FOLLOW THE LEADER?: MARYLAND'S RESPONSE TO THE NEW FEDERAL STEM CELL GUIDELINES

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INTRODUCTION

Billions of dollars have been spent in search of cures for diseases such as cancer,[1] muscular dystrophy,[2] heart disease,[3] diabetes,[4] Alzheimer's,[5] and Parkinson's.[6] Medical research has consistently pushed the envelope to find new ways to tackle old problems, yet, the field of embryonic stem cell research, a field that many believe could be the key to providing new and effective treatments, remains relatively underfunded due to concerns over ethical considerations. This is largely because the biggest financial backer of scientific research is the federal government,[7] and its desire to finance

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1. *Estimates of Funding for Various Research, Condition, and Disease Categories*, NAT'L INSTS. OF HEALTH (Feb. 1, 2010), http://report.nih.gov/rcdc/categories/ [hereinafter *Estimates of Funding*]. The National Institutes of Health's (NIH) financial support for cancer research in 2008 was $5.57 billion. *Id.*

2. *Id.* The NIH's financial support for muscular dystrophy in 2008 was $56 million. *Id. See also Jerry Lewis' Telethon Hits Record*, USA TODAY, Sept. 3, 2007, *available at* http://www.usatoday.com/life/television/news/2007-09-03-jerry-lewis-telethon_N.htm (stating that The Muscular Dystrophy Association Telethon raised $1.46 billion between 1966 and 2007).

3. *Estimates of Funding*, *supra* note 1. The NIH's financial support for heart disease research in 2008 was $1.217 billion. *Id.*

4. *Id.* The NIH's financial support for diabetes research in 2008 was $1.08 billion. *Id.*

5. *Id.* The NIH's financial support for Alzheimer's disease research in 2008 was $412 million. *Id.*

6. *Id.* The NIH's financial support for Parkinson's disease research in 2008 was $152 million. *Id.*

7. *See* James W. Fossett, *Beyond the Low-Hanging Fruit: Stem Cell Research Policy in an Obama Administration*, 9 YALE J. HEALTH POL'Y L. & ETHICS 523, 529 (2009) (finding that states have never felt compelled to support research due to funding from the NIH and other federal agencies being ubiquitous in biomedical research).

embryonic stem cell research has waxed and waned over the years with the changing of administrations and the political climate.[8]

But on January 23, 2009, the Food and Drug Administration (FDA) granted approval to the first clinical trial in the world using human embryonic stem cells (hESCs) on people.[9] Geron Corporation, a biotechnology company in Menlo Park, California, was granted federal approval to test the stem cells on eight to ten patients with severe spinal cord injuries.[10] This authorization to move forward with the trial comes just over ten years after the first human embryonic stem cells were isolated, at the University of Wisconsin in work financed by Geron,[11] and approximately ten months after Geron first applied to the FDA to conduct the trial.[12]

The story of Geron's efforts to push an embryonic stem cell product to market illustrates both the enormous potential and controversy that surrounds embryonic stem cell research. With a goal of ameliorating the devastation caused by spinal cord injuries, Geron hopes their embryonic stem cells will "help repair the protective myelin sheath around the nerve cells, restoring the ability of nerves to carry signals, and perhaps allow damaged cells to regenerate."[13] And despite submitting a record 22,500-page application, the trial was placed in a "clinical hold" by the FDA in August 2009.[14] It is unclear whether this is due to Congress coaxing the FDA in recent years to raise its regulatory hurdles on new products, with some of the most stringent being applied to stem cell products,[15] or due to political considerations from the Bush administration.[16] What is clear is that less controversial stem cells derived from adults and fetuses have been used in clinical trials for years, treating thousands of patients worldwide.[17]

8. *See infra* note 37 and accompanying text (noting that the Obama administration expanded the possibilities for stem cell research relative to what was allowed under the George W. Bush administration but that the new policies are effectively the same as those under President Clinton).

9. Rob Stein, *Government Approves Study Using Human Embryonic Stem Cells*, WASH. POST, Jan. 24, 2009, at A6.

10. *Id.*

11. Andrew Pollack, *Milestone in Research in Stem Cells*, N.Y. TIMES, Jan. 23, 2009, at B1.

12. *Id.*

13. *Id.*

14. Scott Gottlieb, *Stem Cells and the Truth About Medical Intervention*, WALL ST. J., Mar. 14, 2009, at A9.

15. *Id.*

16. Pollack, *supra* note 11.

17. BLOOMBERG NEWS, *Study Using Stem Cells is Delayed*, N.Y. TIMES, Aug. 19, 2009, at B8. On August 18, 2009, the Geron clinical trial was halted by the FDA after Geron shared data from dose escalations studies in animals. *Id.* As of February 20, 2010 the Geron clinical trial was still on hold. Nicholas Wade, *Agency Proposes U.S.-Paid Research on Stem Cells from Early Human Egg*, N.Y. TIMES, Feb. 20, 2010, at A8.

Under President Bush, a moratorium was placed on any research done on cell lines that were created after August 9, 2001.[18] The Bush administration believed that the destruction of human embryos for research purposes was not ethically sound enough to warrant governmental support through the issuing of federal funds.[19] In addition, the Dickey-Wicker Amendment prohibits the Department of Health and Human Services (HHS), which includes the National Institutes of Health (NIH), from funding the creation of embryos for research purposes or from funding research where an embryo would be destroyed, discarded, or knowingly subjected to risk of injury or death.[20] After reviewing the Dickey-Wicker Amendment, the Bush administration felt its policy was in line with this legislative intent.[21] As such, the administration maintained its ethical ground that nascent human life should not be destroyed for research purposes, while allowing for some good to come of the destruction that had already taken place.[22]

With limited cell lines approved for federal funds under the Bush regime, stem cell research was left largely to the states and the private sector as far as funding and determining criteria for what was eligible for state funding.[23] Although some states chose to prohibit stem cell research, or refuse to fund it, a number of states did permit stem cell research,[24] including Maryland.[25] These states established their own guidelines and review boards to advance the field of stem cell research as they saw fit.[26]

Geron's research was neither affected by the Dickey-Wicker Amendment nor by the Bush administration restrictions, because Geron did not use federal funds and the embryonic stem cells were derived from one

18. PRESIDENT'S COUNCIL ON BIOETHICS, MONITORING STEM CELL RESEARCH 189 (2004), *available at* http://www.bioethics.gov/reports/stemcell/pcbe_final_version_monitoring_stem_cell_research.pdf [hereinafter MONITORING STEM CELL RESEARCH].

19. *Id.* at 32.

20. Balanced Budget Downpayment Act of 1996, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34. Embryo includes any organism not protected as a human subject under 45 CFR § 46 "that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes." *Id.*

21. MONITORING STEM CELL RESEARCH, *supra* note 18, at 32.

22. *Id.* at 34.

23. *See* Fossett, *supra* note 7, at 532 (finding that state initiatives have established centers for policymaking for stem cell research independent of federal influence).

24. *Stem Cell Research,* NAT'L CONF. OF ST. LEGISLATURES (2008), http://www.ncsl.org/IssuesResearch/Health/EmbryonicandFetalResearchLaws/tabid/14413/Default.aspx (identifying California, Connecticut, Illinois, Indiana, Iowa, Maryland, Massachusetts, New Jersey, and New York as states that allow some form of stem cell research).

25. *See* MD CODE ANN., ECON. DEV. § 10-429 to 438 (LexisNexis 2008) (setting forth Maryland's rules for stem cell research).

26. Fossett, *supra* note 7, at 532.

of the oldest cell lines, which was eligible for federal funding under Bush's policy.[27] Yet, the Geron application languished in the FDA before its approval in January 2009.[28] Geron's approval coincided with the inauguration of President Obama, who had vowed during his campaign to remove some of the financing restrictions on embryonic stem cell research implemented by the Bush administration.[29] Opinions differ on whether the timing of the approval was mere coincidence. Thomas B. Okarma, chief executive of Geron, stated that he did not think Bush's "objections to embryonic stem cell research played a role in the FDA's delaying approval,"[30] and the FDA insisted that they simply look at the science and approve research based on safety.[31] Yet, Robert N. Klein, the chairman of California's stem cell research program, felt the approval was directly tied to the administration change and even asserted his belief that the Bush administration pressured the FDA to delay the trial.[32]

Following through on one of his campaign platforms to alter federal policy on embryonic stem cell research, on March 9, 2009, President Obama issued an Executive Order lifting certain restrictions placed on stem cell research by the Bush administration.[33] As such, the NIH was given the authority to issue new federal guidelines for stem cell research, which went into effect on July 7, 2009.[34] In light of the newly issued NIH guidelines, any state with their own state guidelines for stem cell research must determine whether they plan on altering its guidelines to fit within the federal scheme.[35] While the assumption might be for states to adopt requirements set forth by these new guidelines in order to be eligible for federal funding, a closer look at the field of stem cell research and its history suggests otherwise.[36]

27. Stein, *supra* note 9.

28. Pollack, *supra* note 11.

29. *Id.*

30. *Id.*

31. Ron Winslow & Alicia Mundy, *Currents – Health: First Embryonic Stem-Cell Trial Gets Approved from the FDA*, WALL ST. J., Jan. 23, 2009, at A12.

32. Pollack, *supra* note 11.

33. Exec. Order No. 13,505, 74 Fed. Reg. 10,667 (Mar. 9, 2009).

34. NATIONAL INSTITUTE OF HEALTH GUIDELINES ON HUMAN STEM CELL RESEARCH, *74 FED. REG. 18,578–80* (Apr. 23, 2009) [hereinafter NIH GUIDELINES]; *National Institutes of Health Guidelines on Human Stem Cell Research*, STEM CELL INFORMATION, http://stemcells.nih.gov/policy/2009guidelines.htm (last visited Aug. 19, 2011).

35. *See* Varnee Murugana, *Embryonic Stem Cell Research: A Decade of Debate from Bush to Obama*, 82 YALE J. BIOLOGY & MED. 101, 102 (2009) ("The new policy allows federally funded researchers to experiment on hundreds of viable ES cell lines restricted under Bush.").

36. *See* Fossett, *supra* note 7, at 523 (discussing the expectation of a major shift in stem cell research policy with the new administration and the difficulty in assessing the significance of the change in federal policy when significant issues were left unresolved).

The NIH guidelines expand the possibilities for stem cell research relative to those under Bush, yet, they effectively return stem cell research to its existence under President Clinton ten years earlier.[37] Though more cell lines may now be approved or be approvable under the new federal guidelines, scientific bodies such as the National Academies (NAS) and International Society for Stem Cell Research (ISSCR) have created guidelines expanding stem cell research that are accepted and utilized internationally.[38]

For Maryland, this is a critical juncture in its stem cell history. It recently announced a collaborative partnership in stem cell research with California at the 2009 World Stem Cell Summit held in Baltimore, with the hopes of generating breakthroughs in the field and obtaining more grant money.[39] How Maryland responds to the new federal guidelines may control how fruitful this collaboration will become. Seen as a pioneer and leader in the field of stem cell research, with a new Center for Stem Cell Biology and Regenerative Medicine, Maryland was seen as a likely site for the Geron trial.[40] If the state intends to maintain this reputation, how it moves forward with its stem cell regulations is critical. In the competition for cutting edge research, Maryland must be wary of limiting itself by blindly abiding by federal guidelines that may lag behind what is accepted in other states, as well as internationally.[41]

37. *Compare* Exec. Order No. 13,505, 74 Fed. Reg. 10,667 (Mar. 9, 2009) (allowing funding for research on newly created stem cell lines), *and* NATIONAL BIOETHICS ADVISORY COMMISSION, ETHICAL ISSUES IN HUMAN STEM CELL RESEARCH – EXECUTIVE SUMMARY 3 (1999), *available at* http://bioethics.georgetown.edu/nbac/execsumm.pdf [hereinafter ETHICAL ISSUES] (finding that federal funding could be used to derive cells or cell lines from cadaveric fetal tissue or embryos remaining after fertility treatments), *with* MONITORING STEM CELL RESEARCH, *supra* note 18, at 189 (stating that federal funds could only be used for research on stem cell lines that existed before Aug. 9, 2001).

38. THE NATIONAL ACADEMIES' GUIDELINES FOR HUMAN EMBRYONIC STEM CELL RESEARCH (2008 Amendments) [hereinafter NAS GUIDELINES], *available at* http://books.nap.edu/openbook.php?record_id=12260&page=R1; THE INTERNATIONAL SOCIETY FOR STEM CELL RESEARCH, GUIDELINES FOR THE CONDUCT OF HUMAN EMBRYONIC STEM CELL RESEARCH (2006) [hereinafter ISSCR GUIDELINES], *available at* http://www.isscr.org/guidelines/ISSCRhESCguidelines2006.pdf.

39. Danielle Ulman, *Maryland Signs Stem Cell Collaboration Deal with California*, THE DAILY RECORD (Balt.), Sept. 22, 2009.

40. Matthew Hay Brown & Stephanie Desmon, *Stem Cell Trials Ok'd; Embryonic Tests in City Possible*, BALTIMORE SUN, Jan. 24, 2009, at A1.

41. *See* Andy Rosen, *Is $12.4M in Stem Cell Funding in MD Enough?*, THE DAILY RECORD, July 27, 2009 ("Comptroller Peter Franchot expressed concern about Maryland's competitive position."); Fossett, *supra* note 7, at 532–33 (discussing how most states modeled their guidelines on those promulgated by the NAS and ISSCR and the competition between states for researchers appears to be increasing).

After providing a brief scientific background in Part I,[42] ethical issues in stem cell research such as embryonic stem cell derivation methods,[43] autonomy and coercion,[44] and procedural concerns[45] will be examined as well. Part II explores the essential differences between the NIH, NAS, and ISSCR guidelines with respect to these ethical considerations and how they relate to procurement of materials,[46] informed consent,[47] and the review process.[48] Part III discusses Maryland's current stem cell guidelines,[49] while part IV suggests model guidelines[50] that Maryland should utilize. In doing so, Part IV will also examine how Maryland's guidelines differ, and what changes Maryland should make to bring its current guidelines closer to the model guidelines.[51]

I. BACKGROUND

A. Scientific Background

Stem cells are important to the field of medical research because they are capable of renewing themselves through cell division for long periods of time, they are undifferentiated, meaning they have not yet developed into a specialized cell type, and they have the potential to become any tissue or organ of the researcher's choosing.[52] Scientists primarily work with two types of stem cells, embryonic stem cells and adult, or somatic, stem cells.[53] Researchers are also beginning to use induced pluripotent stem cells (iPSCs), which are adult stem cells that are genetically reprogrammed to become cells that have embryonic stem cell-like properties.[54]

Embryonic stem cells are typically derived from spare embryos that have been developed through *in vitro* fertilization (IVF) for reproductive purposes and subsequently donated for research purposes when they are no

42. *See infra* Part I.A.
43. *See infra* Part I.B.1.
44. *See infra* Part I.B.2.
45. *See infra* Part I.B.3.
46. *See infra* Part II.A.
47. *See infra* Part II.B.
48. *See infra* Part II.C.
49. *See infra* Part III.
50. *See infra* Part IV.A.
51. *See infra* Part IV.B.
52. NAT'L INSTS. OF HEALTH, STEM CELL BASICS 3 (2009), *available at* http://stemcells.nih.gov/staticresources/info/basics/SCprimer2009.pdf [hereinafter STEM CELL BASICS].
53. *Id.* at 2.
54. *Id.* at 13. The technical term for these cells with embryonic stem cell-like proprieties are human pluripotent stem cells (hPSCs). *Id.*

longer needed for their originally intended use.[55] The human embryonic stem cells (hESCs) are usually taken when the embryos are four to five days old.[56] A cell line is then created after the hESCs have replicated in the "cell culture for six or more months without differentiating, are pluripotent, and appear genetically normal."[57]

The main difference between hESCs and adult stem cells is that hESCs can become a cell of any type, while adult stem cells are thought to be limited to differentiating to the cell types found in their original tissue.[58] In addition, growing hESCs in culture is relatively easy, whereas adult stem cells are difficult to isolate from an adult tissue and growing them in culture is challenging.[59] Despite the promise of iPSCs, it is still unknown whether there are clinically significant differences between the iPSCs and hESCs.[60] A significant portion of stem cell researchers remain skeptical that iPSCs are reliable substitutes for hESCs.[61]

B. Ethical Issues

While hESCs may have more potential than adult stem cells, because of their broader range of differentiation and ease in proliferation, they are more controversial.[62] The ethical implications of using an embryo to derive stem cells are not lost on the nation's populace, nor are they lost on the country's lawmakers.[63] For years the debate over embryos and the beginning of human life has tethered stem cell research to contested issues such as abortion. The moral status of embryos and the rights they deserve are questions that inevitably arise when dealing with where any hESCs come from. The arguments in this context change depending on the source

55. *Id.* at 5.

56. *Id.* The cells are typically taken from a group of cells referred to as the blastocyst. *Id.*

57. *Id.*

58. *Id.* at 12.

59. *Id.* at 13.

60. *Id.*

61. Fossett, *supra* note 7, at 541.

62. *See* Stephen R. Latham, *The Once and Future Debate on Human Embryonic Stem Cell Research*, 9 YALE J. HEALTH POL'Y L. & ETHICS 483, 486 (2009) (identifying the debate surrounding hESCs as concerns about the moral status of the human embryo in vitro against the potential of embryonic stem cell and cloning research to deliver lifesaving and life-enhancing cures).

63. *See* Robert J. Levine, *Federal Funding and the Regulation of Embryonic Stem Cell Research: The Pontius Pilate Maneuver*, 9 YALE J. HEALTH POL'Y L. & ETHICS 552, 553 (2009) (stating that federal officials often try to appeal to both those who believe destruction of embryos or creation of human life artificially is wrong and those who believe potential cures for deadly or disabling diseases should be pursued to the fullest).

of the stem cells.[64] While stem cells can be taken from noncontroversial sources such as cadaveric fetal tissue or adult stem cells, they also can be derived from embryos created by IVF for fertility treatment, embryos created by IVF with gametes donated for research, human somatic cell nuclear transfer (SCNT), and used for chimera research.[65]

1. Objections to Stem Cell Derivation Methods

a. Spare Embryos

Much of the moral objection to embryonic stem cell research resides in the status of the embryo itself. As stated earlier, the destruction of an embryo is seen by many to be the killing of a human being, linking the argument to those made in discussions on abortion.[66] The concept that the human embryo is in fact a human being stems mainly from the religious perspective that life is created at the time of fertilization.[67] The belief that human life begins at the moment of fertilization equates the destruction of an embryo with the murdering of an adult.[68] This religious perspective helped shape the United States' embryonic stem cell policy under President Bush.[69] Seeing the embryo as a human life, President Bush stated in his August 9, 2001 speech on stem cells that "human life is a sacred gift from our creator."[70]

Another view is that while an embryo is not a human being, its potential for life grants it certain moral status that warrants consideration.[71] This typically means that while embryos do not have to be treated on the

64. *See* Latham, *supra* note 63, at 485 (stating that adult stem cell research has been fairly uncontroversial).

65. *See* Stem Cell Basics, *supra* note 52, at 5, 24 (explaining that embryonic stem cells can be derived from embryos created utilizing IVF and somatic cell nuclear transfer); Robert Streiffer, *Human/Non-Human Chimeras*, *in* THE STANFORD ENCYCLOPEDIA OF PHILOSOPHY § 1 (Edward N. Zalta ed., 2010), http://plato.stanford.edu/entries/chimeras/ (discussing how the creation of hESCs increased the range of chimera research).

66. *See* Levine, *supra* note 63, at 563 (discussing how policy makers advocating for embryonic stem cell research may be labeled as condoning the murder of innocent babies).

67. Pope John Paul II, *The Unspeakable Crime of Abortion*, *in* ETHICAL ISSUES IN MODERN MEDICINE 545, 546 (Bonnie Steinbock et. al. eds., 7th ed. 2009).

68. *Id.* at 545.

69. President George W. Bush, *Remarks by President George W. Bush on Stem Cell Research* (Aug. 9, 2001), *in* MONITORING STEM CELL RESEARCH, *supra* note 18, at 183, 186 [hereinafter Remarks by Bush].

70. *Id. See also* Latham, *supra* note 62, at 486 (quoting White House spokesman Tony Snow when asked why President Bush vetoed federal funding for embryonic stem cell research, "The simple answer is he thinks murder is wrong.").

71. *See* Michael J. Sandel, *Embryo Ethics – The Moral Logic of Stem-Cell Research*, 351 New Eng. J. Med. 207, 208 (2004) (stating that personhood is not the only warrant for respect and that to treat an embryo as a mere thing misses its significance as potential human life).

same moral grounds as human beings, their destruction should be for purposes that are appropriate for destroying its potential for life.[72] Some feel that the benefits of embryonic stem cell research are too speculative to justify the destruction of this potential, especially considering the fact that the prospective benefits could possibly be achieved through less controversial forms of stem cell research.[73]

However, this argument for special moral status due to the potential for life is problematic when facing the argument that any single somatic cell or hESC can potentially develop into a human being.[74] Moreover, both an embryo and somatic cell require external factors to realize their potential.[75] For example, a naturally conceived embryo requires nourishment and avoiding dangerous substances while an embryo created through *in vitro* fertilization requires thawing and transferring to a uterus.[76] Since it is unlikely that anyone would argue for the protection of the trillions of cells that contain the potential for life, the argument for special moral status due to an embryo's potential is certainly contested.[77]

b. Research Embryo

While the ethical issues mentioned typically deal with embryos created for infertility and are no longer needed for that purpose, there are separate ethical concerns regarding the creation of embryos for stem cell research. Creating embryos through cloning technologies could potentially allow researchers to better understand genetic diseases as well as address the issue of immune rejection by recipients of stem cell transplants.[78] Yet, some feel that the creation of embryos specifically for the purpose of destroying them for research is not the same as using spare embryos that will most likely be discarded.[79] Creating an embryo for research or therapies is using them as tools from the outset, whereas using embryos that would be discarded is salvaging some benefit since the embryo is bound for destruction.[80] Therefore, the creation and utilization of research embryos for stem cell research raises its own unique ethical concerns.

72. *Id.*

73. Andrew Siegel, *Ethics of Stem Cell Research*, *in* THE STANFORD ENCYCLOPEDIA OF PHILOSOPHY §§ 1, 5 (Edward N. Zalta ed., 2008), http://plato.stanford.edu/entries/stem-cells/.

74. *Id.* at 4.

75. *Id.* at 5.

76. *Id.*

77. *Id.* at 4.

78. *Id.* at 8.

79. *Id.*

80. *Id.*

c. Somatic Cell Nuclear Transfer

One of the methods for creating these types of research embryos is a process known as Somatic Cell Nuclear Transfer (SCNT).[81] This is a technique that combines an egg whose nucleus has been removed with the nucleus of a somatic cell to create an embryo.[82] This method of embryo creation is controversial because of its capability to be used for reproductive cloning.[83] This embryo can be grown to produce a full grown organism with an identical genetic make-up to the organism that donated the somatic cell nucleus.[84] For example, this process was used for the first animal reproductive cloning to create Dolly the sheep in 1996.[85]

While the concept of cloning is highly controversial,[86] the SCNT process could provide an even greater potential in the field of stem cell research in the form of therapeutic cloning.[87] Therapeutic cloning uses the SCNT process to create an embryo with the same genetics as the somatic cell nucleus donor.[88] Therefore, scientists can use these embryos to create stem cells that can be used to generate tissues that match a patient's body.[89] This would likely eliminate the serious concern of tissues being created from stem cells and then having them rejected by the patient's immune system.[90] Yet, some fear that perfecting cloning techniques for therapeutic purposes will enable the pursuit of reproductive cloning, and obtaining the eggs necessary to create the research embryos could lead to exploitation of the women providing those eggs.[91]

d. Chimeras

The other ethical stem cell debate revolves around chimeras, which is an organism composed of cells with different embryonic origins.[92] While the fear and controversy over chimeras can bring about thoughts of human-

81. STEM CELL BASICS, *supra* note 52, at 23–24.

82. *Id* at 23.

83. *Id. See also*, Latham, *supra* note 62, at 486 (stating that therapeutic cloning is controversial because it is uncomfortably close to reproductive cloning).

84. STEM CELL BASICS, *supra* note 52, at 23.

85. *Id.*

86. *Compare* Remarks by Bush, *supra* note 70, at 185 ("I strongly oppose human cloning, as do most Americans."), *with* NAS GUIDELINES, *supra* note 38, § 1.1(a) (covering SCNT, which can be used for therapeutic and, theoretically, reproductive cloning), *and* ISSCR GUIDELINES, *supra* note 38, § 11.1 (allowing for SCNT to be utilized as well).

87. STEM CELL BASICS, *supra* note 52, at 24.

88. *Id.*

89. *Id.*

90. *Id.*

91. Siegel, *supra* note 73, at 8.

92. Streiffer, *supra* note 65, at 2.

animal hybrids, the fact is that each person is most likely a chimera given the fact that other organisms' cells become incorporated into our bodies through processes that leave the cells intact.[93] Other common and naturally occurring examples are pregnant women acquiring cells from their fetuses or mosquitoes transferring blood between victims.[94]

Chimera research is inherently controversial because of the combining of human and animal cells, which carries with it the ethical concerns of animal research ethics as well as the ethical concerns of embryonic stem cell research that were previously discussed.[95] Other more unique ethical concerns may be present, however, given that the use of chimeras in embryonic stem cell research is often met with skepticism and caution, even by advisory boards that maintain its general acceptability.[96] The ethical concerns typically revolve around violating natural species boundaries, existence of entities that cannot be definitely classified as either human or non-human, fear of great apes that have borderline-personhood, affronts to human dignity, and the enhancing of non-human's moral status.[97]

In reality, in terms of embryonic stem cell research, chimera research typically refers to the implantation of stem cells into non-human animals primarily to do experimental research that cannot ethically be performed on humans.[98] For example, to determine whether stem cells are pluripotent they can be injected into blastocyst-stage embryos, the embryo would be brought to term, and then the offspring would be tested for cell potency.[99] Rather than creating a child to ascertain whether hESCs are truly pluripotent, they would be injected into postnatal, immune-deficient mice and see if they give rise to teratomas.[100] Other uses for chimeric research include ascertaining whether certain cells could serve as a source for possible nervous system repair, determining whether a chick embryo could be used as an in vivo system for studying hESC differentiation, and clarifying the bases of diseases by examining the behavior of genetically diseased lines in live animal models.[101]

93. *Id.*
94. *Id.*
95. *Id.* at 3.
96. *Id.*
97. *Id.* at 1.
98. *Id.* at 2–3.
99. *Id.* at 3.
100. *Id.* Teratomas are tumors that consist of disorganized tissue growth of the three germ layers, endoderm, mesoderm, and ectoderm. *Id.*
101. *Id.*

2. Autonomy and Coercion

One of the most important aspects of ensuring ethically sound medical research is the process of informed consent. For consent to be valid, it must be informed and voluntary.[102] These two guiding principles of informed consent help to maintain an individual's right to autonomy and avoid the potential for coercion.[103] Problems arise in the field of embryonic stem cell research because the research is not being performed on the individual giving consent. This raises questions of when consent should be given, who should provide consent, what should the consent cover, and who should be requesting the consent.[104]

The treatment of infertility is a delicate medical process that many suggest should not intermingle with the decision to donate embryos for research purposes.[105] Donation for research then would only be discussed once the infertility treatment is complete and the decision has been made to discard the spare embryos.[106] The thought is that this will avoid taking advantage of people in vulnerable states, and assure that embryos, which might otherwise be donated to others for pregnancy, would not be used for research.[107] A potential problem can arise in cases of "death, divorce, separation, failure to pay storage charges, inability to agree on disposition in the future, or lack of contact with the program."[108] This is why some recommend obtaining written directives at the beginning of the infertility treatment regarding disposition of embryos, with donating to research as an available option.[109]

However, this issue then raises the question of who should provide consent, since decisions regarding gametes and embryos can arise throughout the infertility treatment process.[110] To fully respect the autonomy of all donors, embryos should only be used for research if consent has been obtained by all parties who have contributed biological

102. *See* RUTH R. FADEN & TOM L. BEAUCHAMP, A HISTORY AND THEORY OF INFORMED Consent 155 (Oxford U. Press 1986) (stating that consent must be voluntary and informed).

103. *See id.* at 7 ("Respect for autonomy is the most frequently mentioned moral principle in the literature on informed consent."); Christine Grady, *Money for Research Participation: Does it Jeopardize Informed Consent?*, 1 AM. J. OF BIOETHICS 40, 40 (2001) (discussing how coercion is a threat to the possibility of voluntary informed consent).

104. Bernard Lo et al., *Informed Consent in Human Oocyte, Embryo, and Embryonic Stem Cell Research*, 82 FERTILITY & STERILITY 559, 560 (2004).

105. *See id.* at 562 (stating that certain guidelines find a potential for conflicts of interest if the infertility specialist is the same person requesting embryos for research).

106. *Id.* at 561.

107. *Id.*

108. *Id.*

109. *Id.*

110. *Id.*

material.[111] Alternatively, there are questions about the practicality of obtaining consent from all sperm donors given the widespread use of anonymous frozen sperm.[112] The issue of privacy is also implicated here, given that all identifying information may not be removed, linking the gamete donor with the embryo used for embryonic stem cell derivation.[113]

Generally, it is thought that the consent process should cover "all information that a reasonable person would find pertinent to the decision to donate their embryo to research."[114] Yet, it is unclear what this entails regarding future research that has not been designed or may not even be known at the time of consent.[115] If general categories are used, rather than specific protocols, the question becomes what categories provided would give the most informed consent possible.[116] On the other hand, if the embryo is created for research, rather than created for infertility treatment, the consent content must be different. The consent must be certain to state that the embryo created will not be used to cause a pregnancy.[117] Again, with the importance of privacy, issues surface of how specific can, and should, consent be with regards to who will have access to the genetic information and how long that linking information will be available.[118] An added complication becomes the duration of a genetic link, and how this applies to the ability of donors to withdraw their consent to research.[119]

Finally, the ethical question of who should obtain the consent deals with the physician-patient relationship and whether the donor should be seen as a research subject or simply a patient. The physician-patient relationship is one of trust where the physician is obligated to advocate for the health and well-being of his or her patient.[120] To avoid tainting this

111. *Id.* at 562. This would include SCNT. *Id.* at 560.

112. *Id.* at 560.

113. *Id.* The FDA may require linkage to donors in the future when implanting stem cell lines in people to document that appropriate testing was carried out for infectious and genetic diseases. *Id.*

114. *Id.*

115. *See id.* at 560–61 (noting that donors can consent to general categories of future research).

116. *See id.* at 561 (stating that more empirical research is needed to determine what categories best capture the relevant distinctions among different types of research for donors).

117. *Id.*

118. *See* Jeremy Sugarman, *Human Stem Cell Ethics: Beyond the Embryo*, 2 CELL STEM CELL 529, 530–31 (2008) (finding that there is a legitimate concern regarding privacy of information for those who provide cells when identifiers are often kept in hopes of using the cells or their derivatives in clinical settings).

119. *See* Timothy Caulfield et al., *Informed Consent in Embryonic Stem Cell Research: Are we Following Basic Principles?*, 176 CAN. MED. ASS'N J. 1722, 1723–24 (2007) (discussing the fundamental right to withdraw consent and how it applies to embryonic stem cell research).

120. *See* Lois Snyder & Paul S. Mueller, *Research in the Physician's Office: Navigating the Ethical Minefield*, 38 HASTINGS CENTER REP. 23, 25 (2008) (stating the importance of clinicians putting their patients first).

relationship, or unjustly using it to coerce a trusting patient into donating her embryo for research, some urge that whenever possible, someone other than the treating infertility physician should obtain consent to research donation.[121] This can avoid conflicts of interest and ensure that the reproductive needs are the primary focus of the care.[122] Additionally, the treating physician can ensure that the consent process is actually informed and voluntary.[123]

If it is possible to have the treating physician and the researcher be different individuals, there are compelling reasons to have both parties be the one that obtains the consent. The physician is typically trusted and so depended upon that the patient could simply agree to anything the physician presents.[124] To completely remove the pressure a patient may feel, perhaps the physician should not even be aware of what the patient decides.[125] Alternatively, the physician may be more qualified to deal with the stresses associated with infertility treatment while discussing the option for research donation.[126] Being that patients would typically feel more comfortable with her physician than an unknown researcher, the patient may actually prefer to have the discussion with the physician.[127]

3. Procedural Concerns

Procedural implementations, such as the review process, are utilized to ensure that the ethical concerns raised above are addressed.[128] At the review process the ethical considerations of stem cell derivation have most likely already been decided. If the stem cells were derived in a manner that is legal, the review moves on to the informed consent.[129] It is here that the committee ensures that the consent to research donation was informed and voluntary.[130] This is where issues of conflicts of interest, risks and

121. Lo, *supra* note 104, at 562.

122. *Id.*

123. *Id.*

124. *Id.*

125. *Id.*

126. *See id.* ("Obstetrician-gynecologists, particularly infertility specialists, are accustomed to providing nondirective counseling and respecting a woman's preferences and values.").

127. *See id.* (finding that "a patient's personal physician is considered an impartial source of information and advice").

128. *See* Snyder & Mueller, *supra* note 120, at 24 (stating that a review board such as an IRB should assess all ethical concerns).

129. *See, e.g.,* NIH GUIDELINES, *supra* note 34, § II(A) (stating that once it has been determined that the embryos used were created using *in vitro* fertilization for reproductive purposes but were no longer needed the next step is to review the informed consent process).

130. *Id.* at § II(A)(2).

benefits, confidentiality, and financial coercion are placed under the microscope.[131]

The review process can be done by an Internal Review Board (IRB),[132] a Stem Cell Research Oversight (SCRO) committee,[133] or an Embryonic Stem Cell Research Oversight (ESCRO) committee.[134] The IRB's job is to review a researcher's proposed study to ensure it complies with procedural and ethical requirements, as well as maintaining observation of the research during the study to be certain these requirements are being followed throughout the study.[135] Due to the sensitive and controversial nature of embryonic stem cell research, SCRO and ESCRO committees were recommended and formed to provide an added layer of ethical and scientific review beyond the standard IRB approval.[136]

II. STEM CELL RESEARCH GUIDELINES

In this section, the stem cell guidelines of the National Institute of Health (NIH) will be examined and compared with those provided by both the National Academies (NAS) and the International Society for Stem Cell Research (ISSCR). The NIH guidelines were put forth to indicate what must be followed for research to be eligible for NIH funds.[137] They are not binding on those conducting stem cell research without NIH funds.

The National Academies is a group of organizations that began with the National Academy of Sciences that, under the charter granted to it by Congress in 1863, has a mandate requiring it to advise the federal government on scientific and technical matters.[138] As such, the NAS guidelines are merely advisory rather than binding. The NAS Guidelines were originally put forth in 2005 by the Committee on Guidelines for Human Embryonic Stem Cell Research, but it soon became apparent that clarification was needed as well as frequent updating due to the rapid pace of developments in stem cell research.[139] As a result, the Human

131. *See* Snyder & Mueller, *supra* note 120, at 24 (finding that these types of concerns should be addressed by oversight bodies such as an IRB).

132. 45 C.F.R. § 46.109 (2009).

133. ISSCR GUIDELINES, *supra* note 38, § 8.1.

134. NAS GUIDELINES, *supra* note 38, § 1.3(a).

135. Karen J. Maschke, *Human Research Protections: Time for Regulatory Reform?*, 38 HASTINGS CENTER REP. 19, 20 (2008).

136. Insoo Hyun, *Magic Eggs and the Frontier of Stem Cell Science*, 36 HASTINGS CENTER REP. 16, 17 (2006).

137. NIH GUIDELINES, *supra* note 34, § I.

138. NAS GUIDELINES, *supra* note 38. Other organizations falling under The National Academies include the National Academy of Engineering, The Institute of Medicine, and the National Research Council.

139. *Id.*

Embryonic Stem Cell Research Advisory Committee was created in 2006 and amended the guidelines in 2007 and 2008.[140]

The ISSCR is an independent, nonprofit organization created in 2002 to foster the exchange of information on stem cell research.[141] The ISSCR Task Force formulated its guidelines to articulate the responsibility of scientists to ensure human stem cell research is performed according to rigorous standards of research ethics and to encourage uniform research practices to be followed globally.[142] Again, these guidelines, issued in 2006, are advisory rather than binding.

A. Procurement of Materials

When examining a particular set of guidelines, the first determination should be to ascertain the scope of the guidelines by determining the derivation methods that are covered. The NIH guidelines apply to hESCs and certain uses of iPSCs,[143] defining hESCs as cells that are "derived from the inner cell mass of blastocyst stage human embryos, are capable of dividing without differentiating for a prolonged period in culture, and are known to develop into cells and tissues of the three primary germ layers."[144] The NIH guidelines conclude by making it clear that they are meant to approve research using hESCs derived from nothing more controversial than an IVF embryo created for fertility treatment that is no longer needed.[145] These guidelines reiterate that NIH funding cannot be used for the derivation of stem cells from human embryos due to the Dickey-Wicker Amendment.[146] Also ineligible for federal funding are hESCs derived from sources such as somatic cell nuclear transfer (SCNT), parthenogenesis, and IVF embryos created for research purposes.[147] Research involving chimeras is also labeled as ineligible.[148]

In contrast, the NAS and ISSCR guidelines cover a much wider variety of sources for stem cell research. The NAS guidelines cover all derivation of hESC lines, including those derived from blastocysts made for reproduction and made for research and those derived from somatic cell

140. *Id.*

141. *About the ISSCR*, INTERNATIONAL SOCIETY FOR STEM CELL RESEARCH, http://www.isscr.org/about/index.htm (last visited April 23, 2010).

142. ISSCR GUIDELINES, *supra* note 38, § 2.2–2.3.

143. NIH GUIDELINES, *supra* note 34, § I.

144. *Id.* § II.

145. *See id.* § II(A)(1) ("Research using hESCs derived from other sources, including somatic cell nuclear transfer, parthenogenesis, and/or IVF embryos created for research purposes, is not eligible for NIH funding.").

146. *Id.* § V.

147. *Id.*

148. *Id.* § IV.

nuclear transfer, parthenogenesis, or androgenesis.[149] Similarly, the broad scope of the ISSCR guidelines cover cells from gametes, embryos, or somatic cells, as well as those from oocytes and embryos generated for research purposes, parthenogenesis, androgenesis, nuclear transfer, or other means of somatic cell reprogramming.[150]

B. Informed Consent

Nearly all research regulation is predicated on the necessity of participants giving their informed and voluntary consent. While all of the guidelines give specific details about what needs to be included, and there is some overlap, the content of those specifications differs. To be eligible for NIH funding, assurance and documentation must be provided to show that: all of the options available at that particular infertility facility, including donation, were explained; that no payments were offered; the decision whether to donate would not affect the quality of care; and there was clear separation between the creation and donation of the embryo.[151] To ensure the last requirement of separation is satisfied, the NIH states that the physician responsible for the reproductive clinical care and the researcher deriving the hESCs should not be the same person, unless separation was not practicable.[152] Furthermore, consent for the donation for research should have been given at the time of the donation and donors should be informed that they retain the right to withdraw their consent to donation up until the point where the embryo is actually used or when identifying information linking the embryo is no longer retained.[153]

The content requirements of the donors' informed consent is also specified in the NIH guidelines.[154] The donor must be informed of the following: that the embryos would be used to derive hESCs for research; what would happen to the embryos in deriving the cells; that the hESCs might be kept for many years; that donation was made without restriction or direction; that the research was not intended to provide direct medical benefit to the donor; that results of the research may have commercial potential, but the donor would not receive benefits from that commercial potential; and whether information identifying the donor(s) would be available to researchers.[155]

149. NAS GUIDELINES, *supra* note 38, § 1.1(a).
150. ISSCR GUIDELINES, *supra* note 38, § 11.1.
151. NIH GUIDELINES, *supra* note 34, § II(A)(3).
152. *Id.* § II(A)(3)(d)(i).
153. *Id.* § II(A)(3)(d)(ii)–(iii).
154. *Id.* § II(A)(3)(e).
155. *Id.*

As one would assume from the differentiating scopes, the NAS and NIH guidelines differ in many ways. While there is some overlap with certain criteria,[156] the NAS requirements are much more extensive and the informed consent must be approved by an IRB or foreign equivalent.[157] In some senses the NAS guidelines may be seen as more permissive. For example, there is no requirement to inform the donor of alternatives to donation and it is not explicitly stated that consent must be written.[158] On the other hand, the NAS guidelines require an explanation that the embryo will be destroyed,[159] that cells might be genetically manipulated,[160] that researchers will follow best practices,[161] and there must be a statement of risks.[162] NAS also suggests that in addition to notifying the donors if their identities will be ascertainable, the donor must be given the option of being re-contacted to receive research results, where lines are traceable.[163] Additionally, the NAS guidelines state that the donor should be given the option of consenting to some research and not others to ensure that their wishes are honored.[164] Under the NAS guidelines, informed consent is applicable to all gamete donors, not only those donating the embryo.[165]

The ISSCR specifications for the requirements of informed consent are understandably extensive, given the amount of research the guidelines cover. With a scope more similar to that found in the NAS guidelines, the ISSCR informed consent requirements are largely comparable as well.[166] For example, the ISSCR require explanation that the embryo will be

156. *See* NAS Guidelines, *supra* note 38, § 3.6 (showing that criteria overlapping with the NIH guidelines include the following information: that the decision to donate or not will not affect future medical care; that the embryos will be used to create research hESCs; that the cells or cell lines may be kept for many years; that the donation is made without restriction; that there will be no direct medical benefit to the donor, except under autologous donation which is only available under the NAS guidelines; and that while commercial benefits may come from the research the donor will not be eligible to receive any).

157. *Id.* § 1.3(a).

158. *See id.* § 3.6 (lacking a requirement for informed consent to be written or requiring the donor be told of alternatives to donation).

159. *Id.* § 3.6(j).

160. *Id.* § 3.6(a), (g). Genetic manipulation includes research on human transplantation and mixing of human and non-human cells in animal models.

161. *Id.* § 3.6(e).

162. *Id.* § 3.6(l).

163. *Id.* § 3.6(c)–(d).

164. *Id.* § 3.6.

165. *Id.*

166. ISSCR GUIDELINES, *supra* note 38, § 11.3(a) (including similarities that are found in the NIH and NAS guidelines, such as: that the decision to donate or not will not affect future medical care; that the embryos will be used to create research hESCs; that the cells or cell lines may be kept for many years; that the donation is made without restriction; whether identifying information will be ascertainable; and that there will be no direct medical benefit to the donor).

destroyed,[167] that the cells derived may be used for research involving genetic manipulation,[168] and that the donor may limit their donation to specific research purposes.[169] Moreover, the ISSCR also requires consent be obtained from all gamete donors.[170]

However, there are other areas where the ISSCR finds itself analogous to the NIH guidelines, rather than those of the NAS. One of the similarities between the ISSCR and NIH guidelines is that they both require that consent for donation be obtained at the time the materials are donated to the research team.[171] Yet, the ISSCR allows for a rigorous review by the Stem Cell Research Oversight (SCRO) committee, which is an oversight body equipped to evaluate the unique aspects of the science,[172] to permit the use of materials for which prior consent exists but for which re-consent is prohibitively difficult.[173] Another similarity between the ISSCR and NIH guidelines is their desire to keep the researchers from influencing the donor's decision of consent. The ISSCR states that wherever possible, the treating physician should not also be the researcher when related to the donation of gametes or the creation of embryos for fertility treatment.[174] The ISSCR also leaves open the possibility that consent may be withdrawn at a later date, since donors should be informed that they retain the right to withdraw consent until the materials are actually used in research.[175] The NAS guidelines on the other hand, make no mention of the importance of separating the fertility treatment doctor and researcher, whether consent must be obtained during donation, or if consent can be withdrawn at a later date.[176]

There are certain ISSCR consent requirements that address issues found in the NIH and NAS guidelines, but slight differences distinguish them. For example, the ISSCR guidelines also require the statement that

167. *Id.* § 11.3(a)(ii).

168. *Id.* § 11.3(a)(iv) (including the generation of human-animal chimeras).

169. *Id.* § 11.3(a)(vi) ("[T]he consent shall notify donors, if applicable under governing law, of the possibility that permission for broader uses may later be granted and consent waived under appropriate circumstances by an ethical or institutional review board.").

170. *Id.* § 11.2.

171. *Compare* ISSCR GUIDELINES, *supra* note 38, § 11.2 (requiring consent for donation of materials to research be obtained at the time the materials are transferred), *with* NIH GUIDELINES, *supra* note 34, § II(A)(3)(d)(ii) (stating that consent for donation must be given at the time of donation).

172. ISSCR GUIDELINES, *supra* note 38, § 8.1.

173. *Id.* § 11.2.

174. *Id.* § 11.4.

175. *Id.* § 11.2.

176. *See* NAS GUIDELINES, *supra* note 38, § 3.6 (giving no guidance on who should present the informed consent, when it should be presented, and if it may be withdrawn). Other differences between the NAS guidelines and the ISSCR and NIH guidelines are the inclusion of the statement of risks and a statement that the researchers will use best practices. *Id.*

the derived cell may be kept for many years, but the consent form must state that they will be used for future studies which may not be predictable at this time.[177] The disclosure of potential commercial benefit is required, but the ISSCR guidelines require a statement as to whether the donor will or will not receive any financial benefits.[178] This leaves the door open for donors to receive partial commercial benefits gained from research on their donation, something clearly prohibited by the NIH and NAS. Additionally, the ISSCR guidelines require the consent document to divulge any present or potential future financial benefits to the investigator and the institution.[179]

The ISSCR guidelines also contain requirements not found in either the NIH or NAS guidelines. All possible alternatives to donating found at the infertility facility and elsewhere, must be explained in full.[180] For the donation of embryos, it is required that it be stated that the embryos will not be used to produce a pregnancy.[181] And for experiments in embryonic stem cell derivation, somatic cell nuclear transfer, somatic cell reprogramming, parthenogenesis, or androgenesis, it must be said that the resulting cells would carry some or the donor's entire DNA.[182]

C. The Process of Review

To be eligible for funding under the NIH guidelines, one must first determine if the hESCs were donated in the United States or abroad, and whether they were donated on or after the effective date of the guidelines or before the guidelines were issued. For hESCs donated in the United States on or after the NIH guidelines' effective date, the hESCs should have been derived from human embryos that: were created using IVF for reproductive purposes and no longer needed; were donated by individuals who sought reproductive treatment and gave voluntary consent for the embryos to be used for research; and for which the consent and documentation can be assured.[183] These three requirements are often referred to as satisfying section "IIA," which is utilized as a reference point throughout the NIH guidelines.[184]

For example, hESCs donated in the United States or abroad before the effective date must have been derived from human embryos that comply

177. ISSCR GUIDELINES, *supra* note 38, § 11.3(a)(iii).
178. *Id.* § 11.3(a)(viii).
179. *Id.* § 11.3(a)(ix).
180. *Id.* § 11.3(a)(xii).
181. *Id.* § 11.3(a)(xiii).
182. *Id.* § 11.3(a)(xiv).
183. NIH GUIDELINES, *supra* note 34, § II(A).
184. *See, e.g., id.* (referring to Section II(A) of the guidelines).

with the requirements stated in IIA, or they must be approved by a Working Group of the Advisory Committee to the Director (ACD).[185] The Working Group is comprised of bioethicists, lay persons, and scientists that will make recommendations regarding eligibility to the ACD, who will make recommendations to the NIH Director, who will ultimately make the final decision.[186] For hESCs donated outside of the United States on or after the effective date, they must have been derived according to IIA as well, or there must be assurance that alternative procedures of the foreign country were at least as strict as those in IIA.[187]

While the previously mentioned Working Group will be reviewing numerous applications for federal funding, the more traditional review and approval from an IRB is not made a requirement, as it is with most clinical research. The Guidelines state that IRB review may be required under The Common Rule,[188] if the investigators are engaged in research involving human adult stem cells or the stem cells can be linked to living individuals.[189] This seems peculiar in that local IRBs are typically used in situations like this to weed out the research that is clearly ineligible and lighten the load for the Working Group. This type of review can be found in both the NAS and ISSCR guidelines.[190]

To determine eligibility, the NAS guidelines rely heavily on review committees. Purely *in vitro* hESCs research using previously derived hESC lines must be granted approval by an Embryonic Stem Cell Research Oversight (ESCRO) committee.[191] An IRB must review the application for new procurements of gametes, blastocysts, or somatic cells for the purpose of generating new hESC or hPSC lines.[192] Unlike the NIH guidelines, the NAS allows for hESC and non-hESC research involving nonhuman animals, permitted it receives review and approval from an ESCRO committee and an Institutional Animal Care and Use Committee

185. *Id.* § II(B).

186. *Id.* § II(B)(2).

187. *Id.* § II(C).

188. 45 C.F.R. § 46 (2009).

189. NIH GUIDELINES, *supra* note 34, § I.

190. *See* NAS GUIDELINES, *supra* note 38, § 1.3(a) (stating that an ESCRO committee must approve research with *in vitro* hESCs, which requires an IRB approved informed consent); ISSCR GUIDELINES, *supra* note 38, § 8.2 (discussing that SCRO committee is not meant to replace institutional reviews).

191. NAS GUIDELINES, *supra* note 38, § 1.3(a). The ESCRO committee must receive documentation of the provenance of the cell lines, including documentation of the use of an acceptable informed consent process that was approved by an IRB or foreign equivalent for their derivation and documentation of compliance with any additional required review by an IACUC, Institutional Biosafety Committee (IBC), or other institutionally mandated review. *Id.*

192. *Id.* § 3.1.

(IACUC).[193] According to the NIH guidelines, research using hESCs or iPSCs from eligible sources that are introduced into nonhuman blastocysts is prohibited from receiving federal funding.[194]

The NAS guidelines also go further in what is allowable research by stating that oocytes generated for research through hormonal induction are eligible as long as the donor is reimbursed only for direct expenses acquired as a result of the procedure.[195] This is clearly a distinguishing feature from the NIH guidelines which permit no payments of any kind for the donated embryos.[196]

The ISSCR discusses the importance of creating a Stem Cell Research Oversight (SCRO) committee, along the same lines as that discussed in the NAS guidelines.[197] To be eligible, all experiments using hESC research, human embryos, or embryonic cells must have gone through review, received approval, and be subject to ongoing monitoring by the SCRO committee.[198] In addition, the ISSCR says the same process must be done for experiments that entail incorporating human totipotent or pluripotent cells into animal chimeras.[199] The review must include: appropriate scientific justification for performing the research using the specified material that is required; appropriate expertise and/or training of the investigators to perform the stated experiments; and a discussion of alternative methods and rationale for employing the requested human materials, the proposed methodology, and for performing the experiments in a human rather than animal model system.[200]

When it comes to IRB review, the ISSCR guidelines make it clear that it is necessary due to the fact that derivation of new lines involve the procurement of materials from human subjects.[201] The SCRO review that is recommended by the ISSCR is not to be construed as replacing the

193. *Id.* § 7.3(c)(ii).

194. NIH GUIDELINES, *supra* note 34, § IV(A).

195. NAS GUIDELINES, *supra* note 38, § 3.4(b). Permissible reimbursements include costs associated with "travel, housing, child care, medical care, health insurance, and actual lost wages. No payments beyond reimbursements should be made for donations of sperm for research purposes or of somatic cells for use in NT." *Id.*

196. NIH GUIDELINES, *supra* note 34, § II(A)(3)(b).

197. ISSCR GUIDELINES, *supra* note 38, § 8.1.

198. *Id.*

199. *Id.*

200. *Id.* § 8.3(i)–(iii).

201. *Id.* § 12.1(a). The review must include: scientific rationale for the need to derive new cell lines, justifying the number of embryos needed; researchers must prove appropriate expertise or training; there must be a detailed plan for characterization, storage, banking, and distribution of new lines; embryos made using nuclear transfer, parthenogensis, androgenesis, or other *in vitro* means cannot be transferred to a human or nonhuman uterus or cultured *in vitro* intact as embryos for longer than fourteen days or until formation of the primitive streak; and there must be a plan to safeguard the privacy of the donor information. *Id.* § 12.1(b)-(f).

requirement of IRB approval.[202] In fact, the guidelines clarify that there may be some research that falls into a category where the experiments are permissible after existing and mandated local review, without the SCRO process coming into play.[203] Yet, most forms of research are included in the category of those that are only permissible once there has been SCRO review in addition to IRB review.[204]

III. MARYLAND GUIDELINES

In 2006, Maryland authorized and created state funding for stem cell research by passing the Maryland Stem Cell Research Act.[205] While the Act does not specifically mention human embryonic stem cells, preferring the more politically acceptable term "unused material,"[206] it also states that creation of stem cell lines is not prohibited and it is, therefore, understood to approve of the use of hESCs.[207] This Act created the Stem Cell Research Commission to evaluate and monitor State-wide stem cell research, and put the Commission in charge of adopting regulations and developing and applying criteria to evaluate grant applications.[208] However, the Commission was not intended to be the only body assessing applications, since one of the requirements for eligibility is that an IRB give the protocol its stamp of approval.[209] In addition to the Commission, the Act also created the Maryland Stem Cell Research Fund, whose purpose is to promote State-funded stem cell research through the administering of grants and loans to those applications that the Commission approves.[210]

For researchers to be eligible for State funds, they must meet the eligibility requirements that the Act lays out.[211] However, the requirements

202. *Id.* § 8.2. "Unless the review is specifically designated to be comprehensive, the SCRO process shall not replace other mandated reviews such as institutional reviews that assess the participation of human subjects in research, or the oversight for animal care, biosafety, or the like." *Id.*

203. *Id.* § 10.1.

204. *Id.* § 10.2. These types of research include derivation of new human pluripotent cell lines by any means; where the identity of the donors are readily discoverable or may become known to the investigator; where human totipotent cells or pluripotent stem cells are mixed with pre-implantation human embryos; where cells of totipotent or pluripotent human origin are transplanted into living humans; and research creating chimeric animals using human cells. *Id.* § 10.2(a)–(e).

205. S. 144, 2006 Leg., 424th Sess. (Md. 2006) (codified at MD CODE ANN., ECON. DEV. § 10-429 (2006)).

206. MD CODE ANN., ECON. DEV. § 10-438 (LexisNexis 2006).

207. *Id.* § 10-430.

208. *Id.* § 10-431 (establishing the Maryland Stem Cell Research Commission); *id.* § 10-432 (establishing Maryland Stem Cell Research Commission's duties).

209. *Id.* § 10-435(a)(1).

210. *Id.* § 10-434.

211. *Id.* § 10-438.

are not nearly as detailed as those established in the federal guidelines. For example, the Act requires that individuals considering donation must be provided with sufficient information to allow for an informed and voluntary decision.[212] The Act goes no further in explaining what is necessary to ensure there is informed consent. Yet, the Act does require that the informed consent be written.[213] One area where the Act does show specificity is in the options that must be conveyed to the individual considering donation. The donor must be presented with the options of storing or discarding any unused material, donating any unused material for clinical purposes in the treatment of infertility, donating any unused material for research purposes, and donating any unused material for adoption purposes.[214] The Act also restricts some research by prohibiting unused material that is donated from being an oocyte.[215]

IV. STATE RESPONSE TO FEDERAL CHANGES

A. Model State Guidelines

The question presented by President Obama's Executive Order broadening the scope of federal funding for hESC research is how states should respond. President Obama's order certainly is a relief to researchers who found the Bush limitations of any indirect contact between federal funds and unapproved cell line research cumbersome.[216] However, the advancement of the field of research as a result of the order may be limited. Even President Clinton encouraged researchers to fund the creation of stem cell lines from other sources and then apply for federal funds to continue the research.[217] With a large number of unused embryos currently being stored at fertility clinics likely to be destroyed,[218] the concern of federal funds weighs very little in formulating the model state guidelines described in this section. Instead, the guidelines were determined based on the most advanced levels of stem cell research being conducted throughout the country and the world.

212. *Id.* § 10-438(a)(1).

213. *Id.* § 10-438(c).

214. *Id.* § 10-438(a)(2).

215. *Id.* § 10-438(b).

216. *See* Danielle Ulman, *Maryland Stem Cell Researcher Pleased that Bush Restrictions are Gone*, THE DAILY RECORD, Sept. 21, 2009 (quoting Curt Civin, a doctor nationally renowned for his research on stem cells as saying the Bush restrictions were "a silly restriction" and "an unnatural fence").

217. Fossett, *supra* note 7, at 527.

218. *Id.* at 528.

1. Scope of Material Covered

As seen when comparing the federal guidelines with those of the NAS and ISSCR, the material covered is extremely important in determining what type of research can be done.[219] With the possible ways to create stem cells constantly evolving, it is important not to limit what is eligible. Furthermore, any state wishing to remain in competition for research would be wise not to restrict material qualified for funding beyond what other states have made eligible.[220]

That said, the material eligible should be as ethically expansive as possible. This does not mean allowing any type of stem cell research to be done in the state. Rather, it suggests the need for a sound review process,[221] to determine whether certain research proposals are ethically sound. After reviewing the potential material eligible for funding under the different guidelines, it seems unreasonable to merely allow research on embryos created by IVF for fertility treatment but are no longer needed. Significant scientific progress can be made with embryos created for research as well as SCNT.[222] And while some may consider these methods ethically questionable, guidelines used internationally find them morally acceptable and scientifically sound.[223]

In evaluating its proposals for developing stem cell lines, a state should utilize the more expansive scopes as examples and allow for a review process to limit research deemed questionable. The new federal guidelines return the state of eligible materials to its place under Clinton; yet, even the Clinton guidelines indicated that their recommendations may need to be altered in the future.[224] With regard to embryos created for research, the guidelines stated using this approach was unnecessary at the time because cadaveric fetal tissue and embryos remaining after fertility treatment provided an adequate supply of research resources.[225] Embryos made using SCNT was discussed in a similar manner. It was seen as

219. *See infra* Part II.A (comparing the procurement of material allowed by NIH, NAS, and ISSCR guidelines).

220. Fossett, *supra* note 7, at 541 ("States see themselves, at least rhetorically, as competing with one another for jobs, tax revenue, economic development, and in the case of hESC research, research talent and prestige.").

221. *See supra* I.B.3 (discussing the ethical issues surrounding the review process).

222. *See supra* I.B.1.ii–iii (discussing uses for research embryos and SCNT).

223. *See* NAS GUIDELINES, *supra* note 38, § 1.1(a) (covering procurement of hESCs from blastocysts made specifically for research and using SCNT); ISSCR GUIDELINES, *supra* note 38, § 11.1 (allowing for SCNT to be utilized as well).

224. *See* ETHICAL ISSUES, *supra* note 37, at 5–6 (describing the need to monitor scientific progress and utility of techniques such as SCNT to possibly allow funding of this type of research in the future).

225. *Id.* at 5.

unnecessary to support this type of procedure at the time, but a note was made to the significant therapeutic potential and that scientific progress in this research should be monitored.[226] To avoid being irrelevant in terms of the most up to date research being conducted, a state should aim to keep with the evolution of the science. This means the procurement of gametes, blastocysts, and somatic cells for generating new cell lines should be eligible, including embryos created not only for fertility, but for research purposes as well. Additionally, the SCNT process, as well as parthenogenesis and androgenesis should be eligible for funding. The guidelines should also cover any adult stem cells, of which there are currently little restrictions, as well as pluripotent stem cells derived in any form.

This type of expansive scope allows and encourages collaboration with other states, as well as with potential international partners. With the goal of stem cell research being the exploration of all the potential benefits the science has to offer, this prospective reward should not be overlooked.

2. Informed Consent

Informed consent is an extremely important part of the research process, ensuring documentation that the donor was completely aware of what they were agreeing to. The informed consent should be written, archived, and easily retrievable to provide long-term access to the legal source of materials used. The informed consent is lengthy and detailed, but it is imperative that the donor understand exactly what they are participating in, or at least their understanding should be assured as much as possible.[227]

The informed consent, at a minimum, should contain: all alternatives to donation, not simply those alternatives available at that particular infertility facility; that the decision to donate or not will not affect future care for the patient; that the donation will be used to obtain research hESCs and that the embryos will be destroyed in the process; that the stem cells will be kept for many years and, as a result, may be used in future research that is not yet known; that research may include genetic manipulation, including human transplantation or research with chimeras; that no direct medical benefit will come to the donor except for autologous donation; disclosure of potential commercial benefits for the researcher and that the donor will not receive any commercial benefit; a statement of risks; that the donation is made without restriction; whether identifying information will be available for the researcher; that they retain the right to withdraw consent

226. *Id.* at 5–6.

227. *See, e.g., Moore v. Regents of Univ. of Cal.*, 793 P.2d 479, 483 (Cal. 1990) (holding that the doctor's failure to disclose commercial benefit received from tissue taken from the patient was a breach of fiduciary duty to disclose all pertinent information to provide informed consent).

at any time until identifying material is removed or the material is used in research; and that researchers will follow best practices.

This consent should be obtained from all gamete donors, to avoid potential problems of conflicting interests. For example, consent by a donor in possession of an embryo may not parallel the interests of the gamete donors who created that embryo. A gamete donor may have been willing to consent to the creation of an embryo for fertility treatment, but not for the creation of embryos to be used for hESC research. With potentially identifying information in the embryo related to gamete donors, it is important that they be informed of the donation process. When possible, the fertility treatment doctor and the researcher should not be the same person and the consent should be obtained at the time of donation. If either or both of these are impractical, the review process discussed later will determine if the consent is still acceptable.

3. The Process of Review

The review process on a state level should rely heavily on local review boards such as institutional IRBs to provide much of the proposal assessment. Likewise, the ESCRO or SCRO committees already in place at various research institutions should be utilized in proposal and research evaluations. As stated in the ISSCR guidelines, the specialized stem cell research committees are not meant to replace IRBs or duplicate their efforts, rather they should be employed for this medically complicated and controversial research to add another layer of protection as well as a specialized expertise.[228] This reliance affords a state the ability to be more expansive in their guidelines with certain criteria. For example, the infertility doctor and the stem cell researcher would ideally be separate. However, instead of creating an absolute requirement that they be separate, the state can rely on an extensive review process to allow for situations where separation is impossible to still receive funding approval and create more research possibilities. The multilayered review can properly certify that there was no reason to exclude the research based on conflict of interest or coercion.

The review processes should examine all relevant steps in the research procedure, from obtaining research materials to proposed usage of those materials, in determining whether to fund the project. Furthermore, there should be scientific justification for the proposal as well as corresponding medical expertise and training appropriate to see it to fruition. Finally, the review should assess any and all financial inducements for the donor. This review should ensure that the donor does not receive any undue financial

228. ISSCR GUIDELINES, *supra* note 38, § 8.2.

gains from their decision to donate other than reimbursements justified by the donation. These types of reimbursements may include medical expenses associated with the donation process, lost wages, travel costs, and child care.

B. Why Maryland Should Adopt the Model Guidelines

For Maryland to continue to have a strong presence in the field of stem cell research it is vital that it begins to adjust its guidelines to fit with the model state guidelines suggested above, rather than those recently issued by the NIH. The field of stem cell research is one that operates on a state level, a national level, and a global level. For Maryland to adopt the guidelines set forth by the federal government, they may alienate themselves from the state and global research markets. As shown earlier, the current federal guidelines conflict in several areas with internationally accepted regulations provided by the NAS and ISSCR, which are guidelines that also mirror numerous states within the country.[229] Further examination of the order by President Obama suggests that progress by the federal government is unlikely to be made any time soon.[230] While the important factor in working within the federal guidelines is being eligible for federal funding, this may not be as critical as it would appear.

Evidence of previous funding for embryonic stem cell research, as opposed to stem cell research in general, illustrates that the United States government is not even close to providing the type of financial backing that would warrant a strict adherence to its guidelines.[231] The federal government trails state and private donors in support of hESC research,[232] and the odds of a major shift in funding occurring soon are unlikely.[233] NIH funding for stem cell research has increased steadily over the last six fiscal years to $938 million, yet, funds dedicated to hESC research specifically has increased to approximately nine percent of this, or slightly less than $90 million.[234] While less controversial stem cell research gets

229. *See* Fossett, *supra* note 7, at 532 (discussing how most states have relied heavily on guidelines of the NAS and ISSCR).

230. *See id.* at 537 (stating that the order was narrowly drawn, did not call for an expansion of funding for embryonic stem cell research, and as a result there will most likely be only incremental change).

231. *Id.* at 528. Spending by NIH for all forms of stem cell research is relatively small and hESC support is comparable to that of diagnostic radiology and eye diseases. *Id.*

232. *Id.* at 536. Since state governments and private foundations are outspending the federal government in supporting hESC research they have become major policymakers for stem cell research. *Id.*

233. *Id.* at 524 (noting issues that may preoccupy the government's attention include the national economy, health care, wars in Iraq and Afghanistan, and recent problems in the Middle East).

234. *Id.* at 528.

the bulk of federal funding,[235] advocates of stem cell research have been rewarded with their efforts to increase funding in certain states.[236]

The largest state supporter of hESC research has been California, through the California Institute for Regenerative Medicine (CIRM), which has already allocated over $600 million.[237] This surpasses the NIH's financial commitment, but so does the 2008 appropriation of $100 million by the state of New York.[238] While not all states are financing their hESC research in the same manner, it is clear from these figures, that research on the state level is comparable to, and in some cases exceeds, that on the national level.[239]

If Maryland hopes to truly harness the potential of the first-ever bicoastal agreement they made with California, they should strongly consider altering their state guidelines.[240] By joining forces with California, the largest supporter of hESC research in the world, Maryland is giving itself the opportunity to merge into the international alliances that have been formed between California and Japan, the United Kingdom, Australia, Germany, Canada, and Spain.[241] Yet, adhering to federal guidelines, rather than adopting the model state guidelines described earlier, which are similar to those in California, could hinder the promise this opportunity offers.

The importance of state stem cell guidelines can also be seen in its effect on encouraging researchers to carry out their work in particular states and the effects this can have on the local economy.[242] As a result of its active support of stem cell research, Maryland is strongly attractive to top

235. *Id.*

236. *Id.* at 529.

237. *Id.* at 530.

238. *Id.* at 531.

239. *Id.* Differing financial backing comes from annual appropriations, earmarked bonds, tobacco settlement revenues, and solicitation of donations. *Id.* "Ohio and Minnesota have made one time appropriations for adult stem cell research and capital construction, respectively." *Id.* "New Jersey, Illinois, and Connecticut have allocated research grants of varying sizes," with New Jersey approving funds for the construction of a stem cell laboratory. *Id.* Connecticut also has earmarked $100 million in state funds over the next decade. *Id.* Massachusetts passed a $1 billion life sciences initiative that includes an indeterminate amount for stem cell research, as well as providing a proposal for state support of stem cell research that includes $250 million in private matching funds to be used in conjunction with state funding. *Id.* at 531, 535. California solicited $18 million in donations from private parties to pay CIRM's initial operating expenses. *Id.* at 535.

240. *See Maryland, California Announce First-Ever Bi-Coastal Agreement to Pool Stem Cell Research Grants*, TRANSPLANT NEWS, Oct. 1, 2009 (noting the creation of an agreement that will allow researchers to form teams and submit joint applications for funding).

241. Ulman, *supra* note 39.

242. *See* Latham, *supra* note 62, at 488 (stating that by offering their own funds states hope to gain a competitive advantage in university and industry development).

scientists.[243] However, countries such as the Republic of Singapore have announced stem cell programs of their own, with the aim of recruiting American scientists.[244] Even within the United States, where there is still a struggling economy, more and more states are realizing the potential boost stem cell research can have.[245] Michigan, for example, recently ended a 30 year ban on the destruction of human embryos for stem cell research.[246] One of the main reasons Michigan made this change was that human embryonic stem cell scientists prefer working in states that actively support their research.[247] Similar to Michigan, more states may soon be joining the ranks of those who support stem cell research. This could be problematic for Maryland's hopes of keeping their current scientists given that stem cell scientists are sufficiently mobile and "states with permissive research policies and appealing recruiting packages should stand a chance of successfully attracting researchers."[248] With evidence mounting that state stem cell programs are effective tools for state economic development, Maryland cannot overlook its financial status when determining how to approach its stem cell guidelines.[249]

By following ethical standards set forth by expert groups such as the NAS and ISSCR, Maryland can maintain its position as a leader in stem cell research and provide economic stimulus without sacrificing moral principles by adopting guidelines similar to the model ones described earlier. By broadening the scope of its guidelines to cover protocols involving SCNT, parthenogenesis, and androgenesis, instead of covering merely hESCs and adult stem cells, Maryland can reap the benefits of progressive research while the multilayered review process can ensure unethical science is not being permitted. Furthermore, this will allow smoother coordination with California who allows these types of procedures.[250] This would help maximize the potential benefits of the

243. *See* Danielle Ulman, *World Stem Cell Summit Puts Spotlight on Maryland*, THE DAILY RECORD, Sept. 18, 2009 ("The states that have invested in this accelerating field of science will have a big head start on those that have not.").

244. Fossett, *supra* note 7, at 542.

245. *See id.* at 541–42 (noting that competition among states and between states and foreign countries has encouraged creation of new stem cell initiatives).

246. Elisha Baron, *Proposal 2: Michigan Voters End 30-Year Ban on the Destruction of Human Embryos for Stem Cell Research*, 37 J.L. MED. & ETHICS 155, 155 (2009).

247. *Id.* at 157.

248. *Id.*

249. *See* Fossett, *supra* note 7, at 533 ("[S]tate policies that place few limits on stem cell research have been effective in creating awareness among stem cell scientists of differences among states, causing permissive states to be seen as more attractive research environments.").

250. *The CIRM Medical and Ethical Standards Regulations*, CAL. INST. FOR REGENERATIVE MED., § 100080 (last updated Aug. 13, 2007), *available at* http://www.cirm.ca.gov/workgroups/pdf/Reformatted_MES_Regs.pdf.

collaboration between the two states, rather than having Maryland losing researchers to its new partners.[251]

Another significant difference between the model guidelines and Maryland's is the requirements to provide informed consent. Maryland's consent standards are lacking in detail, and should be given greater specificity to guide researchers in their consent construction as well as those expected to review experimental procedures. The added detail in the consent will also create some restrictiveness to add balance to the expansion of allowable materials. For the scope of the model guidelines may be more liberal in what is allowable, but the addition of certain consent criteria, such as the statement of risks and explanation of all alternatives to donation, go beyond that of the NIH guidelines. Furthermore, the use of local review boards such as IRBs, in addition to the review of the Maryland Stem Cell Research Commission, will ensure that funds are provided to research that not only follows along with the guidelines provided but is free of conflicts of interest and coercion.

CONCLUSION

At first glance, adherence to the new federal guidelines would seem like common sense. Yet, analyzing the history of the progress of embryonic stem cell research on a federal level, as well as the financial support, clearly suggests otherwise.[252] In fact, states lead the way in both funding and policymaking and this is likely to be the norm for the foreseeable future.[253] For these reasons, Maryland should be hesitant to strictly adopt those guidelines recently set forth by the NIH. With its recent collaborative agreement with California, the largest funder of stem cell research in the world, Maryland has the opportunity to join them among the leaders in the field of stem cell research.[254] To fully realize the potential of such a groundbreaking agreement, Maryland should alter its stem cell guidelines to fit within the model suggested in this paper, which is largely an integration of internationally accepted guidelines put forth by the NAS and ISSCR, and very similar to those used in California.

Establishing new guidelines for eligible material, informed consent, and the review process would be a step for Maryland in the direction of

251. *See* Fossett, *supra* note 7, at 542 (noting that CIRM claims at least 45 scientists have relocated to CA from other states).

252. *See id.* at 527 (noting the federal policymaking process has not moved hESC research policy in any particular substantive direction).

253. *See id.* at 524 (stating that most serious policymaking around stem cell research will continue at the state level, rather than through the federal government).

254. *See supra* note 39 and accompanying text (discussing the collaboration deal between Maryland and California, which has committed to putting $3 billion toward stem cell research).

maximizing the agreement with California as well as creating a path for potential future agreements with other states and countries. The alterations of stem cell guidelines would still afford Maryland the opportunity to receive plenty of funding on the state level and from the private sector, while remaining atop the ladder in competing for leading scientists in the stem cell field. The economic potential of stem cell research cannot be overlooked when national and state debts are increasing and countries around the world are joining the fight for top flight stem cell talent. On the heels of the 2009 World Stem Cell Summit held in Baltimore, with states debating how to respond to the new federal guidelines, and with the recent agreement with California, the time for Maryland to make a statement to the stem cell world, and the researchers in it, is now.