

Developing a Stem Cell Research Policy

For more than a decade, Pfizer has been using animal and adult stem cells in its laboratories to help screen new compounds and identify safer and more effective medicines.

Research knowledge about potential use of human stem cells for the development of new medicines and therapies began in the 1960's when scientists discovered certain types of cells could develop into a broad range of tissues. By the 1970's researchers were able to identify stem cells in mice. Almost 20 years later, a team at the University of Wisconsin isolated and created the first human embryonic stem cells (hES cells). "The achievement with human cells was significant because of its implications for improved health. The dual capacity of hES cells for self-renewal and for differentiation into repair cells offers great potential"¹ for curing or slowing the progression of disease and for understanding disease mechanisms.

A 2007 book title describes hES cells best – they are the "Cell of Cells." The hES cell can regenerate into any and all of the body's cells. Because of this power, the "Cell of Cells" is a rich target for research projects around the world. Scientists, patient advocates and members of the public are hopeful hES cell research will assist in the discovery of cures for dreaded diseases such as Parkinson's, Alzheimer's and cancer. The former head of the National Institutes of Health, Dr. Harold Varmus, described the power of embryonic stem cells: "This research has the potential to revolutionize the practice of medicine and improve the quality and length of life...There is almost no realm of medicine that might not be touched."²

While stem cells can be derived from a range of sources such as bone marrow and adult tissues, the use of human embryonic stem cells for research is somewhat controversial, because it touches on the fundamental debate over when life begins with regard to the use of cells from human embryos for research. This paper reviews Pfizer's development of a policy on the ethical use of stem cells for medical research at Pfizer.

¹ "Guidelines for Human Embryonic Stem Cell Research," The National Academies Press. 2005. Available at: http://www.nap.edu/catalog.php?record_id=11278#toc

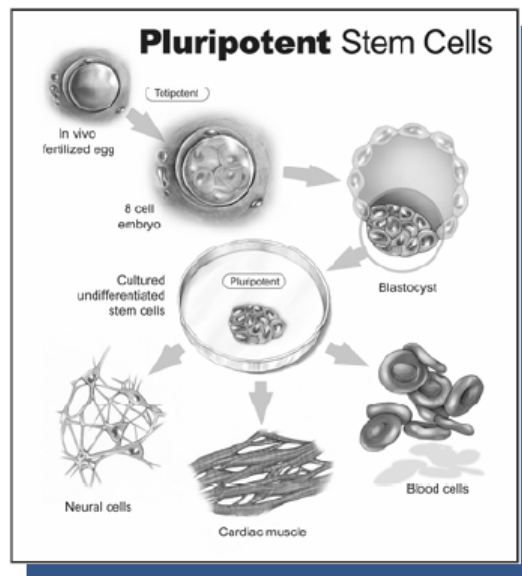
² As quoted in Cynthia Fox, "Cell of Cells: The Global Race to Capture and Control the Stem Cell," (New York: W.W. Norton & Co. Inc., 2007), p. 21.

What are Stem Cells?

Stem cells are “unspecialized” cells derived from several sources including embryos, umbilical marrow, and many embryonic tissues. demonstrate the renew. hES cells are have not yet particular type of through a process differentiation and specialized cells making up blood, cells.³

Under the proper researchers can form the highly that make up our

organs. These traits make stem cells ideal candidates for use in drug development and a potentially valuable source for replacement cells for a variety of diseases, including Alzheimer’s, diabetes, Parkinson’s, and many others.



From the Center for Practical Bioethics³

cord blood, bone other non- All stem cells ability to self-primitive, that is, become a cell. The cells go called then become such as those brain or muscle

conditions, direct stem cells to specialized cells tissues and

What Ethical Issues Arise from Stem Cell Research?

The first hES cells created in Wisconsin were derived from a very early human embryo donated to researchers by a couple who had undergone infertility treatment. Today, virtually all hES cells are derived from human embryos developed for in vitro fertilization and designated for termination. This involves removing the inner cell mass from excess blastocysts (human eggs five days after fertilization) that are unneeded by couples who have completed their fertility treatments. Removing this inner cell mass prevents these blastocysts from further developing. Fertility clinics routinely destroy these blastocysts.

Two significant ethical issues arise for consideration:

1. The moral status of the cells
2. Informed consent for the use of materials generated by fertility treatment

³ “Early Stem Cell Research: The Science, Ethical Issues, and Policy Considerations,” Spring 2005. <http://www.practicalbioethics.org/FileUploads/FINAL%20Stem%20Cell%20Brief%2003-22-05.pdf>

Moral status of the cells

Opponents of stem cell research based on hES believe that because life begins at conception, the use of fertilized eggs, such as those created for in vitro fertilization, should not be used for research and blastocysts should be respected and protected in the same way a fetus would be entitled to such respect and protection.

Proponents of this research do not consider a fertilized egg to be a human life, but merely a collection of cells with the potential to develop until a human life.. Since fertility clinics would otherwise destroy these cells if they are not being used in in-vitro fertilization, using the cells for scientific research is preferable to destroying the cells.

A third view is that the humanity of and ethical deference given to fertilized eggs should be seen on a continuum. As blastocysts progresses toward the status of an embryo, it should be afforded increased ethical deference and protection.

Informed consent

As many of the hES used for stem cell research is from existing blastocysts, current procedures for ensuring researchers have the informed consent of the donor-parents is important. While there are few legal standards for how such consent should or must be obtained, the American Society for Reproductive Medicine has established guidelines for fertility clinics to follow.

**American Society for Reproductive Medicine
Informed Consent Guidelines⁴**

- Information to be conveyed includes:
 - The nature of ES cell derivation
 - The specific research project, if known
 - Possibility of indefinite existence of cell line
 - Source of funding
 - Potential commercial value
 - Anticipated clinical application
- Obtaining consent should:
 - Occur after the couple's infertility needs are met or the couple discontinues therapy
 - By a person other than the fertility specialist

⁴ Ethics Committee, ASRM, "Donating spare embryos for embryonic stem-cell research," *Fertility and Sterility*, Vol. 78, No. 5, November 2002.

<http://www.asrm.org/Media/Ethics/donatingspare.pdf>

The Development of Pfizer's Policy

Pfizer has made significant investments in mouse embryonic stem cells and started working in this area in 1995. Almost a decade later, Pfizer began using human adult stem cells. Some of these stem cell systems are now being employed in our drug discovery efforts, for example:

- Murine ESC-derived neurons are being used to identify compounds may treat schizophrenia.
- Murine ESC-derived and animal/human cardiac stem cells are being used to develop a model system for cardiotoxicity testing.
- Human mesenchymal stem cells are being used to identify new targets of osteogenesis to build understanding of osteoporosis.

Pfizer scientists, like most medical researchers, have reason to believe technologies using stem cells have a great potential to contribute to the development of new medicines and therapies. It is also likely the need to source these stem cells from human embryos will be obviated by new technologies. Pfizer has sought to balance the respect for human life and the imperative to cure disease by establishing a reasonable policy on the ethical use of stem cells in clinical research.

Technology and Policy Worldwide

Pfizer's only major research and development facility outside of the United States is at Sandwich in Kent in the United Kingdom. Thus, Pfizer's policies most closely track the regulatory requirements in the U.S. and U.K.

In December of 1999, a year after the first hES were derived, the U.S. National Institutes of Health released draft guidelines "to help ensure that NIH-funded research in this area [research involving human pluripotent stem cells] is conducted in an ethical and legal manner."⁵ The U.S. Department of Health and Human Services determined the cells were not embryos, but were human fetal tissue, therefore research would be required to follow federal law on fetal tissue research. On August 9, 2001 President George Bush issued an Executive Order limiting federal funding for stem cell work.⁶

After researchers isolate stem cells from a human embryo, the cells often replicate indefinitely, creating a "cell line." The Bush Executive Order made clear that for a cell line already in existence, research would continue to be

⁵ See draft guideline at: <http://stemcells.nih.gov/staticresources/news/newsArchives/fr02de99-43.asp>

⁶ Note: President Barack Obama's administration has confirmed its interest in overturning the ban via executive order, but no such order had been signed as of February 24, 2009.

permissible because destruction of the embryo had already taken place, but the Order refused to allow publicly funded research on any new cell lines, so as to prevent the federal government from acting in a way that would encourage the destruction of human embryos.”⁷

Across Europe, the balance between the sensitivities and opportunities for human embryonic stem cell research plays out differently across the continent. Law and regulations vary in different member states – from *de facto* prohibition to very liberal regulations with strong support from government for the research. The U.K., one of the key countries involved in the development of the technologies underpinning stem cell research, has adopted one of the most enabling regulatory frameworks, specifically designed to encourage expertise and investment in stem cells.

In the U.K., regulation in regards to hES happened in a sort of reverse-order to that in the U.S. Public consultations in the U.K. in the early 1980’s informed the work of the Warnock Committee which helped create a regulatory framework for the treatment of embryos during the process of in vitro fertilization. Many of the Committee’s recommendations became law in the U.K. when the Human Fertilisation and Embryology Act of 1990 was passed.⁸ By the time hES research became technologically possible, the U.K. already had an established and reputable regulatory body and a strong sense of the public’s viewpoint to inform their policies about what research would be permissible.

Policy Status: 2001

U.S. federal policy limited the use of government funding to hES cell lines established and available prior to August 9, 2001, but placed no restrictions on privately funded research.

Though permitted in the U.K. and technically allowed in the U.S., in 2001, Pfizer chose not to conduct any hES research. To date, the firm had been using animal stem cells, but not human stem cells, for two broad-based research purposes: 1) to screen medicines and 2) for direct regenerative medical applications to replace cells due to disease or trauma (for example, research on skin cells for burn victims).

Policy Status: 2007

In 2007 Pfizer established a stem cell research policy to guide external partnerships that might involve the use of human stem cells. By then, the evidence for hES research was compelling and Pfizer decided opportunities to

⁷ American Association for the Advancement of Science, “AAAS Policy Brief: Stem Cell Research.” Updated November 11, 2008. <http://www.aaas.org/spp/cstc/briefs/stemcells/>

⁸ See <http://www.publications.parliament.uk/pa/ld200102/ldselect/ldstem/83/8302.htm#a3>

work with academic, biotechnology and pharmaceutical partners around the world that might utilize human stem cells to develop new medicines, needed to be benchmarked against high ethical standards for this research.”⁹

In its policy, Pfizer committed to adhere to the research guidelines on ethically-derived stem cells established by the National Institutes of Health and the National Academy of Sciences.¹⁰ Pfizer scientists would not create new stem cell lines from human embryos and Pfizer collaborations would not create or use new stem cell lines.

The company knew this policy might need to be revised, given concerns about the NIH guidelines and ongoing critiques of NIH’s guidelines.¹¹ Robert Steiffer, a philosophy professor at the University of Wisconsin, for example, had examined the informed consent documents used to establish which cell lines would be included in the 2001 federal hES policy and found the documents did not meet many of the now well accepted informed consent requirements for donating embryos. In fact, the lack of protections in the documents, his report argues, “provide ethical reasons not to perform several kinds of important research with the NIH lines.”¹²

Policy Status: 2008

In November 2008, Pfizer announced the launch of Pfizer Regenerative Medicine, a new research unit. Scientists at Pfizer Regenerative Medicine were focusing on the use of stem cells to develop future treatments to prevent disability, repair failing organs and treat degenerative diseases. The unit was co-located in Cambridge, U.K. and Cambridge, Massachusetts. The U.K. site focuses on neural and sensory disorders, while the Massachusetts site focuses on endocrine and cardiac research. Pfizer decided that the 2001 policy would need to be expanded, in light of the additional work being planned for the new unit as well as potential engagements with industry and academic partners.

Notably, the U.K. regulations regarding hES research are more permissive than the guidelines set forth in the U.S. Pfizer stem cell research worldwide is therefore governed by policies in line with the U.S. standard. Pfizer does not conduct stem cell research anywhere in the world that would not be permitted in the U.S.

⁹ Pfizer, Inc., “2007 Corporate Responsibility Report,” 2007.

http://media.pfizer.com/files/corporate_citizenship/cr_report_2007.pdf

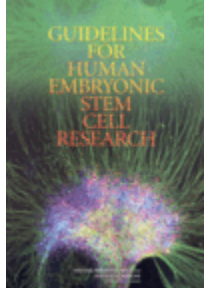
¹⁰ Available at: http://www.nap.edu/catalog.php?record_id=11278#toc

¹¹ Vogel, G and Holden, C, “Ethics Questions Add to Concerns About NIH Lines,” *Science*, 2008. 321:756-757.

¹² Streiffer, R. “Informed Consent and Federal Funding for Stem Cell Research,” *Hastings Center Report*, May-June 2008. <http://www.scienceprogress.org/wp-content/uploads/2008/07/Streiffer-InformedConsent.pdf>

Guidelines for hES Research

The Pfizer Stem Cell Policy guides the company's research activities and meets the highest ethical standards set by leading scientific authorities.¹³



In 2005 the National Academies' National Research Council and Institute of Medicine created a standard set of requirements for deriving, storing, distributing and using embryonic stem cell lines called Guidelines for Human Embryonic Stem Cell Research.¹⁴

Institutional review boards (IRBs) are required by federal law to review the procurement of eggs, sperm, or blastocysts to be used in generating new stem cell lines. The guidelines maintain the IRB requirement, but add a new type of oversight committee to approve the *research* conducted on the cell lines.

Major recommendations include:

- All institutions conducting hES cell research should establish an Embryonic Stem Cell Research Oversight (ESCRO) committee to:
 - Assess which regulations apply to the proposed research
 - Review research proposals and ensure inappropriate research is not conducted and sensitive research is well-reviewed
- ESCRO should review research based on three categories:
 1. Research permissible after notifying ESCRO committee, such as:
 - a. Purely *in vitro* hES cell research with pre-existing coded or anonymous hES cell lines
 2. Research permissible only after additional review, such as:
 - a. Research requiring the creation of new hES lines
 - b. Introduction of hES into nonhuman animals
 3. Research not permitted, such as:
 - a. Research involving *in vitro* culture of embryos longer than 14 days
 - b. Research introducing hES cells to nonhuman primate blastocysts
 - c. Research introducing hES cells into human blastocysts
 - d. Research allowing breeding of animals introduced with hES cells

Other recommendations:

¹³ Available at: http://www.pfizer.com/research/science_policy/stem_cell_research.jsp

¹⁴ Available at: http://books.nap.edu/catalog.php?record_id=11278

- An IRB should review the procurement of gametes, blastocysts, or somatic cells for the purpose of generating new hES cell lines
- Donor consent must be obtained before a blastocyst is used to generate stem cells, and donors should be informed that they have the right to withdraw their consent at any point before a stem cell line is derived
- No payment may be made to donors for research
- Investigators and institutions involved in hES cell research should conduct the research in accordance with all applicable laws and guidelines pertaining to recombinant DNA research and animal care.
- hES cell research leading to potential clinical application must be in compliance with all applicable Food and Drug Administration (FDA) regulations

Discussion Questions

1. What criteria should be used to determine whether stem cells have been “ethically-derived?”
2. What is the relevance of obtaining the informed consent of parent-donors, for the use of embryonic stem cells in research, where the cells would be derived from embryos that the parents had harvested for in-vitro fertilization, but which are no longer needed?
3. If the U.S. NIH policy for use of stem cells for research changes, how should private research firms and institutions respond?
4. Should private research enterprises like Pfizer try to set global policies on ethical issues like stem cell research, in addition to following local laws, or should they instead focus on following local laws and guidelines which may differ in various countries?
5. Should policies for the use of stem cells in research be set by the government, or international organizations, or should it be left to individual researchers, and their institutions?