

BIOETHICS AND STEM CELL BANKING IN CALIFORNIA

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I. INTRODUCTION

Too often, institutionalized bioethics proceeds on the assumption that the existing apparatus of rules is so well fixed that one must only crank new fact patterns through to obtain the correct ethical answer. Holding fast to such a view of bioethics, however, would be to ignore one of the most interesting social aspects of the new life sciences, namely, the way in which new technologies continually confront and unsettle existing dispensations of established bioethical norms.¹ In this regard, recent events in California mark a formative moment for bioethics in the United States.

When voters approved the California Stem Cell Research and Cures Initiative in the November 2004 election, it marked a sea change in the environment for public funding of human embryonic stem cell (hESC) research in the United States.² The U.S. government's human embryonic stem cell policy prohibits the use of federal research money to create new hESC lines, and federally funded researchers may not work on any lines created after August 2001.³ Codified as the California Stem Cell Research

1. See, e.g., David E. Winickoff, *Governing Population Genomics: Law, Bioethics, and Biopolitics in Three Case Studies*, 43 JURIMETRICS J. 187 (2003).

2. Constance Holden, *California's Proposition 71 Launches Stem Cell Gold Rush*, 306 SCI. 1111 (2004).

3. Office for Human Research Protections, Department of Health and Human Services, Guidance for Investigators and Institutional Review Boards Regarding Research Involving Human Embryonic Stem Cells, Germ Cells and Stem Cell-Derived Test Articles (Mar. 19, 2002), <http://www.hhs.gov/ohrp/humansubjects/guidance/stemcell.pdf>

and Cures Bond Act, California's program earmarks \$3 billion in direct state spending, \$6 billion including interest payments, for human embryonic stem cell research and related work over a 10-year period.⁴

Until recently, the question of whether to pursue hESC research has dominated the ethical and political discourse concerning the research. With the passage of the California program, and the development of other state initiatives in its wake,⁵ more explicit attention is now devoted to the ethical and political aspects of its implementation. The California Institute for Regenerative Medicine (CIRM) has been given the legal and bioethical mandate to regulate all research funded by the stem cell initiative.⁶ The roughly two years since the passage of Proposition 71 have been active ones in the formation of the regulatory regimes that will likely be implemented in California and the rest of the United States.

As the first state seriously grappling with implementing hESC research on a large scale, California will likely exert a strong influence on how stem cell research and its associated technologies are regulated nationwide. At a minimum, any regime of ethical oversight and standards in stem cell research will have to govern three distinct facets of the endeavor: (1) the procurement of the gametes, embryos, and other cells from human donors for the generation of new hESC lines; (2) the conditions under which scientists may derive new hESC lines from these materials; and (3) the manner in which already-derived hESC lines are subsequently used.⁷ At least in the United States, systematic thinking in these areas has only recently begun.⁸

(“Research on existing human embryonic stem cell lines may be conducted with Federal support if the cell lines meet the U.S. President’s criteria which he announced on August 9, 2001[.]”).

4. See generally CAL. HEALTH & SAFETY CODE § 125291.10 (2004).

5. See, e.g., John Wagner, *Maryland Approves Fund to Support Medical Stem Cell Research*, WASH. POST, Mar. 30, 2006, at A1.

6. CAL. HEALTH & SAFETY CODE § 125290.35 (2004).

7. Of course, some of these aspects of regulating stem cell research are already regulated in various ways. See discussion of current federal and California regulations *infra* Section II.B.

8. See, e.g., NATIONAL RESEARCH COUNCIL & INSTITUTE OF MEDICINE, GUIDELINES FOR HUMAN EMBRYONIC STEM CELL RESEARCH (2005) [hereinafter NAS GUIDELINES]. There are notable exceptions that confront the ethical concerns of the informed consent process. See, e.g., Bernard Lo et al., *Consent from Donors for Embryo and Stem Cell Research*, 301 SCI. 921 (2003); Bernard Lo et al., *A New Era in the Ethics of Human Embryonic Stem Cell Research*, 23 STEM CELLS 1454 (2005); David Magnus & Mildred K. Cho, *Issues in Oocyte Donation for Stem Cell Research*, 308 SCI. 1747, 1747-48 (2005) [hereinafter *Issues in Oocyte Donation*].

As an early adopter and promoter of hESC technologies, California will necessarily become an early and influential adopter of hESC *governance* as well. In establishing a regulatory regime for its stem cell research program, CIRM will have to develop innovative policies that will in turn carry significant normative implications for the rights of research participants, the collective goals of the state, and the interests of research institutions both in the private and public sector. Decisions in these areas will attempt to balance competing substantive and procedural goals, such as experimental freedom, economic and scientific utility, the autonomy of human donors, and public accountability in bioethical decision-making.

California's decisions in this area play upon the increasingly contested normative terrain of biotechnology, and will surely reshape that terrain. In an age of greater commercialization of clinical medicine and biomedical research, traditional relations among research subjects, researchers, taxpayers, corporations, and research institutions have come under increasing strain, whether around the control of biological samples or intellectual property rights,⁹ the role of human research subjects in ethical oversight,¹⁰ the growing frustration with the pharmaceutical industry,¹¹ or the pricing of medical care.¹² Furthermore, the fact that hESC research implicates a fast-evolving ethical frontier—concerning, for example, the manipulation of nascent human life, egg donation for research on a large scale, “immortalized” cell lines that can, in theory, be propagated indefinitely, and new forms of cross-species experimentation—underscores how California will face bioethical and regulatory questions of first impression. The above ob-

9. See, e.g., *Moore v. Regents of the Univ. of Cal.*, 51 Cal. 3d 120, 129 (1990) (holding a physician must, under informed consent, disclose personal interest unrelated to a patient's health); *Greenberg v. Miami Children's Hosp. Research Inst., Inc.*, 264 F. Supp. 2d 1064, 1074-76 (S.D. Fla. 2003) (failing to recognize a property interest in genetic material given to defendants); *Wash. Univ. v. Catalona*, No. 4:03-CV-01065-SNL, at 49 (E.D. Miss. Mar. 31, 2006) (holding research patients had no proprietary interest in genetic material where it had been donated to the university research program); see also Donna M. Gitter, *Ownership of Human Tissue: A Proposal for Federal Recognition of Human Research Participants' Property Rights in Their Biological Material*, 61 WASH. & LEE L. REV. 257 (2004). For a recent journalistic account of this phenomenon, see Rebecca Skloot, *Taking the Least of You: The Tissue-Industrial Complex*, N.Y. TIMES MAG., Apr. 16, 2006.

10. See, e.g., JENNY REARDON, RACE TO THE FINISH: IDENTITY AND GOVERNANCE IN AN AGE OF GENOMICS (2005) (detailing the struggles over the Human Genome Diversity Project, especially regarding the contested notion of bioethical expertise and oversight).

11. See, e.g., MARCIA ANGELL, THE TRUTH ABOUT THE DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT (2004).

12. See, e.g., DANIEL CALLAHAN, WHAT PRICE BETTER HEALTH? HAZARDS OF THE RESEARCH IMPERATIVE (2003).

servations point to the need for a bioethical analysis that can address the emergent stem cell regime in California through the lenses of democratic governance and political economy, not just with a narrow concern for protecting research subjects.

Part II of this Article explores CIRM's regulatory mandate in relation to pre-existing federal and state rules, and compares recently drafted regulations for the ethics and oversight of stem cell research under the California Initiative against an influential set of research guidelines issued by the National Academies in April 2005. Part III argues that this developing regime of ethical oversight suffers from a number of disadvantages from the perspective of governance, especially around the informed consent process, institutionalized ethical review, and egg donation. Part IV outlines my proposal of a new institutional and legal architecture that would address some of these problems through the creation of a centralized stem cell bank with special rules of participatory governance: The California Stem Cell Biorepository. Such an institution could be established in California by requiring that all new hESC lines created with CIRM funds be deposited there. If set up properly, such an institution could help improve the consent process for donors and the system of ethical oversight, as well as remediate problematic power asymmetries established in the currently proposed regime.

II. THE EMERGENT GOVERNANCE REGIME FOR STEM CELL RESEARCH IN CALIFORNIA

Proposition 71 gave the California Institute for Regenerative Medicine full authority for setting the ethical standards that will govern the new stem cell program. As mentioned above, any regime of ethical oversight and standards in stem cell research will have to govern three distinct facets of the endeavor.

First, any regime of ethical oversight for hESC research will have to govern the procurement of the gametes, embryos, and other cells from human donors for the generation of new cell lines. New lines must be derived from human embryos at an early stage of its development called the blastocyst, and there are three major pathways of donation. The first is in vitro fertilization (IVF), which results in so-called "spare" embryos.¹³ The

13. IVF involves the extraction of eggs and sperm from potential parents or donors, and the creation of embryos *in vitro* for subsequent transplant into the potential mother's womb. "Spare embryos," sometimes called "supernumerary embryos," are those embryos created in the IVF clinic that are not actually implanted in the womb. IVF treatment often

second source of embryos could come from the creation of embryos in vitro from egg and sperm specifically for the purpose of deriving new hESC lines. A third source of stem cell lines would involve somatic cell nuclear transfer, also known as cloning.¹⁴ Rules around procurement will help establish the processes and contexts through which donation of gametes, embryos, and adult cells may occur. These rules will also establish rights and duties between researcher and donor with respect to donated materials and the cell lines to which they give rise.

Second, the governance regime for stem cell research must address the derivation of new hESC lines. Even those who favor hESC research tend to agree that human embryos enjoy some sort of special status and should not be destroyed simply at will, without some specific research justification.¹⁵ The use of somatic cell nuclear transfer to derive new hESC lines is an emerging practice that raises serious ethical questions around the manipulation of early human life. Since the embryos produced through cloning could in theory be used to produce a cloned human being, the use of this technique is more controversial.¹⁶ Many bioethicists and scientists agree that if the use of this technique is to proceed, it should proceed in a regulated fashion.¹⁷

Third, a regime for stem cell oversight might address how already-derived hESC lines are used, an area that is currently only minimally regulated.¹⁸ A number of highly controversial types of research are possible using human embryonic stem cells. Because of their potential to develop into human nerve and brain cells, embryonic stem cells could be used to

involves the creation of more embryos than necessary, because some percentage of created embryos will not be viable.

14. Through this method scientists inject genetic material from an adult cell into an egg cell, stimulating it to reproduce. An advantage of somatic cell nuclear transfer is that it may avoid the problem of rejection that is common in stem cell transplantation procedures. See, e.g., NAS GUIDELINES, *supra* note 8, at 13. It should be noted, however, that an efficient human cloning technique is further away than previously imagined in the wake of the discovery that Dr. Hwang's stunning cloning efficiency in South Korea was a fraud. David Cyranoski & Erika Check, *Koreans Admit Disguising Stem-Cell Lines*, 441 NATURE 790 (2006).

15. For a balanced and useful discussion, see Rebecca Dresser, *Stem Cell Research: The Bigger Picture*, 48 PERSP. BIOLOGY & MED. 184, 184-94 (2005).

16. Indeed, Canada, Spain, Switzerland, Taiwan, The Netherlands, and other countries do not allow somatic cell nuclear transfer for the creation of new hESC lines, but they do allow derivation of new lines from spare embryos. Lori Knowles, *A Regulatory Patchwork—Human ES Cell Oversight*, 22 NATURE BIOTECH. 157 (2004).

17. See NAS GUIDELINES, *supra* note 8.

18. See *infra* Section II.B and accompanying discussion of current federal and California regulations.

create animals with a significant number of human cells. These so-called chimeras may prove useful for conducting biomedical experiments, but they blur the boundary between human and non-human animals, introducing great complexity into the question of human research subject protections as well as animal experimentation.¹⁹ Furthermore, human donors' rights to limit certain research uses are recognized and documented, and it will be necessary to enforce these limitations either contractually, through regulatory oversight, or through some combination of the two.

A. CIRM's Regulatory Mandate

The California Institute for Regenerative Medicine (CIRM) is governed by a twenty-nine member board, the Independent Citizens' Oversight Committee (ICOC), consisting of representatives of public and private universities, non-profit research centers, patient advocacy groups, and biotechnology firms. To help it execute its \$3 billion grant-making authority, the ICOC is advised by three working groups, which include committee members and outside experts. These groups recommend research grants, facilities grants, and ethics standards. Interestingly, the California Stem Cell Initiative established the ICOC's exclusive regulatory authority over "Medical and Scientific Accountability Standards" governing CIRM-funded research.²⁰ This involves a regulatory exemption for CIRM-funded research from pre-existing or future state laws "dealing with the study and research of pluripotent stem cells and/or progenitor cells, or other vital research opportunities."²¹

This exemption is significant. California had been ahead of most states and even the federal government in adopting certain regulations governing stem cell research. For example, federal human research subject regulations cover all federally funded research and also all research conducted at institutions that have granted the federal research agency "assurances" of compliance,²² which covers all major universities. This set of regulations—the so-called "Common Rule"—mandates that an institutional review board (IRB) reviews all covered human subject research protocols, and that research subjects provide informed consent.²³ However, the regu-

19. See Jamie Shreeve, *The Other Stem-cell Debate*, N.Y. TIMES MAG., Apr. 10, 2005 (discussing the controversy surrounding the creation of human animal hybrids). For a discussion of nascent efforts to ban the creation of certain human chimeras, see Christopher Thomas Scott, *Chimeras in the Crosshairs*, 24 NATURE BIOTECH. 487 (2006).

20. CAL. HEALTH & SAFETY CODE § 125290.35 (2004).

21. *Id.* § 125290.35(a).

22. 45 C.F.R. § 46.103 (1991).

23. *Id.* § 46. For a history of federal regulation in this area, see, e.g., RUTH R. FADEN & TOM L. BEAUCHAMP, A HISTORY AND THEORY OF INFORMED CONSENT 151-232

lations permit a waiver of consent (as well as of full IRB review) for the research use of biological samples when the identity of the donors is not “readily ascertained” to the researchers.²⁴ In this case, under federal rules, such donors do not qualify as protected research subjects. In other words, so long as “spare” embryos and gametes donated for research remain sufficiently coded, then federal rules mandating informed consent and institutional review boards for both the derivation and use of stem cell lines do not apply.²⁵

State laws in California governing stem cell research go well beyond federal regulations in a number of ways. First, California mandates IRB evaluation of research involving the derivation and use of hESCs, human embryonic germ cells, adult stem cells, and somatic cell nuclear transfer, even where samples and biological materials remain unidentifiable.²⁶ It also provides for the establishment of a “Human Stem Cell Research Advisory Committee”—a 13-member committee composed of ethicists, lawyers, scientists, and clergy—empowered to generate clear guidelines for the research by January 1, 2005.²⁷ All research involving derivation and use of stem cells in California would have to be approved by an institutional review board in accordance with the guidelines developed by this committee.²⁸ These IRBs must report to the California Department of Health on the number of projects reviewed and their status, as well as on unforeseen or adverse events.²⁹ Finally, California law requires the Department of Health to review IRB reports annually, to reconsider the exist-

(1986); NATIONAL BIOETHICS ADVISORY COMMISSION, ETHICAL & POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS 97-108 (2001) [hereinafter NBAC, RESEARCH SUBJECTS].

24. See U.S. OFFICE FOR HUMAN RESEARCH PROTECTIONS, GUIDANCE ON RESEARCH INVOLVING CODED PRIVATE INFORMATION OF BIOLOGICAL SPECIMENS 3-4 (2004), available at <http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf>.

25. However, it must be noted that this work is not necessarily unregulated by federal agencies in all cases. Absent specific triggers, federal regulation of lab research will not apply. However, if the work is on cell lines aimed at transplantation, it will be regulated by the FDA; if it involves animals, it must be overseen by an Institutional Animal Care and Use Committee (IACUC); and if it involves recombinant DNA work, it must be overseen by an Institutional Biosafety Committee (IBC). Furthermore, the absence of federal IRB jurisdiction in some instances of embryo donation does not necessarily imply an absence of a requirement of consent for use, e.g., through requirements under state common law for property, family, and contract. On the need for regulatory protections for the donors of gametes, embryos, and adult cells in stem cell research, see Bernard Lo et al., *Consent from Donors for Embryo and Stem Cell Research*, *supra* note 8.

26. CAL. HEALTH & SAFETY CODE § 125300 (2002).

27. *Id.* §§ 125118, 125118.5.

28. *Id.* § 125119.

29. *Id.* § 125119.3 (a)-(b).

ing guidelines governing the research, and to report to the California legislature on hESC research activity.³⁰

The text of the Initiative declares exemption from all of these regulations in order “to avoid duplication or conflicts in technical standards for scientific and medical research.” The only relevant statute that was not pre-empted requires that health providers delivering fertility treatment provide adequate information to allow individuals “to make an informed and voluntary choice regarding the disposition of any human embryos remaining following the fertility treatment,” and furnish the clear choices of storing, donating, or discarding unused embryos.³¹ The same statute mandates that embryos cannot be donated for research without “written consent,” and that a list of statements regarding the terms of donation be conveyed to individual embryo donors.³²

In addition to exempting CIRM-funded research from most governing statutes in this area, the Initiative text requires CIRM to establish standards for obtaining the informed consent of research participants, reviewing human subjects research, prohibiting excess payment to research donors or participants (while permitting “reimbursement of expenses”), assuring compliance with patient privacy laws, and setting a limit on the extraction of stem cells from blastocysts.³³ The California Stem Cell Research and Cures Bond Act establishes the Scientific and Medical Accountability Standards Working Group³⁴ to, among other tasks, “recommend to the [Independent Citizens’ Oversight Committee] scientific, medical and ethical standards.”³⁵

The ICOC appointed its Scientific and Medical Accountability Standards Working Group in spring 2005, which met for the first time on July

30. *Id.* § 125119.5 (a)-(b).

31. *Id.* § 125315 (a)-(b).

32. *Id.* § 125315(c). The fact that this statute applies to CIRM-funded research has not been widely appreciated. Under this law, donors of embryos for research in fertility clinics must be told that identifiers associated with the embryos will be removed prior to the derivation of human pluripotent stem cells. Donors will not receive any information about subsequent testing on the embryo or the derived human pluripotent cells. Derived cells or cell lines, with all identifiers removed, may be kept for many years. Donated material may have commercial potential, and donor will not receive financial or any other benefits from any future commercial development. Human pluripotent stem cell research is not intended to provide direct medical benefit to the donor. Early human embryos donated will not be transferred to a woman’s uterus, will not survive the human pluripotent stem cell derivation process, and will be handled respectfully. *See id.* § 125315(c)(1)-(7).

33. California Stem Cell Research and Cures Bond Act, CAL. HEALTH & SAFETY CODE § 125290.35(b) (2004).

34. *Id.* § 125290.50(a)(2).

35. *Id.* § 125290.55(b)(1).

6, 2005.³⁶ The committee adopted a set of interim standards that was based on a new set of guidelines produced in April 2005 by a joint committee of the National Research Council and the Institute of Medicine of the National Academies entitled “Guidelines for Human Embryonic Stem Cell Research” (“NAS Guidelines”).³⁷ The NAS Guidelines focus on the derivation, procurement, banking, and use of hESC lines.³⁸ Co-chairs of the joint NAS committee issuing the Guidelines have urged institutions engaging in hESC research in the U.S. to adopt the voluntary Guidelines, for fear that the research is proceeding without adequate guidance at the federal level.³⁹ This report is a far-ranging and useful document that attempts to summarize ethical thinking in the field. It does, however, leave certain important matters unaddressed.

B. Overview and Comparison of CIRM Regulations and NAS Guidelines

The California Office of Administrative Law published CIRM’s Draft Medical and Ethical Standards Regulations (“CIRM Regulations”) on March 17, 2006, and a public comment period for the proposed regulations concluded on June 29, 2006.⁴⁰ Although CIRM did not adopt the NAS Guidelines in their entirety as it had done for its interim guidelines, the institute did use the NAS Guidelines as a framework.⁴¹ The following pages provide an overview and comparison of these two sets of guidelines.

36. See CIRM, Scientific and Medical Accountability Standards Working Group, http://www.cirm.ca.gov/working_group/standards.asp (last visited Aug. 13, 2006).

37. NAS GUIDELINES, *supra* note 8, at vii. The National Academies is an umbrella organization containing the National Academies of Sciences, National Academies of Engineering, Institute of Medicine (IOM), and the National Research Council (NRC). IOM is the pre-eminent academic society of health professionals, established in 1970 “to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health and the public.” The NRC was organized in 1916 as the principal body of scientific experts involved in advising the government, the public, and scientific and engineering communities. *Id.* at iii; see also The National Academies: About, <http://www.nationalacademies.org/about> (last visited Aug. 13, 2006).

38. For a concise overview and assessment of the NAS GUIDELINES, see Constance Holden & Gretchen Vogel, *Panel Would Entrust Stem Cell Research to Local Oversight*, 308 SCI. 611 (2005).

39. Jonathan D. Moreno & Richard O. Hynes, *Guidelines for Human Embryonic Stem Cell Research*, 23 NATURE BIOTECH. 793 (2005).

40. These rules will be finalized by fall 2006. For an updated timeline and updated proposed changes, see CIRM, Laws/Regulations, <http://www.cirm.ca.gov/laws/> (last visited Aug. 13, 2006).

41. See discussion *infra* pp. 1076-82.

1. Categories of Permissibility for Different Types of hESC Research

The NAS Guidelines set out three categories of permissibility for different types of hESC research, including: (a) research that does not require any additional ethical review but requires notification of relevant research ethics committees; (b) research that is permissible only after review by a hESC Oversight Committee—a new body constituted at the research institutions; and (c) research that “should not be conducted at this time.”⁴² This last category comprises research on any intact human embryo past fourteen days or until formation of the primitive streak begins, and also any research introducing hESCs into non-human primate blastocysts or embryonic stem cells into human blastocysts. The Guidelines also state that no animal into which hESCs have been introduced at any stage of development should be allowed to breed.⁴³ The CIRM Regulations follow these rules by declaring these same types of research ineligible for funding.⁴⁴ Further, both the NAS Guidelines and the CIRM Regulations reaffirm that reproductive cloning should and will not be allowed. Neither set of rules forbids other types of controversial stem cell research, such as the creation of certain kinds of human chimeras.⁴⁵

2. Establishment of hESC Oversight Committees

The NAS Guidelines, which span 131 pages, emphasize procedural matter. They aim to provide for the ethical review of different aspects of hESC research through institutional review boards and the addition of new review entities—local hESC research Oversight Committees (ESCROs)—that fill what is widely perceived as a critical gap in the existing federal rules for the ethical conduct of hESC research.⁴⁶ The NAS Guidelines suggest that each research institution should establish an ESCRO “to provide oversight of all issues related to derivation and use of hES cell lines and to facilitate education of investigators involved in hESC research.”⁴⁷

42. NAS GUIDELINES, *supra* note 8, at 7-8.

43. *Id.* at 8.

44. CAL. CODE REGS. tit. 17 § 100030 (West forthcoming). One minor difference is that CIRM will not fund research involving the introduction of any stem cells (whether embryonic or not) into human embryos. *Id.* § 100030(d).

45. Chimeras are organisms with cells from multiple species. Some leading stem cell researchers see the creation of embryonic chimeras as a promising avenue of research, though it remains controversial. See Shreeve, *supra* note 19. For a discussion of nascent efforts to ban the creation of certain human chimeras, see Scott, *supra* note 19.

46. See Lo, *A New Era in the Ethics of Human Embryonic Stem Cell Research*, *supra* note 8.

47. NAS GUIDELINES, *supra* note 8, at 82.

They recommend that the ESCRO have “suitable scientific, medical, and ethical expertise to conduct its own review” and “should also include at least one person from the community.”⁴⁸

Under the CIRM Regulations, many types of CIRM-funded stem cell research cannot begin without the review and approval in writing of a similar committee, called a Stem Cell Research Oversight Committee (SCRO).⁴⁹ In the CIRM Regulations, there is less emphasis on the need for a separate SCRO at each institution, leaving the door open to create centralized review of some sort.⁵⁰ Further, for CIRM, the SCRO must include one patient advocate in addition to the one community member required under the NAS rules. But as we will see below, the function of the SCRO mirrors that of the ESCRO under the NAS Guidelines.

3. Rules for Procurement of Gametes, Blastocysts, or Adult Cells for hESC Generation

a) Institutional Review Board Review

The NAS recommends that an IRB, as described in the Federal Regulations at 45 C.F.R. § 46.107, should review the procurement of all gametes, blastocysts, or somatic cells for the purpose of generating new hESC lines,⁵¹ even where no review is mandated under federal human research subjects regulations.⁵² Under the CIRM Regulations, any stem cell lines used in CIRM-funded research must be “acceptably derived,” which means already approved by a named institution⁵³ or else derived through a donation process approved by an IRB or equivalent institution.⁵⁴

48. *Id.* at 46.

49. CAL. CODE REGS. tit. 17 § 100070(a) (West forthcoming).

50. *Id.* § 100060(e) (“[A]n SCRO committee may be convened by an institution, a group of institutions, the CIRM or other state agency.”).

51. NAS GUIDELINES, *supra* note 8, at 49.

52. *See supra* note 23 and accompanying text.

53. Under these rules, lines approved by NIH, deposited in the U.K. Stem Cell Bank, U.K. Human Fertilization and Embryology Authority, or derived in accordance with the Canadian Institutes of Health Research Guidelines will be considered “acceptably derived.” CAL. CODE REGS. tit. 17 § 100080 (West forthcoming). It is interesting to note that none of these lines, save those coming via the United Kingdom, would have had obligatory IRB oversight over the procurement process. *See* MEDICAL RESEARCH COUNCIL, UNITED KINGDOM, CODE OF PRACTICE FOR THE USE OF HUMAN STEM CELL LINES, VERSION 2, 15 (2005), available at http://www.mrc.ac.uk/pdf-public-stem_cell_code_of_practice_june2005.pdf; CANADIAN INSTITUTES OF HEALTH RESEARCH, GUIDELINES FOR HUMAN PLURIPOTENT STEM CELL RESEARCH, JUNE 7, 2005, <http://www.cihr-irsc.gc.ca/e/28216.html>. CIRM explains these exceptions as follows:

[T]hese subdivisions are necessary to address the issue of stem cells lines created prior to enactment of Proposition 71 and define the per-

b) Mandated Disclosures in Consent Process

Furthermore, the NAS Guidelines recommend that in all cases of donation for research a number of conditions should be met. Some of the most salient requirements include that consent be obtained from each donor at the time of donation; that where “practicable,” the attending physician responsible for the infertility treatment and the investigator deriving or proposing to use hESCs not be the same person; that the consent process must contain specific disclosures:

- blastocysts or gametes will be used to derive hESCs for research that may include research on human transplantation;
- whether the identities of the donors will be readily ascertainable to those who derive or work with the resulting hESC lines and whether donors wish to be contacted in the future to receive information obtained through studies of the cell lines;
- embryos will be destroyed in the process of deriving hESCs and derived hESCs and/or cell lines might be kept for many years, used in research involving genetic manipulation of the cells or the mixing of human and non-human cells in animal models;
- the possibility that the results of study of the hESCs may have commercial potential, and the donor will not receive financial or any other benefits from any future commercial development; and
- risks involved to the donor.⁵⁵

The CIRM Regulations govern the procurement process of human materials in two major ways, setting up one regime for the procurement process for cell lines not created through CIRM funds, the other for cell lines derived through CIRM funding.

The procurement of stem cell lines derived from donations without CIRM funding get regulated indirectly through Section 100080 defining “acceptable research materials.” As stated above, any stem cell lines used

missible lines for use in CIRM-funded research. This allows needed flexibility and ensures availability of acceptable stem cell lines for CIRM-funded research ensuring proper standards are adhered to.

Notice of Proposed Regulation Adoption and Initial Statement of Reasons, CAL. CODE REGS. tit. 17, div. 4, ch. 2, at 12 (Mar. 17, 2006) [hereinafter Statement of Reasons], available at <http://www.cirm.ca.gov/laws/pdf/OALnoticeadoptionOALREVISIONS1.pdf>.

54. CAL. CODE REGS. tit. 17 § 100080(e)(4) (West forthcoming).

55. NAS GUIDELINES, *supra* note 8, at 90-91.

in CIRM-funded research must be “acceptably derived,” which means already approved by a named institution or else derived through a donation process approved by an IRB or equivalent institution. In lieu of a sister institution’s approval, acceptable derivation also requires acquisition through “voluntary and informed consent.”⁵⁶ This indirect method regulates the procurement process for materials used in the initiative.

Second, if CIRM funds are themselves used to derive new cell lines from gamete, embryo, and adult cell donations, then the SCRO must affirm compliance with specific consent procedures that are in addition to those required by Section 100080(e).⁵⁷ For this context, the CIRM Regulations contain disclosure requirements that are substantially similar to the NAS disclosure recommendations,⁵⁸ although such disclosure requirements may be “determined by the SCRO or institutional review board to be inapplicable.”⁵⁹

Finally, unlike the NAS Guidelines, the CIRM Regulations specify special disclosures that need to be made when CIRM funds pay for deriving new cell lines from donated eggs. This could occur through the donation of extra eggs in the course of IVF treatment, or through the recruitment of donors specifically for stem cell research. The rationale for this distinction in the CIRM Regulations is that egg donation specifically for research is more ethically contested than for treatment of embryo donors in the IVF context or that of sperm and somatic cell donors; egg donors are subjected to greater risks without the prospect of direct benefit.⁶⁰ Risks of egg extraction include pain and emotional stress in the short-term, and a small chance of developing ovarian hyperstimulation syndrome, which can be a serious condition.⁶¹ Accordingly, the CIRM Regulations comprise a number of rules specific to this situation, including disclosure of the foreseeable risks of donation, the nature of the physicians’ relationship

56. CAL. CODE REGS. tit. 17 § 100080(e)(1) (West forthcoming).

57. *See id.* § 100090(a) (requiring that donors have given voluntary and informed consent in accordance with Section 100100).

58. *Id.* § 100100(b)(1-9), (c); NAS GUIDELINES, *supra* note 8, at 102.

59. CAL. CODE REGS. tit. 17 § 100100(b).

60. *See Issues in Oocyte Donation*, *supra* note 8, at 1747. A recent meta-study has concluded that large increases in cancer risk due to ovulation induction have not been established, but that some findings based on small numbers suggest slight increased risk associated with fertility drugs in certain situations. *See Louise A. Brinton et al., Ovulation Induction and Cancer Risk*, 83 FERTILITY & STERILITY 261, 261-74 (2005).

61. *See American Society for Reproductive Medicine, Ovarian Hyperstimulation Syndrome*, 82 FERTILITY & STERILITY (SUPP. 2) S81, S81-S86 (2004); *see also* Abraham Golan et al., *Ovarian Hyperstimulation Syndrome: An Update Review*, 44 OBSTET. GYNECOL. SURV. 430-40 (1989).

to the research, the methods of stem cell line derivation to be used (whether fertilization, somatic cell nuclear transfer, parthenogenesis,⁶² or some other method), and the possibility of recontact to gain more information in the future.⁶³ Effectively, under these recommendations, SCROs would have fairly broad discretion to select their disclosures.

c) Additional Protections for Egg Donors in Procurement Process

The CIRM Regulations feature a number of additional protections for egg donors involved in CIRM-funded cell line derivation. SCROs overseeing derivation must confirm that the following conditions have been met: the donor's fertility treatment has not been compromised; the funded institution has agreed to assume the cost of medical care required as a result of the donation for research; the physician attending the donor and the principal investigator are not the same person (unless approved by the IRB); and the physician performing oocyte retrieval does not have a financial interest in the outcome of the research.⁶⁴

Note however, that these special rules only govern the egg donation process when those eggs will be prospectively collected for use in CIRM-funded research. Recall that research on pre-existing cell lines derived from donated eggs can be used so long as they have been "acceptably derived," that is, derived from reciprocal institutions or assuredly derived after IRB review and informed consent. In other words, CIRM-funded researchers may use lines that have been previously derived from eggs donated specifically for research that were not donated under the more rigorous conditions of Sections 100090(b) and 100100(d).

d) Payment of Donors and for Donated Materials

The CIRM Regulations require that assurances be made to SCROs that no stem cell lines used in CIRM-funded research involved the purchase or sale of gametes, embryos, somatic cells or human tissue,⁶⁵ or the compensation of donors beyond "permissible expenses."⁶⁶ The Regulations define "permissible expenses" as "necessary and reasonable costs directly incurred as a result of donation or participation in research activities," including but not limited to "costs associated with travel, housing, child

62. Parthenogenesis is a form of reproduction in which the ovum develops into a new individual without fertilization.

63. CAL. CODE REGS. tit. 17 § 100100(d) (West forthcoming).

64. *Id.* § 100090(b)(1)-(3).

65. *Id.* § 100080(e)(3).

66. *Id.* § 100080(e)(2).

care, medical care, health insurance and actual lost wages.”⁶⁷ These rules are based on the NAS Guidelines.⁶⁸

4. Rules for the Derivation of New hESC Lines and Use of Oocytes and Embryos

The CIRM Regulations closely follow the NAS Guidelines regarding the proper oversight of new stem cell line derivations. CIRM-funded research involving derivation of new stem cell lines or the use of human oocytes or embryos in the research may not proceed without SCRO committee review and approval in writing.⁶⁹ CIRM-funded researchers must justify the need for new lines and the number of new cell lines needed, and provide special rationale for using somatic cell nuclear transfer.⁷⁰ They must provide documentation of compliance with any required review of the proposed research by an IRB and other already mandated reviews,⁷¹ and document how stem cell lines will be characterized, validated, stored, and distributed to ensure donor confidentiality.⁷² All of these rules track closely the recommendations of the NAS.⁷³

5. Rules Governing the Research Use of hESC Lines

As explained above, federal regulations governing research with human subjects generally do not cover laboratory research with existing hESCs unless the research involves personally identifiable information. The NAS Guidelines state that this research should nevertheless be reviewed by an ESCRO committee, and create a two-tiered system of oversight.⁷⁴ For basic in vitro research on pre-existing hESC lines, ESCRO committees should require “notification” of the research, “documentation of the provenance of all hES cell lines,” and “evidence of institutional review board approval of the procurement process.”⁷⁵ The Guidelines provide that all cross-species transplantation and experimentation be subject to ESCRO pre-approval of protocols.⁷⁶ The rules for CIRM-funded stem cell research follow the recommendations of the NAS fairly closely here.

67. *Id.* § 100020(h).

68. See NAS GUIDELINES, *supra* note 8, at 85-86.

69. CAL. CODE REGS. tit. 17 § 100070(a) (West forthcoming).

70. *Id.* § 100070(a)(1).

71. *Id.* § 100070(a)(3).

72. *Id.* § 100070(a)(4).

73. See Recommendations 4.1-4.4, 4.6, in NAS GUIDELINES, *supra* note 8, at 73.

74. See NAS GUIDELINES, *supra* note 8, at 105-06.

75. See Recommendations 6.0-6.2, in NAS GUIDELINES, *supra* note 8, at 89.

76. See Recommendations 6.4-6.7, in NAS GUIDELINES, *supra* note 8, at 54.

Chimeric research requires SCRO review and pre-approval,⁷⁷ while in vitro research on pre-existing lines requires written “notification” to the SCRO and “assurances” that all lines have been acceptably derived.⁷⁸ Unlike the Guidelines, the CIRM Regulations seem to allow for a waiver of full review by the SCRO committee even where cell lines are identifiable, although such protocols would be subject to IRB review under the federal regulations, and may also trigger the Health Insurance Portability and Accountability Act’s consent requirement. The CIRM Regulations would require establishing registries cataloguing all CIRM-funded research and all materials used in the research, with sufficient detail to establish provenance and disposition.⁷⁹

III. ANALYSIS AND CRITIQUE OF CIRM’S CONSENT AND SCRO REGIME

So what can be said about this emergent regime of bioethics for stem cell research in California, other than the fact that it follows many of the rules advocated by the National Academies and departs from others? The CIRM Regulations represent an impressive body of work and a credible adaptation of the prevailing human subjects protection regime in the United States to a novel context. Nevertheless, I wish to make a number of critiques about this regime, some of which could easily be leveled at other wings of the governance system for biomedical research as well.

First, the consent process under the CIRM Regulations breaks with traditional notions of informed consent in ways that must be acknowledged: the regulations exemplify how informed consent has become a mechanism of expropriating commercial rights from altruistic donors over their biological materials in ways that may undermine meaningful choice. Second, in light of existing experience with IRBS and also the unique questions we face with stem cell research, the regime of ethical oversight by the SCROs suffers from a number of disadvantages from the perspective of governance: the proposed system of SCRO review may reproduce many of the well-documented problems with the decentralized institutional review board system, and suffers from a lack of transparency and public accountability with respect to both the public and donors. Third, although recent bioethical commentaries and the emergent rules discussed above have focused due attention to filling critical regulatory gaps, too

77. CAL. CODE REGS. tit. 17 § 100070(b) (West forthcoming).

78. *Id.* § 100070(c).

79. *Id.* § 100120. Registries are also recommended by NAS. See NAS GUIDELINES, *supra* note 8, at 53-61.

little attention has been paid to the political economy of egg donation in the hESC context—the patterns of extraction, use, and transfer of eggs in relation to markets, power relations, regulation, and collective action. Rules with respect to financial compensation to donors deserve deeper scrutiny in light of the larger political economy of both human eggs and U.S. biomedical research in the twenty-first century.

A. The Regime of Consent: Autonomy, Open Consent, and Commercial Use

Informed consent is the traditional pillar of the protection of autonomy in research involving human subjects.⁸⁰ Articles in the bioethics literature repeatedly state that consent should involve a process of communication, not simply filling out a form.⁸¹ If individual subjects are treated with respect, they will understand the purposes for which their tissue or blood will be used, comprehend the risks and benefits of particular projects, and retain the right to withdraw from the study at any time.⁸² The CIRM Regulations raise two large issues regarding informed consent and autonomy. First, the consent process under the CIRM Regulations breaks with these traditional notions of informed consent in ways that must be acknowledged. Second, the CIRM's consent rules are emblematic of how informed consent has become a mechanism of expropriating commercial rights from altruistic donors over their biological materials in ways that may undermine meaningful choice.

The CIRM Regulations provide that the consent process for derivations of new hESC lines using CIRM funds must include a statement to the effect that resulting cell lines may be used for future studies that are

80. NATIONAL BIOETHICS ADVISORY COMMISSION, RESEARCH INVOLVING HUMAN BIOLOGICAL MATERIALS: ETHICAL ISSUES AND POLICY GUIDANCE, VOL. 1, 47-49 (1999) [hereinafter NBAC, BIOLOGICAL MATERIALS].

Put most simply, to be autonomous is to be one's own person, to be directed by considerations, desires, conditions, and characteristics that are not simply imposed externally upon one, but are part of what can somehow be considered one's authentic self. Autonomy in this sense seems an irrefutable value, especially since its opposite—being guided by forces external to the self and which one cannot authentically embrace—seems to mark the height of oppression.

John Christman, *Autonomy in Moral and Political Philosophy*, in THE STANFORD ENCYCLOPEDIA OF PHILOSOPHY (Edward N. Zalta ed., 2003), available at <http://plato.stanford.edu/archives/fall2003/entries/autonomy-moral>; see also GERALD DWORKIN, THE THEORY AND PRACTICE OF AUTONOMY (1988).

81. George J. Annas, *Reforming Informed Consent to Genetics Research*, 286 JAMA 2326, 2326 (2001).

82. FADEN & BEAUCHAMP, *supra* note 23, at 151-232.

not predictable at this time.⁸³ There remains a hotly contested question in bioethics concerning whether human research subjects should be allowed to grant a broad and “open” consent over future and unspecified uses of their bodily materials.⁸⁴ A broad waiver of control over the future uses of donor cells cannot protect the donor’s autonomy in the way that the traditional mechanism of informed consent was intended. The major virtue of promoting broad consent for unforeseen future uses of biological materials is efficiency: if researchers have to go back to the donor every time a new research project is proposed, the consent process would slow down research and significantly increase transaction costs. But there are also costs in terms of donor autonomy. Open-ended permission makes it difficult for participants to make informed and voluntary decisions throughout their involvement in the research.⁸⁵ There may also be costs in terms of participation: donors may be more reluctant to participate if they are not given a clear idea of how exactly their donations will be used.

This issue of the permissibility of open consent was contested on President Clinton’s National Bioethics Advisory Commission (NBAC).⁸⁶ Some have attempted to balance the interests in efficiency of research and the autonomy of tissue donors by arguing that biobanks’ requests for general permission should be allowed only if certain additional safeguards are in place, including provision of information about subsequent contact, clearly stated time limits for the project, an absolute right of withdrawal, disclosure of details about commercial arrangements, and the ethical review of any subsequent research.⁸⁷ Except for a provision of information

83. CAL. CODE REGS. tit. 17 § 100100(b)(3) (West forthcoming).

84. See Marshall B. Kapp, *Ethical and Legal Issues in Research Involving Human Subjects: Do You Want a Piece of Me?*, 59 J. CLINICAL PATHOLOGY 335, 336 (2006).

85. See, e.g., Henry T. Greely, *Breaking the Stalemate: A Prospective Regulatory Framework for Unforeseen Research Uses of Human Tissue Samples and Health Information*, 34 WAKE FOREST L. REV. 737, 737-66 (1999) (arguing that because it is impossible for the donor to make an informed choice about the risks and benefits of unspecified future research protocols, such permission should never be called informed consent).

86. A majority of the NBAC members recommended that signed consent to unforeseen research uses of biological samples—“open consent”—may be an acceptable alternative to requiring informed consent for each specific use of the sample. *Recommendation 9*, in NBAC, BIOLOGICAL MATERIALS, *supra* note 80, at 64-65. NBAC members Capron and Shapiro rejected the view that patients and donors should be allowed under any circumstances to consent to “any kind of future study.” *Id.* at 65.

87. Greely, *supra* note 85, at 764, stakes out this middle position. Still other bioethicists reject “open consent” unless all DNA samples are stripped of all identifiers. See, e.g., George J. Annas, *Privacy Rules for DNA Databanks: Protecting Coded “Future Diaries”*, 270 JAMA 2346, 2347-48 (1993) (suggesting that individuals might not give

regarding recontact of donors,⁸⁸ the CIRM Regulations lack many of these safeguards. No time limits must be stated. Instead, a statement that the materials will be “kept for many years” is required.⁸⁹ Whereas the NAS Guidelines state that donors “should be informed that they retain the right to withdraw consent until the blastocysts are actually used in cell line derivation,”⁹⁰ the CIRM Regulations require no such disclosure.

Furthermore, neither the NAS Guidelines nor the CIRM Regulations recommend or require the disclosure of details concerning planned commercial uses of derived cell lines. Rather, they both require a general statement that the research may have commercial potential and that donors “will not receive financial or any other benefit from future commercial development.”⁹¹ These rules provide researchers, research institutions, and commercial entities broad leeway for appropriating the commercial value of donations and the cell lines to which they give rise. This marks more of a continuity than a departure from existing practice in the use of biological samples in research.⁹² Nevertheless, the rules provide donors little awareness of whether or not their materials and derivatives will be controlled by commercial entities.

Even after reading statements like those recommended by CIRM, donors may be misled on this score. Empirical studies in the genomic biobanking area suggest that arrangements between medical centers and for-profit biobanks are often insufficient to keep donors apprised of new research uses for their samples. As a result, when patients agree to donate tissue or blood, they sign away their control and oversight. Patients might disagree with a particular commercial or scientific use of their material, but they have no recognized right to be kept informed about it. A number of well publicized cases have emerged in which participants who thought they were participating in an altruistic endeavor subsequently sued their

permission if they knew that the data were being used to study possible genetic correlations to conditions such as alcoholism or homosexuality).

88. CAL. CODE REGS. tit. 17 § 100100(b)(2) (West forthcoming).

89. *Id.* § 100100(b)(1).

90. *See Recommendation 3.2, in* NAS GUIDELINES, *supra* note 8, at 83.

91. *See Recommendation 3.6(h), in* NAS GUIDELINES, *supra* note 8, at 91; CAL. CODE REGS. tit. 17 § 100100(b)(9) (West forthcoming).

92. This waiver of commercial benefits is by now a standard feature of informed consent forms for research protocols involving donated biological samples. *See* Winickoff, *Governing Population Genomics*, *supra* note 1, at 207-14. Even where there is no informed consent on this score, courts have tended to support a default rule at common law that research donors retain no commercial rights after donation. *See* Moore v. Regents of the Univ. of Cal., 51 Cal. 3d 120, 137-38 (1990). Common practice, however, does not necessarily make it a good one.

research institution when its intellectual property practices led to prohibitively expensive pricing or other commercial behavior.⁹³

The drafters of the CIRM Regulations attempted to enhance the degree of choice afforded to materials donors by requiring researchers to offer them the opportunity to express objections to certain types of research. The NAS Guidelines mention the possibility, but not the requirement, that donors be offered the option of agreeing to some forms of hESC research but not others. “For example,” the Guidelines state, “donors might agree to have their materials used for deriving new hES cell lines but might not want their materials used, for example, for [SCNT]. The consent process should fully explore whether donors have objections to any specific forms of research to ensure that their wishes are honored.”⁹⁴ The CIRM Regulations make providing this option to donors a requirement, stating that “researchers *shall* offer donors an opportunity to document their preferences regarding future uses of their donated materials” (emphasis added).⁹⁵ However, the CIRM Regulations take pains to point out that “researchers may choose to use materials only from donors who agree to all future uses.”⁹⁶ Furthermore, no CIRM funds may be used to support research that “violates the documented preferences of donors with regard to their donated materials.”⁹⁷

Despite these specific rules on donor limitation, the CIRM rules evince a spirit of compromise but real ambivalence regarding the powers of donors to exert control over cell lines derived from their materials. The rules do not specify the choices that donors should have regarding which types of research. For example, should donors be explicitly given the choice to opt-out their materials from somatic cell nuclear transfer (cloning) derivations and chimeric experiments? Should consent forms have check-boxes next to these “sensitive” techniques, or simply allow for open-ended objections? CIRM rules seem to imagine a regime of blanket disclosure of a

93. While *Moore v. Regents* is the canonical case, there have been other recent cases. For example, when a group of Canavan’s patients and their families agreed to participate in research on their disease, they were subsequently shocked to find out that a diagnostic test discovered through their participation had been patented, and that many members of the group were incapable of affording the test at market prices. *Greenberg v. Miami Children’s Hosp. Research Inst., Inc.*, 264 F. Supp. 2d 1064, 1067 (S.D. Fla. 2003). This case recently settled out of court. *See also Skloot, supra* note 9.

94. NAS GUIDELINES, *supra* note 8, at 91.

95. CAL. CODE REGS. tit. 17 § 100100(c) (West forthcoming).

96. *Id.*

97. *Id.* § 100100(b).

large range of types of research, without facilitating donor choice.⁹⁸ Although a strong efficiency rationale for framing, indeed constructing, donor autonomy in this way exists, perhaps we really don't believe that donors have a deep claim in determining how the materials derived from their cells are used. However, an argument otherwise will be developed below. Even so, different consent procedures construct, as much as embody, different visions of research participant subjectivity. It should be acknowledged that there were many ways a more autonomous research donor might have been imagined.

B. The Regime of SCROs

Following the model of the NAS Guidelines, the CIRM Regulations attempt to fill gaps in existing research oversight by creating Stem Cell Oversight Committees (SCROs). In a structural sense, this mechanism of research oversight mimics the existing federal institutional review board regime in a number of ways. First, oversight bodies will tend to be localized at the research institution, although the regulations permit institutional sharing. Second, the regulations set minimum standards that local oversight bodies must follow, but not precise standards of review. Third, the system of oversight is enforced through contractual mechanisms tied to research funding. While having such an oversight system is better than having none at all, and is certainly a credible attempt to adapt the existing IRB model to stem cell research oversight, such a system has a number of important shortcomings.

1. *Reproducing the Institutional Review Board's Well-Known Problems*

Localized IRB oversight has some well-known advantages.⁹⁹ However, the proposed system of SCRO review may reproduce many of the well-documented problems with the decentralized institutional review board system, which is widely believed to be inadequate.¹⁰⁰ Many U.S.

98. The level of detail in the regulations would be going beyond what is typical for regulatory language and is more typical of the close details governed at the IRB or SCRO level. Nevertheless, the regulatory-level guidelines do construct the normative frameworks for local review board activities, and it would be highly unlikely for individual review boards to enact consent mechanisms that do more than is required in terms of offering choices to research participants.

99. NBAC, RESEARCH SUBJECTS, *supra* note 23, at 30 (discussing the advantages and disadvantages of a centralized, as opposed to localized, IRB system and noting that localized review helps provide important contact and proximity to those involved in the daily conduct of research).

100. See, e.g., Ezekiel J. Emanuel et al., *Oversight of Human Participants Research: Identifying Problems to Evaluate Reform Proposals*, 141 ANNALS INTERNAL MED. 282,

agencies and professional organizations have already proposed remedies for major problems such as uneven standards, poor enforcement, and the scarcity of IRB resources.¹⁰¹ Because of these problems, NBAC discussed at length the desirability of centralized accountability and standardization across the IRB system.¹⁰²

Creating yet another ethical review body within the research institutions themselves would also suffer from an emergent problem afflicting institutional review boards in the modern era of academic-industry relations, namely that of institutional conflicts of interest.¹⁰³ Institutional conflicts of interest between the SCROs, research donors, and “the public” would be most pronounced in CIRM-funded entities organized as commercial enterprises. Nevertheless, another problem, which the Jesse Gelsinger incident at the University of Pennsylvania has come to symbolize, increasingly abounds, namely that of conflicts at non-profit hospitals, clinics, and other research entities themselves possessing investments or financial interests in the human subjects research being conducted.¹⁰⁴ SCRO members are likely to be department chairs, deans, and mid- and high-level administrators from the research institution itself. Such members would likely appreciate the value of these investments to the institution, and may be influenced by the desire to protect the overall fiscal health of the entity.¹⁰⁵

282-86 (2004). See generally JUNE GIBBS BROWN, INSPECTOR GENERAL, DHHS, INSTITUTIONAL REVIEW BOARDS: A TIME FOR REFORM (1998), available at <http://oig.hhs.gov/oei/reports/oei-01-97-00193.pdf>.

101. See, e.g., Emanuel, *supra* note 100; see also INSTITUTE OF MEDICINE, PRESERVING PUBLIC TRUST: ACCREDITATION AND HUMAN RESEARCH PARTICIPATION PROGRAMS (2001).

102. NBAC, RESEARCH SUBJECTS, *supra* note 23, at 28-64.

103. See, e.g., Ezekiel J. Emanuel & Daniel Steiner, *Institutional Conflict of Interest*, 332 NEW ENG. J. MED. 262, 262-67 (1995).

104. See Mark Barnes & Patrick S. Florencio, *Investigator, IRB and Institutional Financial Conflicts of Interest in Human-Subjects Research: Past, Present and Future*, 32 SETON HALL L. REV. 525, 547-48 (2002). The 1999 death of 18-year-old Jesse Gelsinger, a research subject in a gene therapy trial for a rare metabolic disorder, caused the government and research institutions to scrutinize the profitable relationships that researchers and their academic institutions have with companies that are financing their research. Gelsinger died in an experiment at the University of Pennsylvania’s gene therapy program led by Dr. James Wilson, who founded a company that funded part of the research. The company, Genovo Inc., was later sold to a bigger company and Wilson received a reported \$13.5 million in stock. See also Robert Gatter, *Walking the Talk of Trust in Human Subjects Research: The Challenge of Regulating Financial Conflicts of Interest*, 52 EMORY L.J. 327, 330-342 (2003).

105. For a discussion of these conflicts in the IRB context, see Barnes, *supra* note 104, at 544-48.

2. Transparency, Accountability, and Trust

The SCRO regime also has a number of shortcomings in terms of transparency and public accountability, problems that may undermine public trust in the oversight system over the long term. As discussed above, hESC research will likely involve procedures—such as somatic cell nuclear transfer, or cloning, as well as mixing human stem cells into non-human organisms to create chimeras—that remain ethically controversial in the public at large. Under the NAS Guidelines and the CIRM Regulations, the local stem cell oversight committee would have the discretion to approve or disapprove of new stem cell line derivations, whichever technique is used, and also chimeric experiments. Many countries currently forbid somatic cell nuclear transfer techniques with human cells.¹⁰⁶ Others, such as the United Kingdom, allow research using these techniques but only after researchers receive a license from a centralized regulatory authority.¹⁰⁷ Although the Independent Citizens' Oversight Committee and the Scientific and Medical Accountability Standards Working Group must both conduct their meetings in public, the work of the SCROs will not be conducted in public. There is a danger that the SCRO system of oversight could create the perception that crucial ethical decisions are being made in the dark backrooms of the very institutions that stand to gain from large CIRM grants. Because the research is occurring on a fast-changing ethical landscape, there is a strong push to proceed quickly in California. Moreover, because the system of assurances involves self-reporting only, the danger of undermining public trust in the proposed stem cell research governance regime is especially high.

Focusing on the composition of membership on ethical oversight committees may engender public representation, accountability, and trust. The CIRM Regulations specify that in addition to having “persons with expertise in, including but not limited to, developmental biology, stem cell research, molecular biology, assisted reproduction, and ethical issues in stem cell research,” the SCRO should also have a public representative from a non-scientific background and also at least one patient advocate. This seems a rather meager nod to public representation. In pointed contrast, the Human Fertilisation and Embryology Authority in the United

106. Shaun D. Pattinson & Timothy Caulfield, *Variations and Voids: the Regulation of Human Cloning Around the World*, 5 BMC MED. ETHICS 1, 1-8 (2004), available at <http://www.biomedcentral.com/1472-6939/5/9>.

107. See Knowles, *supra* note 16, at 160.

Kingdom contains a majority of non-physicians and scientists in related areas.¹⁰⁸

3. *Donor Participation in Oversight*

As currently imagined, SCROs suffer from a lack of accountability not only with respect to the public at large, but also with respect to the donor group. In the field of biobanking for genetics and other research, both accountability to and representation of the donor group have emerged as important norms and active areas of policy development.¹⁰⁹ Recent controversies involving donor groups, researchers, and commercial entities around ethical decision-making have led to lawsuits and the collapse of projects.¹¹⁰ Institutional review board decision-making has become less tenable in the absence of donor representation when there are commercial rights at stake, and disparate risks and benefits will be distributed across different constituencies, whether they are commercial interests, research interests, or the participants themselves.¹¹¹ The interests of research par-

108. See Human Fertilisation and Embryology Act 1990, Schedules, http://www.opsi.gov.uk/acts/acts1990/Ukpga_19900037_en_3.htm#sdiv1 (last visited Aug. 21, 2006). The relevant provision states:

- (3) The following persons are disqualified for being appointed as chairman or deputy chairman of the Authority—
 - (a) any person who is, or has been, a medical practitioner registered under the [1983 c. 54.] Medical Act 1983 (whether fully, provisionally or with limited registration), or under any repealed enactment from which a provision of that Act is derived,
 - (b) any person who is, or has been, concerned with keeping or using gametes or embryos outside the body, and
 - (c) any person who is, or has been, directly concerned with commissioning or funding any research involving such keeping or use, or who has actively participated in any decision to do so.
- (4) The Secretary of State shall secure that at least one-third but fewer than half of the other members of the Authority fall within subparagraph (3)(a), (b) or (c) above, and that at least one member falls within each of paragraphs (a) and (b).

Id.

109. See REARDON, *supra* note 10; see also Winickoff, *Governing Population Genomics*, *supra* note 1, at 196-201 (arguing that the struggles over the Human Genome Diversity Project highlight how expert ethical review can usually be reframed as not just an expert, but also a political space, one requiring political representation of participants especially where group interests—whether financial or cultural—are at stake).

110. See, e.g., REARDON, *supra* note 10; see also Eric Niiler, *Collapse of Framingham Data Deal Highlights Lack of Cooperative Model*, 19 NATURE BIOTECH. 103 (2001); Gitter, *supra* note 9.

111. See Winickoff, *Governing Population Genomics*, *supra* note 1, at 192-93, 226-28.

ticipant groups are often not commercial. For instance, a number of disease groups have actively constructed their own biobanks in order to steer research to the particular diseases they are interested in.¹¹²

The controversies over donor accountability and representation in IRB review underscore the ways in which the CIRM Regulations are problematic. Recall that CIRM Regulations recommend ethical review of subsequent research on CIRM-derived cell lines only for the most sensitive of research applications; otherwise mere notification suffices. Furthermore, if researchers in California send cells out to non-CIRM-funded researchers, then any subsequent SCRO oversight would be purely voluntary. No formal legal requirement would exist that research funded outside of CIRM, but on CIRM-derived lines, be subject to any institutional oversight. If donors wish to limit the types of research that can be conducted using their materials, it will be left to researchers' own materials transfer agreements, and no SCRO oversight, to help ensure that these limitations are enforced. But the CIRM Regulations do not make this obligation of researchers related to distributing CIRM-funded cell lines explicit.

This lack of accountability to and representation of the donor group is especially problematic for women who donate eggs, as this group of women will incur a greater proportion of the physical risks involved in this research, as discussed below.¹¹³

C. The Regime of Property, Power, and Egg Donation

As stated above, both the NAS Guidelines and the CIRM Regulations recommend an altruistic regime of egg donation that compensates donors only for direct expenses. This regime contrasts with that of donation in the IVF context, at least in the United States, where more of an open market prevails in which women can be paid in excess of \$5,000 per procedure.¹¹⁴ Limiting the free market in this context is not unreasonable; inducing egg donors with money would tend to shift disproportionately the health burdens of supplying eggs onto poorer women, resulting in possible economic coercion.¹¹⁵ However, the donation regime proposed by the NAS Guide-

112. See *id.* at 222-26.

113. See discussion *infra* Section III.C.

114. Kenneth Baum, *Golden Eggs: Towards the Rational Regulation of Oocyte Donation*, 2001 B.Y.U. L. REV. 107, 108 (2001). For a recent journalistic account of the emerging market for eggs in the IVF context, see Carlene Hempel, *Golden Eggs*, BOSTON GLOBE MAG., June 25, 2006.

115. There is extensive literature on how to distinguish between a coercive, as opposed to an enticing but ethical offer. In practice, the line may not be clear. See, e.g., Neal Dicker & Christine Grady, *What's the Price of a Research Subject? Approaches to Payment for Research Participation*, 341 NEW ENG. J. MED. 198-203 (1999); Evan G. DeR-

lines—and largely enacted in California—raises at least three ethical problems that have been inadequately addressed by policymakers.¹¹⁶

First, there is the problem of what might be called “asymmetrical altruism.” Under the NAS Guidelines and the CIRM Regulations, the regime of altruism is deployed asymmetrically with respect to donors and researchers: while altruism is required of donors, it is not required of research institutions or corporations that may profit from the donations. As mentioned before, this asymmetry might be justified by the possibility of coercion raised by payment. But if society is so worried about the possible coerciveness of paying women for eggs, or about the commodification of body parts, why are payments in excess of \$5,000 allowed in the IVF context? Although such asymmetry is not new in biomedical research, it is more troublesome in this context where the risk and time-burden of donation is significant, and where the commercial value of the resulting products—new human embryonic cell lines—are likely to be significant.

Second, the NAS Guidelines fail to address compensation of donors who are harmed in the process of donation, and the proposed rules in California do so insufficiently. Existing federal research policies do not require compensation for injured research participants, and the NAS Guidelines are silent about the issue. However, a compensation system is warranted in large-scale programs of state-sponsored egg donation as a matter of fairness. CIRM has moved part of the way towards closing this gap in a set of proposed research standards in which funded institutions would have to agree to “assume the cost of any medical care required as a direct and proximate result of oocyte donation for research.”¹¹⁷ But because some of the health problems that may be associated with egg retrieval do not show up in the short term, such as infertility or ovarian diseases, this provision may prove inadequate.¹¹⁸ Large state funding programs like California’s should make sure that research institutions provide insurance to egg donors that cover both short and long-term risks associated with

enzo, *Coercion in the Recruitment and Retention of Human Research Subjects, Pharmaceutical Industry Payments to Physician Investigators, and the Moral Courage of the IRB*, 22 IRB: A REVIEW OF HUMAN SUBJECTS RESEARCH 1, 1-5 (2000).

116. This section is based on David E. Winickoff, *Governing Stem Cell Research in California and the USA: Towards a Social Infrastructure*, 24 TRENDS IN BIOTECH. 390 (Sept. 2006).

117. CAL. CODE REGS. tit. 17 § 100080 (West forthcoming).

118. See, e.g., Brinton, *supra* note 60, at 261-74; American Society for Reproductive Medicine, *supra* note 61, at S81-S86; Golan, *supra* note 61, at 430-40.

egg extraction, though more research on these long-term risks will undoubtedly be necessary.¹¹⁹

Finally, there is a strong argument to be made from the perspective of procedural justice that altruistic donors should be represented as a group in the regime of ethical oversight, especially where the power to benefit financially from donation is denied to individual donors. Neither the NAS Guidelines nor the proposed CIRM Regulations would allow donors to exercise any collective power in the governance of the research. The NAS Guidelines recommend that local oversight committees include “at least one member of the community,” but there is little or no discussion of the collective representation of egg donors in the regime of ethical oversight.¹²⁰ But the contributions of charitable egg donors to public hESC projects arguably give rise to special duties of political accountability and representation to this group of women, which might mean donor representation both on ethics committees and committees setting funding priorities. These committees are charged with weighing collective scientific benefits of particular forms of research against potential harms to this group of donors, who arguably should be represented in this process as a matter of legitimacy. Research participants on the whole are not usually represented on ethics review committees in other contexts, but this does not necessarily justify the practice from a political theory point of view. Further, the claim of representation for the donor group in the egg donation context is arguably greater than in other forms of research participation. The significance of the donor group in the hESC research context, the denial of financial compensation, and the historic neglect of women’s health issues in research¹²¹ all suggest how a more participatory form of governance may be appropriate, useful, and fair.

IV. THE CALIFORNIA STEM CELL BIOREPOSITORY (CSCB)

This Part explores my proposal for stem cell policy that would strengthen hESC research governance in important ways: the construction of a centralized public stem cell bank in California, to be linked up with

119. Compensating for long-term risks associated with egg donation, however, does raise the problem of uncertainty in causation, a well-known problem in toxic tort litigation. Clearly, more data and study is needed in this area before claims could be adjudicated fairly and efficiently.

120. NAS GUIDELINES, *supra* note 8, at 55. However, note that later in the report, the recommendation is for the ESCROS to “include representatives of the public,” indicating that one might not be sufficient. *Id.* at 100.

121. See generally SUSAN SHERWIN, NO LONGER PATIENT: FEMINIST ETHICS AND HEALTH CARE (1992).

national and international networks of similar banks in the future, with particular structures designed to render policies more transparent, accountable, and effective. The NAS Guidelines set out a number of standards for the banking of hESC lines, and commend efforts that have begun to encourage the sharing and dissemination of cell lines and other research materials.¹²² These recommendations suggest that each cell line repository establish uniform guidelines for quality control, standardized consent and IRB procedures, tracking procedures, privacy assurances, and consistent rules for deposits and withdrawals. They also develop a committee for policy and oversight.¹²³ Nascent efforts to build such facilities have begun in both the United Kingdom and Wisconsin with some success,¹²⁴ and the NAS Guidelines focus on the U.K. Stem Cell Bank.¹²⁵ However, whereas the centralized stem cell bank plays a crucial role in the governance architecture in the U.K., it seems to play a much smaller governance role within the NAS's imagined regulatory regime. Furthermore, the idea of centralized banking of stem cell lines, though perceived as a probable eventuality by CIRM, has not been discussed as a feature of stem cell governance.

The ways in which the stem cell bank could be an efficient and effective vehicle for better governance over stem cell research in California deserve exploration. Indeed, the U.K. model might be adapted to the California context and extended in a way that actually addresses existing shortcomings in the regulatory regimes discussed above.

A. The Role of Stem Cell Banks in Governance: The U.K. Model

Concerned with research involving both embryonic and adult stem cells, the U.K. Stem Cell Bank is a repository aiming to facilitate the sharing of well-characterized and high-quality cell lines with the clinical and research communities in order to support research and the development of

122. NAS GUIDELINES, *supra* note 8, at 76-79.

123. See Recommendations 22-23, in NAS GUIDELINES, *supra* note 8, at 128-29.

124. See STEERING COMMITTEE FOR THE UK STEM CELL BANK AND FOR THE USE OF STEM CELL LINES, FIRST ANNUAL REPORT FROM THE UK STEM CELL BANK (2004), available at http://www.mrc.ac.uk/pdf-stemcell_steer_comm_annrep.pdf; Associated Press, *Wisconsin Group to Run Stem Cell Bank: Federal Program Will Store and Distribute Cells for Research*, Oct. 4, 2005. The federally-funded stem cell bank in Wisconsin is limited to storing and distributing lines approved under Bush's policy, a fact that has hampered the bank's importance. Harvard University, for instance, now distributes far more batches of cell lines than this national bank. Rob Waters & John Laureman, *Harvard Stem Cells Favored Over Those Produced With U.S. Funds*, BLOOMBERG.COM, July 13, 2006, <http://www.bloomberg.com/apps/news?pid=20601103&sid=aeyb8GOm8Md8&refer=us>.

125. NAS GUIDELINES, *supra* note 8, at 76.

new therapies to treat serious disease.¹²⁶ Funded by the Medical Research Council (MRC) and the Biotechnology and Biological Sciences Research Council pursuant to recommendations made by a House of Lords Select Committee, the U.K. Stem Cell Bank (UKSCB) plays a central role in the governance regime for stem cell research in the United Kingdom. The UKSCB's institutional structure and practices help demonstrate that stem cell banks may be useful for ethical oversight and governance in stem cell research.

1. *Institutional History*

Exactly how the UKSCB became a crucial site of research governance in the U.K. deserves review. In the early 1980s, the United Kingdom worked as a pioneer in the area of new reproductive technologies. The U.K. made new scientific and clinical advancements in the field, but also discussed relevant legal and ethical issues related to such research with the publication of the *Warnock Report* in 1985.¹²⁷ The Human Fertilisation and Embryology Act of 1990, passed on recommendations made in the *Warnock* report, created a licensing body for research involving embryos known as the Human Fertilisation and Embryology Authority (HFEA). The governing policy of the Act attempts to promote open and effective regulation of embryo research, delineating that the HFEA should license work only if it is necessary in relation to approved statutory purposes, and that research on embryos should not run beyond fourteen days.¹²⁸ Acceptable goals for the research originally included either promoting the advancement in the treatment of fertility, increasing knowledge about disease or miscarriages, developing more effective techniques for contraception, or developing methods for detecting gene or chromosome abnormalities.¹²⁹

Advances in stem cell research throughout the 1990s prompted HFEA officials to revisit regulations and consider whether licenses for stem cell research could be issued under the 1990 Act's originally stated purposes. In 2001, the HFEA released new regulations that added new purposes to embryo research in order to facilitate work on stem cells. These new purposes included increasing knowledge about embryo development or serious disease and its treatment.¹³⁰ With the release of the regulations, con-

126. CODE OF PRACTICE, *supra* note 53.

127. See Matthew Herder, *The UK Model: Setting a Standard for Embryonic Stem Cell Research?*, 10 HEALTH L. REV. 14, 14-24 (2001).

128. Roger Brownsword, *Stem Cells, Superman, and the Report of the Select Committee*, 65 MOD. L. REV. 568, 571 (2002).

129. Human Fertilisation and Embryology Act 1990, *supra* note 108.

130. *Id.*; Brownsword, *supra* note 128, at 572.

cerns were raised as to whether cloned human embryos produced by somatic cell nuclear transfer fell within the definition of embryo in the Act and would therefore not be subject to the new HFEA provisions.¹³¹

In response to this concern, the House of Lords agreed to appoint a committee “to consider and report on the issues connected with human cloning and stem cell research arising from the Human Fertilisation and Embryology (Research Purposes) Regulations.”¹³² The House of Lords Select Committee addressed a number of central issues, including the potential benefits of stem cell research, alternatives to research on human embryos, the moral status of the early embryo, distinctions among categories of embryos (surplus embryos left over from IVF treatment, embryos created by IVF, and embryos created via CNR), commercial involvement, and the possible need for the regulation of stem cell lines derived from embryos.¹³³

The House of Lords Select Committee decided that the government should continue to engage in stem cell research in order to understand scientific developments within the field and recommended that the Department of Health and the MRC establish a centralized stem cell bank to provide scientists access to high quality stem cell lines. Furthermore, the committee recommended that a steering committee establish rules governing withdrawals from and deposits in the bank.¹³⁴ The following Section discusses the governance structure of the UKSCB.

2. *Institutional Governance*

The UKSCB Steering Committee oversees the bank’s operations and governance. A non-statutory body that meets three times per year and reports annually to the MRC, the Steering Committee ensures that the research associated with the UKSCB is carried out in a transparent and ethical manner. Lord Naren Patel currently heads the Steering Committee, and membership of the committee includes experts in science, ethics, theology, and medicine, regulatory and funding agency representatives, and public lay persons.¹³⁵ The Steering Committee is responsible for developing a code of practice for the UKSCB and the use of stem cell lines, reviewing on a case by case basis applications to deposit or access embryonic and

131. HOUSE OF LORDS SELECT COMM. FOR STEM CELL RESEARCH, STEM CELL RESEARCH-REPORT (2002). In the U.K., somatic cell nuclear *transfer* is usually called somatic cell nuclear *replacement*, or CNR.

132. *Id.* at ch. 1, § 1.15.

133. *Id.* at ch. 1, § 1.19.

134. *Id.* at Summary of Conclusions, § xxvi.

135. CODE OF PRACTICE, *supra* note 53, at 10.

adult stem cell lines, ensuring that strategies are in place to manage risk and issues reported by the Bank Management and User and Clinical Liaison Committees, reporting annually to the MRC, and annually briefing Health and Science Ministers on stem cell research.¹³⁶ The UKSCB has a number of other important committees involved in the active management and governance of the repository.¹³⁷

Researchers who wish to derive new hESC lines must first obtain a license from the HFEA, a prerequisite for the UKSCB to accept new lines from researchers for banking. The Steering Committee must review that the cell lines have been ethically sourced, with fully informed donor consent,¹³⁸ and that the lines present a valuable resource to the research community. Bank researchers are requested to complete an application form in

136. Steering Committee for the UK Stem Cell Bank and for the Use of Stem Cell Lines, http://www.mrc.ac.uk/index/strategy-strategy/strategy-science_strategy/strategy-strategy_implementation/strategy-government_spending_review_initiatives/strategy-stem_cells/strategy-stem_cell_governance/public-stemcell_governance_steering.htm (last visited Aug. 13, 2006).

137. A “User and Clinical Liaison Committee,” for example, includes stem cell researchers and clinicians from academia and the industry. This group provides a forum for discussion and consultation on issues relating to oversight of stem cell research and therapy development in the UKSCB. A “Bank Management Committee” meets every six months and directly oversees the UKSCB; it monitors operational issues related to the UKSCB and assists in developing longer term management strategy. The committee is chaired by the NIBSC Director and membership includes stem cell experts from the UKSCB and external experts, professionals, lay members, and funding agency representatives. The committee receives annual reports from UKSCB and reports them formally to the Steering Committee. Currently, the Management Committee has established a number of subgroups that meet more regularly to support day to day functioning of the UKSCB and address specific issues. These include separate working groups to manage public relations, to involve stem cell biologists in providing advice on characterization procedures for the UKSCB, to review proposed procedures for safety testing and potential sources of cell contamination, and to establish appropriate processes and procedures enabling “quick and appropriate response in the event of an adverse discovery relating to a donor or a cell line.” See STEERING COMMITTEE, FIRST ANNUAL REPORT, *supra* note 124.

138. Patients making embryo donations must be provided with comprehensive information such that it allows a free and informed decision. Written information and consent forms must be reviewed by a Local Ethics Committee, and for research involving embryos, HFEA approval is also required. The HFEA and the Steering Committee for the UKSCB have developed a list of criteria that must be presented to donors in information leaflets: only a few stem cell lines will be successfully derived from embryos; stem cell lines may be used in various research projects and donors may not restrict research conducted on such lines; cell lines may be used for future treatment purposes; embryos will be coded and researchers will not have access to donors’ identifying information; and the decision to donate is voluntary and will not affect donors’ treatment in any way. CODE OF PRACTICE, *supra* note 53, at 15-16.

order to aid the Steering Committee. The depositor and the UKSCB must sign a “Materials Deposition Agreement” in order to make stem cell lines available to requestors on terms of access negotiated by depositor and requestor in the Material Use License.¹³⁹ Depositors remain closely involved in the deposition process through a Project Team. The Project Team, composed of Bank staff and scientists and technicians from the depositor’s institution or laboratory, is responsible for the transfer of stem cell lines, along with techniques and skills, to the UKSCB. In addition, the depositor is requested to test cell lines and provide comments on their consistency, a process that gives requestors confidence in the cell lines.¹⁴⁰

Researchers wishing to access stem cell lines from the UKSCB must meet HFEA requirements for stem cell research. More specifically, researchers requesting the use of banked lines must provide assurances that the experiments are likely to increase knowledge about embryo development or serious disease, and basic research must underpin these aforementioned aims or lead to the development of cell-based therapies for clinical trials.¹⁴¹ It is expected that proposals for research be subjected to peer review; evidence of this process must be presented to the Steering Committee. Institutional review board (called the Research Ethics Committee in the U.K.) approval must be obtained as part of the HFEA research license process, for research involving human tissues and for clinical trials of all stem cell derived products. The Steering Committee does not require IRB approval for research involving established embryonic stem cell lines.¹⁴²

B. Adapting the U.K. Model to California to Address Governance

Drawing from the new UKSCB, the proposed California Stem Cell Biorepository (CSCB) would offer a vital resource to support this research (both academic and commercial), while establishing governance mechanisms useful for protecting the covenant between donors and the scientific community.¹⁴³ The CSCB would be a new non-profit foundation that is funded by and works closely with CIRM, but which is governed independently by a Steering Committee for Public Policy and a Board of Trustees composed of individuals free of conflicts of interest. Members of this body might include directors of CIRM and the ICOC, donor representatives, state senators, and rotating public ombudspeople. The leading features of this institution would be: (1) a centralized biorepository for the

139. *Id.* at 13.

140. STEERING COMMITTEE, FIRST ANNUAL REPORT, *supra* note 124.

141. CODE OF PRACTICE, *supra* note 53, at 13-14.

142. *Id.* at 13.

143. See NAS GUIDELINES, *supra* note 8.

characterization, standardization, propagation, and distribution (at cost) of new hESC lines developed under CIRM funding; (2) a Centralized Embryonic Stem Cell Research Oversight Committee (CESCRO) that will consider all research protocols requesting CIRM funds, and also any research protocols requesting materials from the biorepository; and (3) a donor advisory group with procedural rights in the development of CSCB policy and ethics review.

In California, a centralized stem cell bank should be built by requiring that all new hESC lines created with CIRM funds be deposited there. Additionally, to achieve greater coverage over all stem cell research in the state, the legislature should mandate that all stem cell research that is conducted in the state be on cell lines that have either been banked at or approved through reciprocity by the CSCB.¹⁴⁴

At the bank's physical repository, staff should have the task of propagating the cell lines, keeping a coded cell line registry, and handling distribution to researchers who seek access, freeing many scientists from administrative burden. Centralized banking is also likely to expedite standardization, quality control, and uniform characterization of cell lines,¹⁴⁵ as well as the management of genetic diversity in the archive of therapeutic materials for people with divergent haplotypes.¹⁴⁶ Operational costs should be shared by funding agencies and research institutions themselves, which will save the expense of developing separate banking and distribution facilities. Eventually, such a public stem cell bank in California should be linked into a larger network of hESC banks in the United States and abroad, including the UKSCB.

Previous authors have discussed thoroughly the scientific advantages to centralized banking. Centrally banking and cataloguing new stem cell lines and material-based research tools, and making these widely available for research at cost, would maximize scientific and therapeutic value of CIRM funds. In Recommendation 23, the NAS Guidelines propose a se-

144. This latter policy could be challenged on the basis of rights of contract and freedom of association. However, the state's sovereign police powers and regulatory power over health would likely overcome these claims.

145. See Ali H. Brivanlou et al., *Setting Standards for Human Embryonic Stem Cells*, 300 SCI. 913, 916 (2003).

146. See Ruth Faden et al., *Public Stem Cell Banks: Considerations of Justice in Stem Cell Therapy*, 23 HASTINGS CENTER REP. 13, 19-20 (2003). Stem cell therapies will involve transplanting tissues derived from stem cells, or the stem cells themselves. Since patient immune systems will try to eliminate cells with foreign antigens, matches will have to be found. Since the relevant antigens tend to correlate with race, the authors argue there are important racial justice issues inherent in the management of cell line diversity. *Id.*

ries of best practices for any lab or institution planning to bank stem cell lines. These include: (a) creating a committee for policy and oversight purposes and creation of clear and standardized protocols for banking and withdrawals; (b) establishing documentation requirements for investigators and sites that deposit cell lines; (c) establishing a secure system for protecting the privacy of donors when materials retain codes or identifiable information; and (d) setting out clear criteria for the distribution of cell lines, including evidence of approval of the research by an embryonic stem cell research oversight committee or equivalent body at the recipient institution. Establishing the CSCB would accomplish these goals efficiently. The CSCB would also promote access to high-quality materials and thereby of stem cell therapies, and reduce the burden on individual labs to distribute cell lines, allowing them to focus on their laboratory work. Finally, centralization would facilitate the creation of a centralized and searchable database and registry for eventual therapeutic use.

The new insight in this Article is that the CSCB would help address some of the inadequacies in the governance regime for stem cell research addressed above. First, as a threshold matter, maintaining a public hESC repository in California would reduce the number of egg donors required to support an expanded program of research. Because of the significant risks of donating, such a policy has distinct ethical advantages over maintaining decentralized stem cell banks at each research institution. Since hESC lines can be perpetuated *ad infinitum*, or at least for a period of many years, a central bank could generate a ready hESC supply with fewer cell lines. To the extent that fewer academic researchers would be forced to derive their own cell lines from egg donations, this would reduce the number of donors. If researchers were to allow non-restrictive licensing of the materials, either through voluntary or mandatory rules, then this advantage of a central repository would be enhanced. Finding a way to minimize the number of women undergoing egg extraction for research alone would translate into an ethical imperative to do so.

Second, standardization afforded by the centralization of ethical review would bring more effective review of new hESC research in California, and would help avoid institutional conflicts of interest, both real and perceived. The group of researchers engaging in this line of work at each particular institution is small enough such that well-documented conflicts of interest problems with IRBs would be exacerbated. Attaching a centralized ethics review board to the stem cell bank would facilitate the maintenance of independence crucial for the ethical review body's legitimacy and efficacy. Furthermore, the ethics review body at the bank could maintain a regular dialogue with the ethics policy makers on the Steering

Committee, which would be designed to interface with scientists and the public on complex issues as they arise. This system would mean that non-CIRM-funded researchers would have to apply to the CSCB for access to lines developed from CIRM funds, bringing needed oversight to this work that the CIRM Regulations leave uncovered.¹⁴⁷

Third, there are strong reasons for centralizing banking and ethical review from the perspective of administrative efficiency. Although some arguments for keeping ethical review on the local institutional level exist,¹⁴⁸ centralized review would be more efficient and less expensive than the use of localized SCROs. It also may be unrealistic to imagine that each institution would be able to find the necessary scientists, personnel, and members of the public with sufficient expertise. One of the main advantages of centralizing a repository of new stem cell lines and other donated materials for research is that the additional ethical oversight required to do this research could be centralized, standardized, and overseen in a publicly accountable institution.

Fourth, from the perspective of transparency and public accountability, this proposal has significant advantages. This system would avoid the perception that crucial ethical decisions are being made in the backrooms of the very institutions that stand to gain from large CIRM grants. This centralized review panel would have the independence necessary to achieve public confidence, would make the ethical review more transparent, and would ultimately lead to a more legitimate policymaking process at the level of the Steering Committee. It would create a nodal point for public engagement, education, and deliberation where one is lacking. It would create a better forum for an iterative communication process between the Centralized Embryonic Stem Cell Research Oversight Committee and the Steering Committee in a way that would position the California initiative to deal with new ethical questions and particular controversies as they emerge.

Fifth, the CSCB as proposed would address the dearth of representation of the donor community in the governance of stem cell research by enhancing the membership of donor representatives and lay people on the Steering Committee, Board of Trustees, and CESCR. Alternatively, the institutional structure of public stem cell banks could be used to develop a participatory role for the donor group. As discussed above, in the field of biobanking for population genomics, new norms of participation in research governance by donor communities have emerged. These norms

147. See discussion *supra* Section III.B.3.

148. See NBAC, RESEARCH SUBJECTS, *supra* note 23, at 111-31.

should apply in the stem cell biobanking context, where the physical and emotional investment of donors and the privacy risks are arguably more significant, especially for egg donors. Important and vexing ethical issues relevant to the donor group will likely arise, including those surrounding the retention and management of coded identities, and the possible recontact of donors in the future.

The central banking institution could house an egg donor group to advise and interact with the bank's central ethics committee, empowering donors to participate in deliberations over costs and benefits of the hESC research under review. Representatives could be selected in a similar way as shareholder representatives on corporate boards, or alumni representatives on university corporate committees. In this way, the ethics committee's duty to promote beneficence could be brought into line with the altruistic expectations of the donor group. This arrangement would foster more representative governance and a more meaningful dialogue among key partners in the collective endeavor of hESC research.

Sixth, the collective organization of research donors entailed by these features could help mitigate the problem of "open consent" in two ways. First, through direct representation on repository committees, donors as a group would enjoy greater control over the future uses of their samples, giving donors a voice in decision making over uses of their materials that were "unforeseen" at the time of donation. If a particularly controversial use emerged, representatives of the donor community could contact donors for a sense vote on whether such research should be permitted. A stronger way of addressing the loss of autonomy entailed by open consent would be to allow donors whose materials resulted in useful cell lines to retain a right of refusal to participate in new research projects. Through a repository website, donors could be kept apprised of research protocols requesting cells from the repository. New requests for cells would be posted on the website, giving donors notice to opt out. Donors could be given a window of time to opt out of particular projects, such as one month, after the posting of the new protocol on the web. This mechanism has been proposed before, in the context of tissue donation in genomics research, as middle ground between open consent and informed consent for each new research project.¹⁴⁹

Seventh, a centralized repository would make characterization of the overall genetic coverage of the new stem cell lines easier, facilitating important distributive justice and ethnic equality goals. Developing stem cell

149. David E. Winickoff & Richard N. Winickoff, *The Charitable Trust as a Model for Genomic Biobanks*, 349 NEW ENG. J. MED. 1180, 1183 (2003).

therapies will necessitate finding genetic matches among diverse genotypes, and some predict that patients may require ethnic-specific lines for transplant.¹⁵⁰ Centralized banking could help guide CIRM as it sets targets for funding the creation of new hESC lines, enhancing CIRM's capacity to develop and track a diverse archive.

In sum, if set up properly, such institutions could help improve the consent process for donors and the system of ethical oversight. Overall, they would help correct the power asymmetries towards egg donors established in the currently proposed regime. This idea of using stem cell banks to drive governance should not replace the development of binding regulations subjecting human embryonic stem cell research to institutional review board oversight and other controls. However, in a political climate in which the federal government is unlikely to create a new national regulatory architecture for stem cell research, state government and charitable funders could achieve better governance for hESC research through an infrastructure of public stem cell banks. In California, such an institution, if governed transparently and according to the best scientific and ethical thinking, could set a high standard both for the science and the ethical oversight of stem cell research.

V. CONCLUSION

The California Stem Cell Initiative has enormous potential to advance basic science and clinical therapy for a wide range of diseases, but achieving these goals will require careful ethical planning. The NAS Guidelines are a useful starting point for addressing the complex ethical issues involved in conducting embryonic stem cell research, and leaders at CIRM have adapted these recommendations to the California context in credible ways. However, these guidelines should only be a starting point for California, where much more robust structures are imaginable because of the research program's centralization and public character.

While it would be easier for California to simply adapt and apply existing consent and IRB structures onto the field of stem cell research, California would lose an opportunity to innovate and lead not just in biotechnology, but also in bioethics. Taking a cue from the United Kingdom, centralized stem cell banking in California would bring general gains in efficiency while creating a pragmatic opportunity to construct an ethical and legal architecture for long-term public return. This vision of stem cell banking would provide useful flexibility in the face of a fast-evolving

150. Faden, *supra* note 146, at 21-23.

ethical frontier, and help build trust between scientific institutions and society. Such a collaborative vision of biotechnological governance would be economically feasible, socially preferable, and scientifically advantageous.

