) with variations in conflict of interest policies. Almost all ESCRO committees reported having oversight obligations beyond the approval of research, such as an annual review. She stated that although ESCRO committees generally rely on the NAS guidelines, some noted practical problems with the application of the guidelines, or had not formally adopted the guidelines. There was also substantial variation with regard to payment policies.

Dr. Powell advised members that most respondents expressed an interest in receiving educational materials for their ESCRO committee, including scientific training materials for ethicists and other non-scientists, as well as ethics materials for the scientists. She concluded stating that since ESCRO committees in New York State are in a formative stage, this would be an appropriate time to offer guidance on design, governance, and scope. However, since ESCRO committees are fairly new entities, there is relatively little experience upon which to base best-practice advice.

Presentation: ESCRO Committee Issues and Oversight

Dr. Daines introduced Dr. Henry Greely, who is the Deane F. and Kate Edelman Johnson Professor of Law at Stanford University and chairs the California Advisory Committee on Human Embryonic Stem Cell Research. Dr. Greely presented information on the California experience in the oversight of human embryonic stem cell research and offered advice to the Committee.

Dr. Greely noted that California has regulations that are applicable to research funded through the California Institute of Regenerative Medicine (CIRM) and separate guidelines developed by the State Department of Health Services that apply to all human embryonic stem cell research (hESC), regardless of whether it receives state funding.

Dr. Greely recommended that New York State require the review of stem cell research by ESCROs or SCROs, rather than by IRBs, because of the unique nature of the cells involved and the moral and ethical questions raised by the use of human embryos in research. He also suggested that the pluripotency of the cells makes a difference in at least two respects. One is the safety issues raised when the cells are used in clinical trials, and the other is the unpredictability of what the cells may become, especially when used in human/non-human chimeric research.

Dr Greely recommended that New York State be flexible in the standards it develops because the federal government may have a less restrictive view on human embryonic stem cell research after the change of administration next January. If that happens, the federal government is likely to adopt different standards to which the states will be required to react to.

Dr. Greely recommended the Committee give serious thought to the types of stem cell research it wants to cover in any standards. He noted that CIRM's regulations are so over-broad that they regulate hematopoietic stem cells that have been commonly used in medical treatments for decades. He suggested that the Committee focus only on pluripotent stem cells, but noted it may also want to oversee the use of neuro-progenitor cells and gonadic progenitor cells because of the uncertainty of where injected cells may wind up and what they may become. He noted that induced pluripotent stem cells may not give rise to the same level of concern, but suggested some oversight is appropriate because it is unclear whether they could become the equivalent of an embryo. Dr. Greely also suggested that stem cells derived from hESC lines should be regulated because of the potential for de-differentiation.

Dr. Greely suggested that when standards are developed, it is probably appropriate to consider establishing a sunset clause of ten to fifteen years because hESC research may become less controversial with changes in technology and attitudes over time.

Dr. Greely also provided his thoughts on a variety of issues where New York may, or may not, want to follow the lead of California. On the issue of compensation of gamete donors, he recommended the Committee not follow California's lead because of how restrictive their policy is. He suggested New York should allow some compensation for gamete donation because it is not unethical for women to receive some compensation for their pain, suffering and time. However, he also recommended establishing some type of limit on the amount of compensation paid to donors.

Dr. Greely also suggested that New York should not be as restrictive as California on the issue of confidentiality and anonymity because the federal Food and Drug Administration (FDA) will require information about donors for health and safety reasons when therapies go to clinical trial. However, he suggested New York should follow California's lead in relying on many standards applicable to IRBs and on the guidelines established by NAS and the International Society for Stem Cell Research (ISSCR). For the review of research by an ESCRO or SCRO committee, he suggested that New York establish a quorum requirement to ensure that the review and approval of all research include a person from each of the categories of membership recommended for ESCRO composition.

Dr. Greely responded to questions from Committee members on a variety of issues including the wisdom of providing compensation to ESCRO committee members, whether California imposed a gender requirement on ESCRO membership, the appropriate level of compensation for donors, special concerns for research involving chimeras, the

effectiveness and appropriateness of multi-institutional ESCRO committees, and problems in coordinating reviews with IRBs.

Dr. Daines thanked Dr. Greely for an excellent presentation and taking the time to share his expertise in this area with the Committee.

Discussion and Development of ESCRO Committee Standards

Dr. Daines noted that the Committee had expressed an interest in developing some additional standards for ESCRO committees relating to committee membership, conflicts of interest, recordkeeping and oversight. He advised members that Wadsworth staff had developed some draft language to provide a starting point for their discussions on these issues. He noted that most of the draft language had been modeled after the federal requirements for IRBs, which were also included in the agenda books under tab 4. He then turned the floor over to Dr. Powell to lead the discussion regarding potential additional standards for ESCRO committees.

Dr. Powell referred members of the Committee to the draft language under tab 8 of their agenda books. She noted the first section of the draft document addressed the issue of membership and solicited input from Committee members. Several members expressed support for including recommendations or requirements for diversity of membership, including diversity of gender. Members also expressed support for maintaining a requirement for a community or independent member to serve on the ESCRO committee. The Committee discussed the purpose of such a member and the problems of community members often being marginalized on IRBs. Several members expressed a preference for characterizing the person as an independent member of the committee that would not be affiliated with the institution. In response to questions on how these standards would relate to the existing recommendations contained in the NAS Guidelines and ISSCR Guidelines, members were advised that these provisions were expected to supplement, rather than supplant, those guidelines. It was suggested that the draft language be provided in the future in the context of the existing provisions of those guidelines.

In discussing the composition of ESCRO committees, some members questioned whether there is a need to require a separate entity to review human embryonic stem cell research, or whether this review function could be performed by an institution's existing IRB. Dr. Daines and Dr. Powell noted that Dr. Greely had recommended a separate organization perform this function, at least in the near term. Several members expressed strong support for the creation of a separate committee to review stem cell research due to concerns about current IRB review processes, federal limitations on human embryonic stem research, potential impact on collaborations with scientists outside the State, and the unique issues raised by stem cell research that require a different level of expertise and focus than typically exists in IRBs. Dr. Sulmasy commented that since the name of the review committee includes the word "embryonic," it presupposes the types of research to be funded when the Committee had not discussed that issue. Dr. Powell noted that California has required the creation of Stem Cell Research Oversight (SCRO) committees, which are

required to review other types of stem cell research beyond human embryonic stem cell research and suggested the Committee should take up that issue after consideration of the rest of the draft language.

Dr. Powell then suggested the Committee consider the draft conflict of interest language. Members supported requiring ESCRO committees to adopt policies to address potential conflict of interest issues. However, most members felt the draft language defining a conflict of interest was problematic, potentially being both over-inclusive and under-inclusive. Some members expressed an interest in following the federal regulations applicable to IRBs without expanding upon the definition of “conflict of interest.” Several members expressed support for requiring ESCRO committees to adopt conflict of interest policies that are in alignment with the institutional conflict of interest policy and the Committee reached general agreement that was an appropriate approach.

Dr. Powell then directed members to the proposed language on recordkeeping. Support was expressed imposing requirements that were in alignment with the recordkeeping requirements applicable to IRBs. Ms. Dubler noted that the federal Office for Human Research Protections (OHRP) provides additional guidance on the IRB requirements and suggested that ESCRO committees be directed to comply with those regulations and the guidance issued by that office. It was also suggested that since the types of records required to be retained include the IRB’s policies and procedures for review of research, model policies should also be developed for ESCRO committees. It was noted that ESCRO review extends beyond human research subject protection and that there may be other issues and records unique to ESCRO committees that should also be maintained, including records concerning the provenance of the cell lines used, consent to gamete donation, and unexpected outcomes and adverse events relating to the research. Dr. Gorovitz questioned whether the three year record retention requirement was adequate and suggested a longer retention time. Several members preferred a retention period of at least six years, and some suggested that the retention period be longer.

Dr. Powell then encouraged members to return to the question of the work to be performed by ESCRO committees. She inquired whether the Committee thought oversight responsibility should be extended to research involving other pluripotent or totipotent stem cells as California had done. Several members expressed support for extending the review to pluripotent and other stem cells, but acknowledged that could lead to some types of research, such as that involving bone marrow stem cells, being unnecessarily subjected to an additional level of review. It was suggested that most organ-system specific stem cells should be exempted from the types of stem cell research subject to this type of oversight. However, it was also noted that some system-specific stem cells, such as neuroprogenitor stem cells and gonadic progenitor stem cells present some potentially unique and sensitive issues that should be subject to additional review. Other members suggested that the Committee develop a policy that includes all pluripotent and totipotent stem cells and carves out what should be exempted from ESCRO committee review. Mr. Swidler inquired whether the Committee was rejecting the structure contained in the National Academies’ guidelines and cautioned against creating standards that do not mesh with those guidelines and the categorization of review. Dr. Hohn suggested that this was an issue that the

Committee could work on with members of the Funding Committee and offered to help develop language and share it with scientists for their input. Ms. Dubler suggested that Dr. Greely be contacted to determine whether the July meeting in California, which considered a variety of issues relating to stem cell research oversight, has shed any light on these issues.

Funding Committee Report

In response to a request made by Committee members at the January 17th meeting, Dr. Sturman provided a brief report on the types of research being funded through the initial institutional development grant. He advised members that based upon the descriptions of research provided in the applications, of the seventy-four research projects being funded through the initial round of grant awards, six institutions had projects that involved hESC research. Of those, fifteen investigators were planning to use stem cell lines that are on the registry of approved lines that could be used in research funded by the National Institutes of Health (NIH), and nine investigators at two institutions planned to use stem cell lines that were not on the NIH-approved registry. Dr. Sturman stated that none of the applications submitted requested funding to derive new hESC lines.

Dr. Sturman also provided members with information on the status of the awards, noting that about half of contracts for the grants awarded had been forwarded to the Office of the State Comptroller and the Office of the Attorney General, and the remaining grants were awaiting different types of documentation from the applicants.

Intellectual Property – Background and Policy Considerations

Dr. Daines noted that the Committee, at its November 30, 2007 meeting, expressed an interest in examining certain intellectual property issues. He turned the floor over to Dr. Willey to present the information members had requested.

Dr. Willey advised members that the intellectual property policies currently applicable to research funded through the Empire State Stem Cell Trust Fund (Fund) are contained in Appendix A-2, which could be found in their agenda books under tab 9. She noted that these policies have been revised to provide for increased disclosure and access to the results of research supported through the Fund.

Dr. Willey then briefly provided members with information on the status of the patents held by the Wisconsin Alumni Research Foundation (WARF), which were issued to the inventor, Dr. Thompson, who claimed to be the first person to successfully derive pluripotent stem cells from human embryos. Dr. Willey referred members to the information contained in their agenda books under tab 10 which provided abstracts of the patents. She advised members that the patents have been challenged by groups in New York and California. The federal Patent and Trademark Office disqualified some of the claims of the patents, but they have not invalidated the patents. WARF has challenged that determination and the appeal is pending. She noted that WARF aggressively protects the

inventions of its staff and they hold, or have applied for, 173 patents relevant to stem cell research. However, they also provide access to other academic researchers by no-cost license agreements. She also advised Committee members that WARF had recently licensed all of the patents to a for-profit company, through a non-exclusive license that still allows WARF to make the materials available to other researchers.

Dr. Willey reminded members they had also asked for information on federal legislation that might affect patents for stem cell research. She advised members that there are two patent law bills pending that are of interest. One would prohibit patenting of human genes, and the other would make it easier for individuals to challenge patents in the first twelve months after they are issued.

Dr. Willey then provided members with information about the intellectual property policies of other state stem cell funding programs with regard to two areas they expressed an interest in considering further: 1. Return on the state investment; and 2. Access to new discoveries and treatments. She advised members that only California has an extensive, explicit policy in these areas. Dr. Willey explained that California has adopted different policies for not-for-profits and for-profit entities but has not yet funded research conducted by for-profit entities. She advised members that both policies require extensive recordkeeping regarding the specific activities supported with state funds, as well as the revenues generated from successful commercialization of the resulting discoveries.

The formula for not-for-profits first requires the calculation of the net revenues received by the institution from the invention, which is then prorated based upon the investment of state funds in the underlying research. The institution is then entitled to keep a threshold amount of approximately a half million dollars of the prorated state share of the net revenues and then pay 25 % of the remainder back to the state. For for-profits, the percentage of the prorated state share of the net revenues paid to the state is 17%. Dr. Willey noted that the net revenues will be a higher percentage of the entire revenues generated by the invention because for-profits do not tend to pay their employees royalties for their inventions. Dr. Willey explained that California also has “blockbuster” provisions that would allow the state to recover higher amounts, which could be as much as six times the total amount of the original grant plus 1% of all royalties for the life of the patent, if certain thresholds and conditions are met. They must also make any resulting therapeutic product available at the predetermined MediCal rate. She also explained that the institutions are expected to police their partners in assuring a return on the investment. Dr. Willey noted that these provisions are viewed as a real disincentive for funded entities to pursue translational research and the development of any kind of commercialized product involving stem cells.

Committee members expressed an interest in exploring other models that would not serve as a disincentive to commercialization or require as much recordkeeping. Dr. Sulmasy noted that there has been some resentment that pharmaceutical companies have been making huge profits off of AIDS drugs that were developed with government funding. Several members expressed an interest in pursuing a policy that would provide for a return to the state when there has been a “blockbuster,” but without the kind of substantial

recordkeeping requirements relied upon in the California program. Ms. Dubler also expressed support for including a no cost license arrangement requirement in the contract attached to the funding. Some members suggested that a return on investment policy that relies on trust, rather than recordkeeping may work and cited examples where an honor system worked well. Members expressed concern that the state not adopt a policy that would drive industry away and favored exploring creative solutions.

Strategic Planning Progress and Discussion

Dr. Daines then turned the floor over to Drs. Sturman and Stocker to present the draft outline of the strategic plan. Dr. Stocker briefly reported on the activities of the Strategic Planning Coordinating Committee that resulted in the development of the outline provided to them. He stated that at the next meeting of the Ethics Committee on March 13th he expected to provide members with an expanded version of the plan but wanted to get their input on the mission, goals and initiatives presented in the outline. He noted that a copy of the latest version of a proposed mission statement had been handed out to the members and solicited their input.

Dr. Gorovitz suggested the mission statement be modified to reflect that one of the long-range goals is to deepen our understanding of the world we live in and engage in the basic pursuit of knowledge. Mr. Conway suggested the Committee should be careful to make sure the mission statement is consistent with the Board's statutory mandate. It was suggested that Dr. Gorovitz's comments could be part of a subset of goals, rather than a part of the mission statement.

Some members suggested that the list included in the chapter on ethics should be expanded to include research involving chimeras and the ethics of regenerative medicine, and expressly acknowledge that the list of issues presented in that chapter is not necessarily complete and is open to the emergence of new issues in the future. Several members noted that the chapter should include an express statement that the Ethics Committee's primary role is to make recommendations about the medical, ethical and scientific standards that should be applied to funded research. Dr. Sulmasy noted that the draft plan indicates the Board will be supporting research involving hESC and somatic cell nuclear transfer when the Committee had not yet had that conversation and come to a consensus that this type of research reaches the highest ethical standards.

Ms. Dubler suggested the document probably needs some elaboration from the perspective of the Ethics Committee and the process the Committee thinks it should engage in for identifying options and weighing choices. Ms. Dubler also stated she thought one of the goals is to encourage and support a wide public dialogue about this kind of research and its social and ethical implications and thought that should be stated in the document.

In response to a question about the proposed expenditure of funds to conduct an economic impact assessment, Dr. Stocker noted that many people had expressed an interest in identifying the potential return on the investment to the state and it was felt that the

Board could not address those concerns without engaging outside experts to evaluate that. Ms. Doesschate noted that this assessment ties into the statutory language that suggests the return on investment is a factor the Board should be considering in developing policies.

Mr. Swidler expressed a desire to see a greater emphasis on moving towards a cure for Parkinson's disease, diabetes, spinal cord injury, and the promise of regenerative medicine. He thought that would be inspiring. He also suggested that the chapter on administration include a bullet on supporting research in accordance with the highest standards.

Dr. Sturman observed that New York State is not a leader in stem cell research, but that is not to say that we don't have the excellence or the expertise. It is hoped that this investment of resources both in mission directed science and in discovery science will lead to an increased leadership role for the state. Dr. Sturman also stated he viewed the strategic plan as a 'living' document that will be reviewed annually.

Dr. Daines thanked members for their input and stated staff would be attempting to incorporate the comments into the redraft of the strategic plan.

Next Steps

Dr. Daines summarized the decisions reached by the Committee, advised members that staff would be following up on those recommendations, and then asked for a motion to adjourn. Dr. Gorovitz so moved; Dr. Klitzman seconded the motion. The motion passed unanimously.

Approved: March 13, 2008