Empire State Stem Cell Board
Ethics Committee Meeting Minutes
September 27, 2010

The Empire State Stem Cell Board Ethics Committee held a meeting on Monday, September 27, 2010, at the Offices of the New York State Department of Health, 90 Church Street, New York, New York. Commissioner Richard F. Daines, M.D., presided as Chairperson.

Ethics Committee Members Present:
Dr. Richard F. Daines
Dr. Robert Klitzman
Ms. Brooke Ellison
Dr. Samuel Gorovitz
Rev. Dr. H. Hugh Maynard-Reid
Fr. Thomas Berg
Mr. Robert Swidler
Dr. Samuel Packer
Ms. Nancy Dubler

Ethics Committee Members Absent:
Dr. Vivian Lee
Dr. David Hohn

Department of Health Staff Present:
Ms. Beth Roxland
Ms. Judy Doesschate
Ms. Susie Han
Ms. Lakia Rucker
Dr. Lawrence Sturman
Ms. Janet Cohn
Ms. Carrie Zoubul
Dr. Kathy Chou

Observers Present:
Dr. Willy Lensch

Opening Remarks and Summary of Ethics Committee Activities to Date

Dr. Daines opened the meeting with a review of the Board's accomplishments during its first three years. He noted that the Full Board has met six times, the Ethics Committee 22 times, and the Funding Committee 16 times, for a total of 34 meetings over three years.

Dr. Daines stated that the Ethics Committee had deliberated on a number of important topics including the moral status of the embryo; standards for human embryonic stem cell research; standards for informed consent for gamete and embryo donors; compensation of oocyte donors; methods to increase public awareness and understanding of stem cell research; intellectual property issues; funding mechanisms for increasing knowledge of stem cell research; and the ethical, legal, and social implications of stem cell research.

The Funding Committee recommended the approval of 17 Requests for Applications (RFAs) totaling approximately $332 million. It has made 227 awards of $196 million to183 investigators at 37 separate institutions throughout New York State, many of which received more than one award. The Funding Committee adopted state-of-the-art standards for review of

RFAs by independent outside experts, ethical stem cell research, informed consent, compensation of donors, and intellectual property rights of awardees.

Dr. Daines informed members that the Board had worked with NYSTEM staff to develop and improve the Board's bylaws and that an exemplary strategic plan was in place to guide initiatives. In addition, the Board released a statement on the proposed NIH guidelines for human embryonic stem cell research and a statement on the compensation of oocycte donors for stem cell research. The latter statement was a ground-breaking document that received attention worldwide.

Although the Board has been in existence for less than three years, Dr. Daines acknowledged the significant progress it has made toward the mission of creating a robust stem cell research program in New York. The NYSTEM-funded research community was accelerating the growth of scientific knowledge about stem cell biology and the development of therapies and diagnostic methods for the purpose of alleviating disease and improving human health, while maintaining the highest ethical, scientific, and medical standards.

NYSTEM Contractor Status and Accomplishments

Dr. Daines reported that there have been 71 peer-reviewed scientific publications and related articles published with NYSTEM support. NYSTEM awardees generated several induced pluripotent stem cell lines that included the first models for Alzheimer's disease, familial dysautonomia, Leopard and Noonan syndromes, Charlotte-Marie tooth disease, long QT syndrome, and Parkinson's disease. NYSTEM support permitted researchers to investigate disease mechanisms and to identify chemical compounds that may alleviate or reverse symptoms.

Dr. Daines informed members that in May 2010, more than 150 researchers and interested individuals attended a two-day NYSTEM sponsored meeting to share data from NYSTEM-funded research and to engage in productive dialogue. Researchers endorsed the importance of NYSTEM-funded shared research facilities.

Introduction of Janet Cohn

Dr. Daines announced that Ms. Doesshate was retiring after many years of exemplary service to the Department and to NYSTEM. He then introduced Janet Cohn, the new Director of Board Operations for the Empire State Stem Cell Board and the Director of Policy and Planning for Wadsworth Center. For the last three years, Ms. Cohn was the Deputy General Counsel in the Department of Health, Division of Legal Affairs, where she worked on many issues and in particular on improvements to the medical malpractice system. She was responsible for the acquisition of a $3 million AHRQ grant to improve patient safety and achieve medical malpractice liability reform. Before joining the Department, Ms. Cohn served eight years as Chief of the Criminal Prosecution Bureau in the New York State Office of the Attorney General.

Report on Recent Funding Committee Activities

Dr. Daines stated that the Funding Committee met on September 17, 2010 and recommended the approval of four awards totaling $7.4 million. These awards were for the Empire State institutional training programs in stem cell research for pre-doctoral and post-doctoral fellows. The Funding Committee was impressed with the quality of applications and decided to approve the reissuance of this RFA to allow for the funding of four additional awards, which would commit another $7.5 million.

In addition, the Funding Committee approved an RFA for journalism programs, which had been recommended by the Ethics Committee. The RFA would commit $4 million to support up to four programs at post-secondary institutions to create unique opportunities for journalism students to increase scientific knowledge of stem cell biology and regenerative medicine, understand the process and timeline of translating bench discoveries into bedside applications, and recognize the ethical, legal, and social implications of stem cell research. Dr. Klitzman commented that this RFA would be of interest to groups who normally do not consider applying for NYSTEM awards and recommended that outreach be conducted to inform them.

An earlier presentation by Dr. David Anders on trans-differentiation research led to consideration of funding this area. The Funding Committee concluded that the researchers in this area would already be eligible for funding through other initiatives and awards, and consequently the Board decided not to issue a specially targeted RFA.

Approval of the May 21, 2010 Meeting Minutes of the Ethics Committee

The minutes of the May 21, 2010 Ethics Committee were approved.

Program Updates

Dr. Sturman stated that the Committee received a copy of the current fiscal report reflecting the status of awards and contracts. He noted that Dr. Daines had already reported on the awards recommended for funding at the September 17, 2010 Funding Committee meeting.

Dr. Sturman provided information about current RFAs and RFPs and reported that the Consortia to Accelerate Therapeutic Applications of Stem Cells RFA had been approved by the Funding Committee for $80 million. He anticipated that the RFA would be released shortly and recommendations for awards would be made at the May 2011 meeting. A related RFP would be issued for activities related to scientific oversight of the consortia to provide ongoing guidance to NYSTEM regarding the progress and success of the consortia contracts. A third round of Investigator Initiated Research Projects and Innovative, Developmental or Exploratory Activities applications was approved for $25 million and would be issued in the coming months. Finally, the Short Term Faculty Training Opportunities and Research Training for Medical, Dental and Veterinary Students RFAs would be issued shortly, representing an additional $2.5 million in funding.

Dr. Sturman informed the Committee that NYSTEM staff had followed up on a request from investigators at the annual awardees meeting that NYSTEM facilitate information-sharing related to the Shared Facilities and Equipment awards by creating a centralized database. He reported that the information will be available shortly on the NYSTEM website under the "research" section and will be listed according to the type of facility. The information will include a brief description of the shared resource, the website for the related laboratory and contact information.

Dr. Sturman advised the Committee that planning for next year's scientific meeting had begun and would be held at the CUNY Graduate Center on May 24 and 25, 2011.

Dr. Sturman continued with a description of the education workgroup, which he reminded members was convened after the Board, particularly the Ethics Committee, had identified the need to engage diverse communities to advance public understanding of stem cell research and to provide opportunities for education on stem cell science and its societal impact. The workgroup, chaired by Robin Elliot and composed of four board members and three community representatives, planned to consider informal science learning opportunities and would make recommendations to the Board.

Dr. Klitzman expressed concern about the lag following the award of the $189 million of total funds contracted and the reimbursement of the $43 million requested, and whether this needed to be addressed or would be resolved over time. Dr. Sturman stated that there were two sources of delay. The first was a product of the state's multi-step contract process, which required awardees to provide information to the extramural grant administration office, followed by steps involving the offices of the Controller and Attorney General. The second was caused by the voucher-based funding of awards, which was performed quarterly. Consequently, awardees did not receive moneys until the first quarter after the award was given.

Thus, both delays were inherent in the state contract process. Dr. Daines added that there had been internal meetings focused on reducing delays, but that given current fiscal constraints progress would be difficult to achieve. With this, Dr. Daines turned to Ms. Roxland to provide the update on the legal issues.

Federal Update

Ms. Roxland began with a short history of the *Sherley v. Sebelius* case. The original complaint, filed in August 2009, included a number of named plaintiffs, including Nightlight Christian Adoptions, Embryos, and Adult Stem Cell Researchers.

The complaint, filed in the Federal District Court of the District of Columbia, challenged the new NIH Guidelines for stem cell research on two grounds. The plaintiffs alleged that the guidelines: (1) violated the Dickey-Wicker Amendment, which prohibits federal funding of research involving the creation or destruction of an embryo or fetus; and (2) were issued in violation of the Administrative Procedures Act because they did not incorporate public comment, particularly when it expressed opposition.

Initially, the District Court dismissed the case because the plaintiffs lacked standing to sue. On appeal, the Court of Appeals for the District of Columbia reversed the ruling as to the adult stem cell researchers only, allowing their case to proceed. Despite its significance, the appellate decision received little media attention.

The appellate court based its standing decision on the claim by the adult stem cell researcher plaintiffs that the change in NIH policy subjected them to increased competition for funding. Because the ruling might be interpreted to establish standing for any researcher who applies for NIH funding, the Court attempted to narrow the decision by stating that "[the adult stem cell researchers] are more likely to lose funding to projects involving ESCs than are researchers who do not work with stem cells because [adult stem cells] and ESCs are substitutes in some uses."

The case went back to the District Court, and on August 23, 2010, it issued a preliminary injunction suspending NIH funding of stem cell research. Ms. Roxland explained that a preliminary injunction was an extraordinary remedy, which required plaintiffs to show that: (1) there was a substantial likelihood of success on the merits; (2) the plaintiffs would suffer an irreparable injury if the injunction was not put in place; (3) the injunction would not substantially injure other parties; and (4) that the injunction was in the public interest.

The District Court found that because research is a process, one should not distinguish among the various steps in the process. Therefore, because hESC research required the destruction of an embryo at some point in the research process, Dickey-Wicker prohibited federal funds from supporting research using hESC lines regardless of whether the individual funded project involved the derivation of the line from an embryo.

Ms. Roxland said that the District Court's reasoning in its preliminary injunction opinion could be read to prohibit not only funding pursuant to the new NIH Guidelines, but also to funding of research on the Bush Administration lines, since those were also hESC lines. For this reason, the NIH issued a directive to halt all research involving human embryonic stem cells, including research involving the Bush Administration lines.

On September 7, 2010, the District Court denied the government's request for a stay of the preliminary injunction pending appeal. In its opinion, the Court noted that the plaintiffs had not challenged the Bush Administration stem cell lines or previously-funded research projects, so the initial ruling could not be read to include them.

The Government appealed the decision to the Court of Appeals and filed an emergency motion to stay the preliminary injunction. On September 9, 2010, the Court granted an administrative stay of the injunction pending its review of the motion for an emergency stay. On September 27, 2010, the day of the Ethics Committee meeting, the emergency stay motion was to be argued before the appeals court. Meanwhile, the merits of the case still remain before the District Court.

Dr. Klitzman asked whether both courts would address the merits of the case. Ms. Roxland clarified that a motion for summary judgment, for which the entire record would be

reviewed, was proceeding simultaneously before the District Court while the appeal of the preliminary injunction was handled by the Court of Appeals. Fr. Berg inquired when the merits of the case would be discussed in the District Court. Ms. Roxland answered that a date had not yet been set, but she estimated that it would be in the next couple of months. She stated that a decision from the Court of Appeals could be expected fairly soon.

Dr. Lensch asked which interpretation of the reach of the preliminary injunction would apply if sustained. Ms. Roxland replied that the District Court had made it clear that the legality of funding the Bush Administration stem cell lines and previously funded NIH projects was not before the court, and therefore, could continue. However, she noted that if the logic of the original opinion was applied, even this funding was in jeopardy. Mr. Swidler added that the decision opens the door for researchers to challenge funding of the Bush lines.

Ms. Dubler commented that by issuing the preliminary injunction, any NIH researcher in a particular area could question any new area of funding. Dr. Klitzman asked about the legal status of the Dickey-Wicker amendment and related Congressional action. Ms. Dubler responded that Congress did vote to limit it, but the action was vetoed by President Bush. Ms. Roxland added that there were two similar bills currently pending in the Congress. Fr. Berg commented that the only way forward for advocates of human embryonic stem cell research would be to repeal Dickey-Wicker.

Mr. Swidler noted that in the light of this case, federal funding was in jeopardy, highlighting the importance of state funding. Dr. Daines agreed and added that Dickey-Wicker would be tested in Congress. He expressed that even while federal funding was debated, there was consensus to continue to keep state funds available.

Standards for Chimera Research

Dr. Daines moved the discussion to the development of standards for research involving chimeras. He noted the two excellent presentations to the Committee on this topic by Dr. John Gearhart from the University of Pennsylvania and by Dr. Willy Lensch from the Harvard Stem Cell Institute and Children's Hospital Boston. Dr. Daines asked Ms. Roxland to lead the discussion.

Ms. Roxland provided a brief summary of the Committee's previous discussions on chimeras. She reviewed the issues presented by chimera research—level of ESCRO review, type of animal used, developmental stage of the animal/degree to which the hES cells would be incorporated, type of tissue involved, and breeding of the chimeric animal. She suggested that the Committee approach the selection of standards of oversight and conduct of chimera research in one of four ways: 1) default to NAS or ISSCR guidelines, 2) mandate only NAS, 3) mandate only ISSCR, or 4) create new standards for researchers to follow.

Ms. Roxland reminded the Committee that Appendix A-2 did not specifically address chimera research; instead it simply permitted researchers to adhere to either NAS or ISSCR guidelines on all issues that were not explicitly addressed in the NYSTEM contract or law. Ms.

Doesschate stated that if the Committee chose to allow researchers to comply with either NAS or ISSCR guidelines for chimera research, standards applicable to funding would not change.

Mr. Swidler asked Dr. Sturman whether a research proposal would indicate whether chimera research was involved and therefore subject to review for chimeric components by both the funding reviewers and an ESCRO committee. Dr. Sturman clarified that the Funding Committee did not review the research proposals, but an outside group reviewed the proposals. He also stated that none of the ethical discussions regarding chimera research (such as transplanting pluripotent cells into blastocysts) that have been discussed at the previous Committee meetings were currently being funded. Dr. Chou stated that the research being funded to date only involves differentiated hES cells that are being inserted into adult mice.

Dr. Sturman asked Dr. Lensch for an estimate of how many researchers in the world were doing advanced chimera research. Dr. Lensch replied that he believed few researchers were performing this type of research, but the amount of research in this field should not preclude funding for this area. In addition, Dr. Lensch later pointed out that while NAS required a full ESCRO review for any type of chimera research, ISSCR distinguished chimera research that would suffice with an expedited review versus that requiring full review. For example, ISSCR permitted teratoma assays, a very common form of chimera research, to fall under expedited ESCRO review.

Dr. Klitzman asked Dr. Lensch to explain the scientific and moral reasons to permit specific types of chimera research and the presumed dangers that would be involved in drawing limits for certain types of research. Dr. Lensch responded that the reasons to permit or deny certain types of chimera research were not purely scientifically- or morally-based, but an amalgamation of both. He stated that the ISSCR guidelines were more flexible. ISSCR gave researchers the opportunity to provide evidence for the need to conduct specific types of research. NAS guidelines may be perceived to limit research; but they merely provide that certain research was not permitted "at this time," and that in the future these restrictions may be removed.

Dr. Klitzman asked Dr. Lensch for his opinion on whether NAS or ISSCR was too restrictive or permissive with respect to chimera research. Dr. Lensch disclosed that while he was a member of the ISSCR committee that developed the guidelines on chimera research, he thought both guidelines were strong and thoughtful. He emphasized that both guidelines stated what research was not permitted, but more importantly, permitted certain types of research only when a convincing argument was advanced.

Ms. Ellison asked Dr. Lensch if either the NAS or ISSCR guidelines had any limitations that were unduly prohibitive. Dr. Lensch commented that he personally favored ISSCR because the NAS guidelines could be interpreted to be too restrictive. He stated that ISSCR permitted a broader range of possibilities of research and gave the local review committees the authority to decide whether the research would be permitted.

Dr. Daines commented that while it seemed obvious why there would be limits to hESC research that may contribute to the germ line, and related restrictions on breeding of these

animals, the guidelines on chimeric research involving hES cells that may contribute to the central nervous system (CNS) seemed less clear and depended on the degree and complexity of the hES cell contribution. Dr. Lensch indicated that, although the guidelines did not issue specific restrictions, review committees require solid scientific rationale to justify why the research should be approved. He reaffirmed that no committee would ever simply "rubber stamp" research for approval without detailed review.

Dr. Gorovitz asked, with respect to the 14-day limitation on research, if there were any animals that developed faster (*i.e.*, before the end of the 14-day limit). Dr. Lensch replied that the14-day limit only applied to human embryos in culture and not to animals. Dr. Gorovitz responded that since the public had anxiety about chimeras, especially science fiction perceptions, the Committee should mandate limitations on certain types of chimera research to reassure the public. Dr. Lensch replied that since much of the public's anxiety was about scientifically implausible research, it may not be in the best interest of science to give too much weight to this concern. He further stated that since almost all species were unable to cross breed, such chimeric science fiction products would never occur. In addition, for the few species that could cross breed, such as horses and donkeys, the offspring of such breeding are always infertile.

Mr. Swidler asked Dr. Lensch if there were similar restrictions by NAS regarding the use of iPS cells in chimera research. Dr. Lensch stated that because the derivation of iPS cells did not involve a human embryo, NAS did not require ESCRO review for this procedure. However, if these cells were to be used in chimera research, the same NAS restrictions would apply, including ESCRO review. Ms. Roxland noted that there were NAS guidelines on the use of iPS cells in chimera research. Dr. Lensch affirmed that many of the hypothetical research questions posed by Committee members applied also to iPS cells in chimera research.

Fr. Berg asked whether NAS or ISSCR had guidelines on using human embryos in chimera research. Ms. Roxland stated that NAS did, but that she would have to confirm as to ISSCR. She commented that ISSCR may permit this type of research as long as the research was done *in vitro*, did not extend beyond 14 days, and the product was not implanted into a uterus. Dr. Lensch clarified that although it would be difficult to predict what future research involving a human embryo with animal genetic material would entail, it could be that this type of research would be useful in determining which cells control which functions. For example, animal genes are routinely inserted into human cells, *e.g.*, using sea anemone green fluorescent cells to track where certain cells migrate.

Fr. Berg suggested that the public needed to be involved in the discussion of chimera research, and that perhaps the Committee could issue a statement on such research for public comment. Ms. Dubler responded that in her opinion, she would rather not seek public comment because it would give voice to an extreme, science fiction perspective from individuals who did not have an accurate understanding of the complex nature of chimera research. Fr. Berg commented that he believed that reasoned feedback could be made by those who opposed this type of research, which would contribute to thoughtful discussion. Ms. Ellison concurred with Ms. Dubler and said that although she was a proponent of public debate, the usefulness of public feedback on this topic would be limited since the public did not have a clear understanding of

this research area. Dr. Kliztman replied that public debate and comment were already occurring and that there were deep cultural fears of mixing species, which had nothing to do with science, ethics, or today's discussion. Rev. Dr. Maynard-Reid stated that the Committee could consider releasing educational materials about the value of chimera research, such as how this type of research could advance understanding of various CNS diseases.

Dr. Daines reminded the Committee that the goal of today's discussion was to propose recommendations for chimera research guidelines to the Funding Committee; and that if no recommendations were made, the current language in Appendix A-2, permitting researchers to abide by either NAS or ISSCR guidelines, would apply.

Fr. Berg asked whether the Funding Committee would be open to adopting new standards that the Ethics Committee formulated. Dr. Daines replied that from a practical perspective, the Funding Committee would most likely defer to either NAS or ISSCR guidelines, especially since most researchers worked in both national and international arenas, but that the Funding Committee would likely be open to adopting new standards for chimera research if the Ethics Committee provided a substantial case for why new standards were needed.

Dr. Klitzman asked Dr. Lensch if there were any problems or dangers in current chimera research that the Committee should consider which may encourage the development of additional guidelines for Appendix A-2. Dr. Lensch replied that both the NAS and ISSCR guidelines reflected a solid understanding of the risks involved and that since chimera research had been performed for many years, with heavy institutional review and oversight, there were no "new" dangers for the Committee to consider.

Dr. Gorovitz commented that depending on how the Committee phrased its guidelines on chimeras, it could affect both public perception and how the guidelines were interpreted by researchers. Dr. Lensch agreed and pointed out that both the NAS and ISSCR guidelines were intentionally somewhat vague, to allow for some flexibility as the science and technology evolved, and to give review committees, who would be best informed of the scientific possibilities at the time of their review, the power to decide if the research should go forward.

Ms. Dubler commented that she was comfortable with the NAS guidelines and asked Fr. Berg if there was a specific provision or issue that the guidelines did not address. Fr. Berg reiterated his opposition to hES cell research, which also encompassed chimera research, but stated that he would like more time to consider possible areas of concern and what research limitations may be needed. Dr. Klitzman noted that he was inclined to follow one of the established set of guidelines rather than draft new guidelines and that ISSCR seemed to be more permissive in the types of chimera research allowed than NAS.

Ms. Dubler commented that the NAS and ISSCR guidelines seemed sufficiently specific to guide ESCROs in such a way to protect against science fiction chimera research. In addition, the risk-averse climate surrounding this type of research would cause review committees to be more sensitive to the concerns of the public. Ms. Dubler stated that both sets of guidelines were sufficient for the Committee's purpose and new guidelines should not be created unless absolutely necessary, because it would be confusing for researchers and a barrier to multi-

institutional research. Ms. Ellison concurred with Ms. Dubler that the Committee should adopt either NAS or ISSCR.

Dr. Klitzman suggested that in addition to giving researchers the option to follow NAS or ISSCR, the Committee could consider adding language that would state that since chimera research was relatively new, review committees should provide feedback to the Ethics Committee about any questions or problems they experienced when reviewing chimera research protocols. Mr. Swidler stated that he agreed with other members to permit researchers to utilize either set of guidelines and that Appendix A-2 should contain specific language regarding chimera research. He also suggested that the Committee periodically revisit the issue in the future, to account for new scientific developments.

Dr. Daines concluded that the Committee was comfortable with permitting researchers to abide by either NAS or ISSCR guidelines in connection with chimera research. He asked the Committee whether there should be separate language in Appendix A-2 that was specific to chimera research or whether the Committee should be silent on this topic, with the understanding that since Appendix A-2 already contained language that permitted researchers to choose which guidelines to follow, no additional language was needed. Mr. Swidler stated that the Committee should add specific language regarding chimera research in Appendix A-2 that would permit researchers to follow either set of guidelines.

Mr. Swidler made a motion for the Committee to recommend that a new provision be added to the NYSTEM contract requiring grantees who conduct chimera research to comply with the chimera provisions in either NAS or ISSCR guidelines. Rev. Dr. Maynard-Reid seconded the motion. The Committee voted in favor of the recommendation, with one abstention by Fr. Berg.

Model Informed Consent Forms

Dr. Daines introduced the final topic on the agenda, the development of model informed consent forms for donation of biological materials to stem cell research. He stated that use of the forms would not be mandatory and that they would instead serve as models. Dr. Daines turned to Ms. Roxland to facilitate the informed consent discussion.

Ms. Roxland directed the Committee's attention to an updated version of a form governing donation of oocytes for stem cell research purposes. While there were additional forms being developed, including a form governing donation of excess IVF-created embryos, the Committee began with the form for the donation of oocytes because it was the most complex. Once that form was finalized, the other model consent forms would be conformed appropriately.

Ms. Roxland stated that the forms were based on the model forms issued by ISSCR, and that a workgroup composed of Ethics Committee members (Nancy Dubler, Robert Swidler, and Dan Sulmasy) drafted forms and brought them back to the Committee for review. Since the last time the forms were circulated, comments from Committee members, the informed consent requirements of Appendix A-2, workgroup input, and comments from DOH staff have been incorporated. However, DOH had not officially reviewed the form, so there may be outstanding

legal issues that would need to be incorporated. Additionally, the forms were updated to reflect current medical literature on risk, and with respect to the risk section, had been compared to forms from other institutions.

Dr. Gorovitz inquired about the language on page seven regarding compensation for research-related injuries, the standard for determining what qualifies as a research-related injury, and whether the form conveyed the possibility that an injury might occur that would not be covered. Ms. Roxland explained that the standard, taken from the language in Appendix A-2, covered injuries resulting "directly and proximately" from participation. The language appeared in a footnote rather than the form itself and Ms. Roxland inquired whether the Committee wanted the form to contain the legal language.

Ms. Dubler stated that there was no legal standard or case law governing what constituted a research injury. Dr. Klitzman commented that IRBs regularly confront the issue of defining adverse events. Mr. Swidler agreed that additional information would not be helpful to the participant, and commented that if an injury were to occur, the researchers would either cover it or the parties would litigate the case. He stated that the form was very good, and his only concern was its length, therefore this was not an area that should be expanded.

Ms. Roxland pointed out that the Committee had instituted a requirement that researchers be financially responsible for both associated medical procedures and for research-related injuries through the "directly and proximately" provision in Appendix A-2. Ms. Dubler responded that she agreed with that approach, but that it should be made clear to institutions that they must assume this responsibility in addition to their other regulatory obligations. Ms. Roxland stated that the forms were optional, and that the institution had discretion about whether to use them. Ms. Dubler opined that the language was a requirement of A-2, therefore contractors must use it, and recommended that the exact language be included in the form.

Mr. Swidler asked whether the form was flexible enough to accommodate an egg-sharing proposal, *i.e.*, a situation where a researcher offered to discount fertility services in exchange for eggs. Ms. Roxland responded that while the Committee had previously discussed egg sharing, it did not make specific recommendations. However, she believed the Committee made several statements that it did not view the practice favorably. Dr. Klitzman stated that it may be worth revisiting this topic at a later date.

Ms. Dubler inquired about the risk language in the form and whether it was comparable to what might appear in a clinical consent form. Ms. Roxland replied that with respect to the risk section, it had been completely revised to contain a detailed description of risk based on medical literature and sample consent forms from other institutions. She added that the risk disclosure in the current form exceeded what was contained in the other institutions' forms.

Ms. Dubler asked whether it was the intent of the Committee for the risk section to be a model for clinical consent forms generally. The Committee discussed whether requiring the clinical community to adhere to certain risk language fell within its purview, and it was generally agreed that it did. Ms. Roxland asked if there were other thoughts about how the form should be used—whether it should be used with other medical consent forms that already exist in

clinicians' offices and clinics, or stand alone as a comprehensive form. She pointed out that the issue had been discussed but never clarified by the Committee, although it would ultimately be decided by the institution.

Fr. Berg remarked that the form did not contain a provision governing the options available to a woman who donated her eggs for research, which were subsequently fertilized via IVF, who afterwards changed her mind before the embryo was used in research. Ms. Roxland stated that this was covered on the page 9, "What If I Change My Mind," section, which stated that consent could be withdrawn at any time during the egg retrieval process, or after the retrieval was complete, but before the eggs were used in research. Mr. Swidler also pointed out that page 8 of the form addressed alternatives to research donation and stated the options. Ms. Roxland stated that Appendix A-2 required that a donor be advised there were alternatives to research donation available, including embryo adoption. Embryo adoption was not listed as an alternative in this informed consent form, however.

Fr. Berg replied that he was concerned about the donor's ability to change her mind once an embryo had been formed with her egg for research purposes, rather than during or after the egg retrieval. Dr. Gorovitz clarified the point and reframed the question: if an egg had been fertilized, creating an embryo, did this mean the research had begun and the woman could no longer change her mind? Fr. Berg stated that the form did not seem to allow a woman to assert a claim over an embryo that might be formed with her donated egg.

Dr. Lensch commented that even if an embryo was formed in the situation described, it was not clear that the egg donor would have dispositional rights over it as opposed to the sperm donor. Ms. Roxland acknowledged this point and stated that it was unclear from a legal standpoint what an egg donor's rights were. Ms. Ellison suggested that once a woman donated her eggs to research, she relinquished control of a future embryo at that point. Dr. Klitzman responded that one could argue that there was joint "ownership" of the embryo based on related case law. Ms. Ellison asked whether the embryos that were the subject of such disputes were created for research, to which Dr. Klitzman responded that they were not.

Ms. Roxland commented that there was quite a bit of case law from the family law context on the subject of embryo disposition when the divorcing couple could not agree. Ms. Dubler commented that the case, *Davis v. Davis*, referred often to the concept of ownership, but that the problem could be avoided by clarifying the point where research began. She suggested that the form should be clear on this point, and contain the following statement: "once the egg has been entered into a process of fertilization, the research has begun."

Fr. Berg suggested it may not be as simple as the Committee deciding when research began, and perhaps some legal analysis of the disposition issue was warranted. A Committee member suggested that the question of when transfer of control of the egg occurs was more of a contractual matter with the donor, to which Ms. Dubler replied that in these cases, the consent form was the contract, and the terms and conditions were clear.

Ms. Roxland stated that if the Committee agreed to allow a woman to rescind consent after an embryo had been created with her egg, this may require a revision of Appendix A-2 as

well. She offered to explore the disposition issue from a legal standpoint to determine whether it was considered a property right or some other interest that could be extinguished by contract.

Another Committee member inquired whether the 14-day window could be utilized as the period where a donor might change her mind, or whether an embryo was frozen soon after formation for future use. Dr. Lensch explained that the 14-day limit was theoretical, as most embryos fall apart *in vitro* before the end of this period and that stem cells were usually derived from embryos between three and seven days after formation. He stated that it was possible that the embryo would be frozen for future research use. Mr. Swidler noted that it was his understanding that there was a need for fresh embryos as opposed to frozen, so that the time frame was likely to be on the shorter side.

Fr. Berg asked Dr. Lensch if he knew of any researchers that were developing new stem cell lines utilizing embryos created from donated eggs, as opposed to excess embryos from IVF treatments. Dr. Lensch replied that he only knew of a couple of lines derived specifically for research, due to the practical fact that there were numerous IVF embryos available for research. He stated that in his opinion, stem cell research with donated eggs would be more likely to utilize Somatic Cell Nuclear Transfer (SCNT) and parthenogenesis, neither of which would result in embryos suitable for fertility purposes.

Committee members reached a consensus that research began when there was an intervention with the embryo. Dr. Daines stated that it may be necessary to draw the line there for practical reasons, and encouraged the next iteration of the form to reflect this conclusion. Ms. Roxland informed Committee members that she would redistribute the form, with a specific request for comments.

Discussion of Future Agendas

Dr. Daines moved the conversation to the discussion of future agendas. He noted that the consent forms would be revisited, and mentioned that egg-sharing was raised as a potential area for further discussion. The Committee also planned to revisit the issue of research standards governing chimeras as the science evolved.

Ms. Dubler suggested that the Committee discuss standards and/or guidelines to govern clinical stem cell research protocols, specifically whether the Board would issue guidelines to assist ethical review committees when they evaluate these proposals. Rev. Dr. Maynard-Reid suggested discussion of financial conflicts of interest in light of new literature and the effort at NIH to revise its conflict of interest rules. He also suggested the related issue of intellectual property rights. Fr. Berg suggested the topic of hybrids and cybrids.

Dr. Klitzman stated the Committee may want to solicit input from ESCROs to obtain feedback about where further guidance might be necessary. He also suggested inviting a few NYSTEM awardees to a meeting to engage in a dialogue with the Committee. Finally, he requested information about what issues other members of the IASCR were working on, and Ms. Roxland stated that she would be attending the upcoming annual IASCR meeting and could provide that information at the next meeting.

Adjourn

Dr. Lensch thanked the Committee and commended the members on its work, commitment, and the depth of issues it reviewed. Committee members once again acknowledged Ms. Doesschate's work with the Board, and Dr. Daines entertained a motion to adjourn the Ethics Committee meeting. A Committee member so moved and Dr. Gorovitz seconded the motion. All were in favor, and the meeting was adjourned.

s/
Janet Cohn, J.D.
Executive Secretary to the
Empire State Stem Cell Board
Approved: December 17, 2010