

**Interstate Alliance on Stem Cell Research, Fall 2008 Meeting**  
**September 9-10**  
**University of Maryland Biotechnology Institute**  
**Baltimore, MD**

**Meeting Summary**

**Participants:**

*States*

California	Connecticut	Illinois	Massachusetts
Maryland	New Jersey	New York	
Ohio	Rhode Island	Wisconsin	

*Countries*

Canada	United Kingdom
--------	----------------

*Organizations*

International Society for Stem Cell Research  
National Academies

*Guest Organizations*

RESOLVE - The National Infertility Association

**Major Focus Items:**

- Intellectual Property Policy:
  1. Provide an overview of recent state legislation and policy
  2. Consider how state and national partners can support information needs regarding IP policy
  
- Registries and Banking:
  1. Provide an overview of current registry and banking initiatives nationally and internationally
  2. Consider how state and national partners and/or IASCR can support the registering of cell lines
  
- Chimeras:
  1. Understand the role of chimeras in research supporting the development of cell based therapies
  2. Review current guidelines and policies governing transplantation of human cells to animals

## State and Partner Updates

**CT:** A total of \$9.8 million in state funding will be made available to the research community on or after April 1, 2009 in the third installment of grants from the Stem Cell Research Fund created by statute in 2005. On May 27, 2008, Governor Rell signed Public Act No. 08-80, effective October 1, 2008, making changes in Connecticut's stem cell research law to reflect acknowledgment of, and compliance with, the "National Academies' Guidelines for Human Embryonic Stem Cell Research". The legislation is the direct result of interstate discussions at the IASCR meetings.

**Issues:** Status of NIH lines given recent revelations on donor consent; WiCell MTAs; genetic privacy; are other states doing neural stem cell implantation into primates?; medical tourism; commercial ESCROs.

**CA:** The CIRM governing board approved two new regulations on an interim basis (270 days). One provides for a petition for designating a cell line as acceptably derived. The other grandfathers the use of paid eggs from donors for research use if made before August 2008. CA is forging international collaborations with Australia and Canada. July workshop on using stem cells for predictive toxicology went well, report expected out soon.

**Issues:** CA is also getting a lot of questions about the NIH lines re consent, but CIRM is not reconsidering its authorization of use of these lines.

**IL:** IL is having a "budgetary pause" due to a \$2 billion shortfall. A report on progress to date is expected to be out soon.

**MA:** Massachusetts Governor Deval Patrick signed the 10 year, \$1 billion Life Sciences Investment Act in June. It establishes numerous programs to strengthen the life sciences industry in Massachusetts, including capital funding, support for loans, grants, fellowships, and investments in R&D, tax incentives, and a program to expand employment in the life sciences sector and promote health-related innovations. The Massachusetts Department of Public Health also received an inquiry from the research community as to allowing the practice of egg-sharing for research under Massachusetts law. A draft analysis of this issue is currently under review by the Biotechnology Research Advisory Council BRAC and the Department.

**MD:** In 2008, another 58 projects were funded for a new total of 82, including post doctoral fellows. In 2009, MD will have \$19 million and beginning in 2010, \$20 million/year. MD supported projects are beginning to be successful at leveraging additional funds, e.g., from NIH. Karen Rothenberg is the new chair of the stem cell commission.

**Issues:** Conflict of interest for reviewers; MD is trying to address factors that go beyond scientific merit, e.g., stem cell type, disease or condition addressed, institution, demographics, public vs. private, and where else investigators may be getting funding.

Finally, concern about “specialness” of stem cell research, are integrating their stem cell research into larger life sciences framework.

**MO:** Repeal attempt failed, so there have been no steps backward. MO has no state regulations nor any state funding, all SCR done in MO with federal or private funding.

**NJ:** The bond issue failure in late March was a major setback and funds for bricks and mortar to build a stem cell center were lost. But NJ is still supporting research, with \$11 million in an RFP that just closed. One hundred applications were in review at the time of the IASCR meeting.

**NY:** In May the NYSTEM program issued four RFAs for nearly \$109 million in funding. See meeting handout at [www.iascr.org](http://www.iascr.org) for a description of the focus areas. Two additional RFAs will be released this fall to support student internships and undergrad curriculum development. The Empire State Stem Cell Board strategic plan was approved in June and scheduled for final publication in early October 2008. The Board’s Ethics Committee is expected to develop guidance and model informed consent forms to assist grantees and on payments to gamete donors. NYSTEM will hold its first grantee conference on June 12 2009 in Albany.

**OH:** The state of Ohio has funded stem cell research through the Third Frontier Program, including a stem cell center based at Case Western with collaboration from the Cleveland Clinic and other institutions. Thus far, research has focused on adult stem cells. The efforts are also linked to another initiative in tissue engineering and there is also a linkage to the Armed Forces Institute of Regenerative Medicine, with 20+ clinical trials on-going. Ohio has no ESCRO committees as yet, but with interest in moving into embryonic cell lines growing, they will consider establishing the appropriate oversight.

**RI:** The Rhode Island Umbilical Cord Blood Bank Act was passed and signed into law. It requires hospitals and other obstetrical facilities and professionals to inform patients of the option of donating or storing umbilical cord blood in banks. An income tax check-off program for contributions to the RI Blood Center’s Umbilical Cord Blood Bank Initiative was drafted in the 2008 legislative session and would be a state tax check-off form that filers can elect to include with their state income tax return to have donations automatically deducted from their refund checks for whatever amount they wish to give. This bill has not passed as yet. RI Public Law 2008 Chapter 153 was enacted July 1, 2008; it establishes funding streams for Public Cord Blood, for which there will be a pilot project for 2008-09. Rhode Island is also currently looking into a \$100 million dollar bond proposal through the Economic Development Corporation and the Science Technology Advisory Council for life-sciences. This group is composed of public and private researchers, universities, laboratories and hospitals.

**WI:** To keep WI at the pinnacle of ground-breaking research and new life-saving innovations, Governor Doyle has outlined an ambitious but achievable goal to capture 10 percent of the national stem cell market by 2015. To meet this goal, WI is working to harness talent and innovation from every corner of the state. Key partners in the public and private sectors, such as the University of Wisconsin’s researchers, University Research Park, the Wisconsin Alumni Research Foundation, WiCell Research Institute, patient advocate

groups, and the many private businesses that work in the stem cell area are working with state government to continue to blaze the future of stem cells and biotechnology. The success of their researchers and the value they provide through outreach and training is paying dividends for state's economy. According to a research study by NorthStar Economics, the overall annual economic impact of human embryonic stem cell research and commercial activity in 2006-2007 was \$44.5 million, which was generated from research activities at UW and the commercial activity and research of a number of stem cell start-up companies. In addition to the overall economic impact, stem cell research and commercial activity created hundreds of high paying jobs throughout the state. See the handout for these meeting notes at [www.iascr.org](http://www.iascr.org) for more details.

**ISSCR:** 2009 meeting will be in Barcelona, Spain, co-sponsored by the CRG and CMRB; 2010 meeting in San Francisco co-sponsored by CIRM. Their Guidelines for the Clinical Translation of Stem Cells are out for public comment. They are also planning on staging two regional meetings a year to have more translational research focus, with the first one set up for Argentina. The ISSCR annual report, published in Cell Stem Cell, is available online: [http://images.cell.com/images/Edimages/stem/isscr\\_annual\\_report.pdf](http://images.cell.com/images/Edimages/stem/isscr_annual_report.pdf).

**Canada:** Concern about shift in views with October 14 election. There is an eastern Canada/eastern US initiative for research. Also a new agreement is being developed with CIRM for cancer stem cell research.

**UK:** HFEA bill went through the House of Commons. The most controversial provisions were the ones on chimeras, which did pass. But the bill was tabled until Commons comes back in the fall.

**Intellectual Property Policy discussion:** Ed Penhoet, Scott Tocher, Nancy Koch, California Institute for Regenerative Medicine (See accompanying handout)

By law, CA must receive monetary benefit from stem cell products market while not hindering research. Private sector is key to developing therapies and cures for commercialization, but this sector does not like provision that they must give back the same amount whether they received a small amount of CIRM funding or a large amount. Industry wants return to the state to be proportional to the level of support they got from the state, which CA refuses to do. Still IP is owned by grantee and not the state – policies consistent with Bayh-Dole. But even though the grantees own the IP, state still gets a return: (1) access plan – grantees must submit plan to address uninsured patients in CA; (2) price guarantees - drug prices must be set according to states' discount program; (3) revenue sharing – CIRM gets 25% of licensing revenues >\$500K, etc. (See handout for details.)

CIRM grantees must also share publication-related materials for research and CIRM retains right to assume licensing control to prevent underutilization of CIRM-funded inventions. But CIRM rejected a research rule. CA is also looking at collaborative funding opportunities with organizations such as JDRF, Canadian Cancer Stem Cell

Consortium, State of Victoria, Australia (all under MOUs). There will be more discussion on these collaborations at the next (May 5) meeting.

### **Stem Cell Banking and Registries – Rosario Isasi**

International Stem Cell Forum (ISCI) is a worldwide collaborative effort to establish basic criteria and techniques to underpin development of applications for hES cells in human medicine. Led by Peter Andrews.

International Stem Cell Banking Initiative (ISCBI) is establishing an agreed upon set of minimum standards for banking, characterization, and testing. Also creating a solid ethical framework for international banking and research. Will serve as an umbrella under which international agreements can be established. Adoption of “consensus guidance.” ISCBI is hosted by UK stem cell bank. Convergence is merging, generally consistent with general policy frameworks related to permissibility of SCR. Majority of institutions accept cell lines of different origins and grades (research vs. clinical) but in some countries (e.g., US) there are special restrictions. But the requirements for international sharing are murky. Clinical-grade lines will take longer to sort out because they are much more specialized. Some banks are likely to have separate facilities for research and clinical lines. Seeking to harmonize ethical approach to what banks can accept, although there is lots of variability across banks and what they can and cannot take. Article summarizing all this due out, maybe in Nature, Rosie will share with group.

Discussion: Geoff Lomax serves on ISSCR registry steering group, deals with provenance, not scientific aspects, which are being addressed in a separate context.

Erik Forberg: US National Stem Cell Bank: operated by Wisconsin, contains only NIH-approved lines. But might serve as a model for other banks. WiCell also has a separate bank for “non-presidential” lines.

Geoff Lomax distributed a discussion draft for a CIRM Model Oversight Committee Certification form. Could IASCR adopt this as a recommended approach across all states? A discussion was begun here, but no decisions were expected at the meeting. Should the form have more detail on informed consent? Susan Stayn recommended adding a line for restrictions in case there are any that need to be recorded.

**Collaboration with the IVF Community:** Barbara Collura, Executive Director, RESOLVE, The National Infertility Association, and Margaret (Peggy) Swain, attorney specializing in family practice law

Collura: RESOLVE provides patient support, information, and advocacy, in business 34 years. They are also proponents for insurance coverage, IVF is generally not covered. So they make it their business to rack legislative action at the state level through their nationwide network. For example, Colorado’s “personhood” amendment would change the CO constitution to define a person as originating at the moment of conception. This would not exempt IVF practices, storage, donation, etc. Eight other states have

comparable legislation in play. While these things may not pass, they are signs of opposition not just to SCR, but to IVF and how it operates.

Embryo disposition work: have three HHS grants related to embryo adoption/donation. HHS has supported such grants since 2001 to raise awareness about this. The majority of this funding has gone to faith-based organizations that promote adoption. RESOLVE has put together a Guide to Embryo Donation for Professionals (copies are available, or see the RESOLVE website). State laws on adoption of children (after birth of child) highly variable, and it is difficult to apply “adoption” regulations to embryos. This is a problematic area of the law. Note that “adoption” and “donation” are not interchangeable, although HHS grants use these terms that way.

[www.resolve.org](http://www.resolve.org): This site has all their policy statements. They have a stem cell/cloning policy very similar to that of CAMR.

Swain: Informed Consent and Patients’ Rights – Informed consent is to allow patients to make good decisions about their own care. This should be a joint process between the patient and the physician. But ART has special aspects on top of general features. ART is elective, and there are risks to patient and offspring. May involve third party collaborations whose behavior is not under patient’s control. Financial aspects also critical, since insurance usually doesn’t cover and cost to patient can be \$25-30K. In general, not a lot of US tax breaks for this, either, although there is a 50% tax break in Canada.

In US, federal reporting to CDC is required. This includes success rates. Disposition options include donation for research, but usually this is not more detailed or specific than that. Emotional aspects of disposition choices should not be underestimated, either. In short, there is very little regulation of any of this, including storage and disposition of unused embryos. ASRM recommends destruction/disposal after 5 years but clinics rarely do this for fear of liabilities. Cryopreservation triggers costs, etc. Cases of divorce have produced court decisions. Courts have thus far not forced an unwilling spouse to parent, but at least 2 courts have viewed cryopreservation agreement as a contract. “Abandoned” embryos cannot just be donated for any other because may not be able to track down owners to get consent. See Swain’s slides for several interesting scenarios.

### **Chimeras: Panel Discussion**

John Gearhart (see accompanying slides): Clarified definitions of chimera, mosaic, hybrid, clone, transgenic. Primary chimeras made at earliest stages of embryogenesis or develop naturally and these are very powerful tools for research in developmental biology. Secondary chimeras – anyone who has received a transfusion of blood or bone marrow, heart valves, etc. is one of these. Animal/human chimeras: animal receives human cells, tissues or organs. “Humanized” animals – e.g., animals with human immune systems due to insertion of human tissue into animal. Not a great deal of moral concern about most of these.

Stem cells and chimeras: how many cells? Germ cells and the brain are the areas in which concern is focused. Factors to be considered with possible humanizing of the brain – stage of development, number of human cells, site of graft, relatedness of host to human.

Why are chimeras essential? If we are to get stem cells into therapies, we must test them for efficacy, safety, etc. *in vivo*. Hence this must be done in chimeras. FDA requires it! Although we have to go this route, the paradigm is not without inherent concerns and will require a lot of effort and money to make it safe.

**Willy Lensch, ISSCR:** In its guideline deliberations, ISSCR wanted to refrain from saying that certain areas of research should not be allowed and leave most decisions to local authorities. ISSCR Category 1 research includes *in vitro* chimera research that does not require much oversight and Category 2 chimera work requires some oversight to look at the integration of human cells into animal models. But Category 3 research covers things that they felt should be off the table: no breeding of animals that might have germ line involvement. Otherwise, advised not to shy away from experiments but to give them full and adequate consideration. But draw the line at implantation for non-human primates.

**James Lawford Davies, UK:** Debate in the UK has been about creating human embryos that contain animal cells. A House of Commons report on reproductive technologies and the law allowed hybrid and chimeras, but subject to 14 day rule. In 2005, government announced another review of legislation, including “hybrids” research. HFEA said human=animal hybrids were already allowed and sometimes necessary and desirable. In Nov. 2006, licenses applied for to derive stem cells from human-animal hybrids, which initiated a high level of public engagement. In Dec. 2006, the government issued a white paper proposing a ban in mixing human and animal cells. There was a campaign to stop this from moving forward, with overwhelming, but very balanced (and even pro-science) media coverage that helped build public understanding and acceptance. More recently, HFEA announced its decision to treat hybrids as “human” and stated that there was no basis for a government ban, HFEA would regulate. IN Oct. 2007, all types of hybrid/chimera research were declared allowable, but the terminology was changed to “admixed” embryos. Two other bills were voted on in May of 2008, both trying for a ban and both defeated.

Cybrids – although mitochondrial DNA is still in enucleated animal eggs, it is eventually lost and replaced by human mitochondria. (?)

### **Wrap-up: List of issues for future discussion**

- **Administrative oversight: Administrative structure at state level**
- **NIH lines and consent; what if they don't conform to consent standards?**

- **WiCell MTA agreements: Do MTAs impact what research can be done?**
- **Genetic privacy: Does the consent process need to be revised to reflect privacy requirements?**
- **Neural transplantation in primates**
- **Stem cell tourism: What should the response be?**
- **Commercial ESCROs: Any experience with these?**
- **International partnerships and how these are developing, how are they working?**
- **Conflict of interest: What happens when institutional members run into COI considerations? Does IASCR need to consider this as a topic for members?**
- **Research focus: Where are folks putting their funding? Bioscience framing vs. stem cell research; hESC research vs. other types of SCR; basic research, translational, clinical? What is the state of progress and where are the discoveries?**
- **Private sector: Are there barriers to participation in state programs? What about other mechanisms for investment in research, e.g. tax credits**
- **Education and outreach on embryo donation, continue dialogue with IVF community**