STEM CELL RESEARCH-LOOKING AHEAD

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EXECUTIVE SUMMARY

Through this detailed examination of stem cell research and the federal regulations that should govern this research, it has became obvious that there are few more difficult policy questions in the field of public policy. This topic borders the most "hot-button" social topics of abortion, medical ethics, religion and religious differences, health policy, and technological development. It has proven extraordinarily difficult to fashion a policy that coherently addresses the need to develop a policy governing this practice.

One of the first aspects of stem cell research to understand is that there is not one single policy that governs this research but rather differing policies that are tailored to the source from where a given stem cell line comes. This study has differentiated nine sources of stem cell lines, all of which much be judged differently and therefore, the policy towards those nine lines must correspondingly be different. This analysis examines each of these nine sources, judges them, and recommends specific and individualized policies that are to govern each of those sources of stem cells.

We have developed an approach that effectively recommends governmental action where appropriate. The United States federal government is an instrument by which American public health can be addressed and improved. We have recommended federal involvement and funding for research on stem cells where potentially beneficial to the American public health, cost effective for the United States federal government and most importantly, morally acceptable. We recommend allowing some stem cell research practices to continue development in the private sector without grants from the federal government. We also recommend federal laws that ban practices that relate to stem cell research where they are morally unjustifiable.

More importantly, we recognized that the contemporary contexts for some of the sources of stem cells simply are not ripe for a coherent policy. Therefore, a governmental policy and action is not possible. It is in these situations that there is more work to be done before developing a complete stem cell research policy.

Stem cells have a great potential benefit to society in their capacity to help the ill. But they are still only one of many different medicines that are being developed to treat the illnesses that affect America. Stem cells are a part, not the entirety, of the medical solutions to illness.

America is not a land where the ends justify the means. Americans will not disregard their moral sensibilities. So when looking at the issue of stem cell research and the governmental policies that should govern this research, we will support policies that both improve the public health and uphold the values of a moral society. Policymakers and leaders that are responsible for how this debate over stem cell research policy develops owe the nation the obligation to stop talking past each other and to confront the issues directly. This analysis factually confronts the issues that are important for this debate along with policy recommendations that follow those issues. It is up to political leaders to have the courage to follow recommendations like the ones that you will read below.

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CHAPTER I - INTRODUCTION

When Dr. John Gearhart announced that his medical research team had created stem cell lines from embryos solely for research purposes, a national uproar ensued. Because harvesting stem cells destroys the embryo, stem cell research has become ensnared in the abortion (or pro-life) debate. Supporters contend that since the cells will be destroyed anyway why not use the lines to research ways to improve the quality of life of the living? Opponents say it destroys a human life or the potential thereof.

WHY THIS TOPIC IS IMPORTANT

When President Bush laid out a policy governing federal funding of stem cell research, this matter was only temporarily decided. A more long-term policy is needed to set the guidelines by which the future of stem cell research is conducted. It is simply not good enough for a government to wait for the private sector to create unregulated technologies. The states of this debate are as high as over any debate occurring in politics today. Many proponents of stem cell research believe that embryonic stem cell research may eventually lead to therapies that could be used to treat diseases that afflict approximately 128 million Americans.[1] However, opponents of the means by which these stem cells are derived contend that living humans are being destroyed in order for the scientists to acquire their research booty. The battle lines are drawn.

DESCRIPTION OF CURRENT STEM CELL TECHNOLOGY

The most significant hope created by stem cell research is the development of cell therapy. Cell therapy is where cultured and grown stem cells are used to repair degenerated or destroyed human tissue.[2] In theory, pluripotent stem cells could be coxed into forming specialized cells to replace tissue destroyed by Alzheimer's disease, Parkinson's disease, spinal cord injury, and other destroyed cells. However, controversy swarms embryonic stem cell research though scientists maintain faith in the potential solutions found in their work.

A History of Stem Cell Research

Media reports on stem cell biology trace the field's origin to two key papers published in 1981. These two papers are G.R. Martin's "Isolation of a Pluripotent Cell Line from Early Mouse Embryos Cultured in Medium Conditioned by Teratocarcinoma Stem Cells," and M. Evans and M.H. Kaufman's "Establishment in Culture of Pluripotential Stem Cells from Mouse Embryos." However, Leroy Stevens at the Jackson Laboratory in Bar Harbor, Maine, laid the groundwork in mice feeder cells from the 1950s through the 1970s. Stevens manipulated bizarre growths called embryoid bodies to see what these cells would become. Embryoid bodies formed when cancer cells were transplanted into mouse abdomens. At first they appeared to be a ring of cells enclosing blood, debris, and a few unspecialized cells. Over time, differentiated cells would appear, sometimes even forming a beating mass of contractile tissue, as well as other hints of body components.[3]

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[1] US Senate Fact Sheet. Senate Subcommittee Hearing on Health and Human Services. August 9, 2001.
[2] Canadian Institutes of Health Research, "Human Stem Cell Research: Opportunities for Health and Ethical Perspectives", 2001.
[3] R. Lewis, "New Workhorses of Stem Cell Technology", The Scientist, 15[2]:17, Jan. 22, 2001.

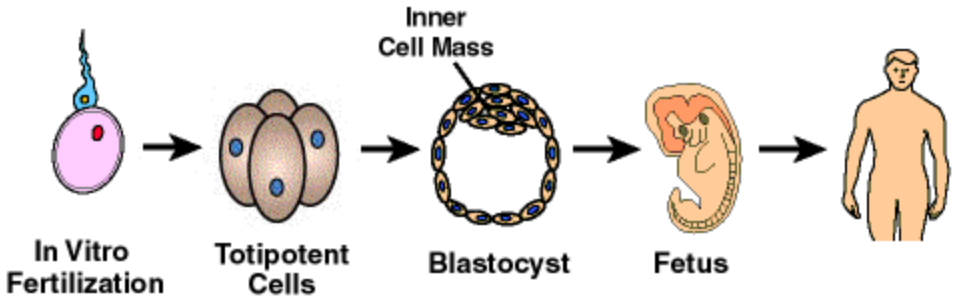
Scientists have been studying stem cells derived from mice for over twenty years. These studies have been quite useful for understanding mammalian development and specialized gene roles.[4] There was a significant breakthrough in stem cell research in 1998 when U.S. scientists derived pluripotent stem cells from human sources.

Explaining the Terms :
Stem cells are found at various stages in human development. These cells have a distinct ability to divide into multiple cells while maintaining their stem cell identity. This characteristic called self-renewal is unique from all other cell types derived from mammalian tissue.[5] They can be divided indefinitely and cultured perpetually. Furthermore, in response to certain stimuli, stem cells can differentiate to form more specialized cells.[6] There are three categories of stem cells based upon this ability to specialize.

Stem cells in the earliest stages (3 to 22 days) of development seem to have the greatest potential for cell theory. These stem cells have the greatest potential to develop into an embryo. Stem cells found shortly after the union of an egg and a sperm in the earliest stage are called totipotent.

Totipotent Stem Cells
Human development begins when a sperm fertilizes an egg. The fertilized egg is totipotent; its development potential is total. Within hours after fertilization the cell divides into identical totipotent cells. Each totipotent cell can develop into an individual embryo. The cell is totipotent from day one until about day three.

About four days after fertilization and several cell divisions, totipotent cells begin to specialize and form a blastocyst. The blastocyst has an outer layer of cells that form a hollow sphere. Enclosed within the sphere is a cluster of cells called the inner cell mass. This mass, if left alone, will go on to form essentially every cell type found in the human body. The outer shell will form the body's various tissues. The inner cell mass cells can specialize into many different cell types, but not all. They are thus called pluripotent.[7]



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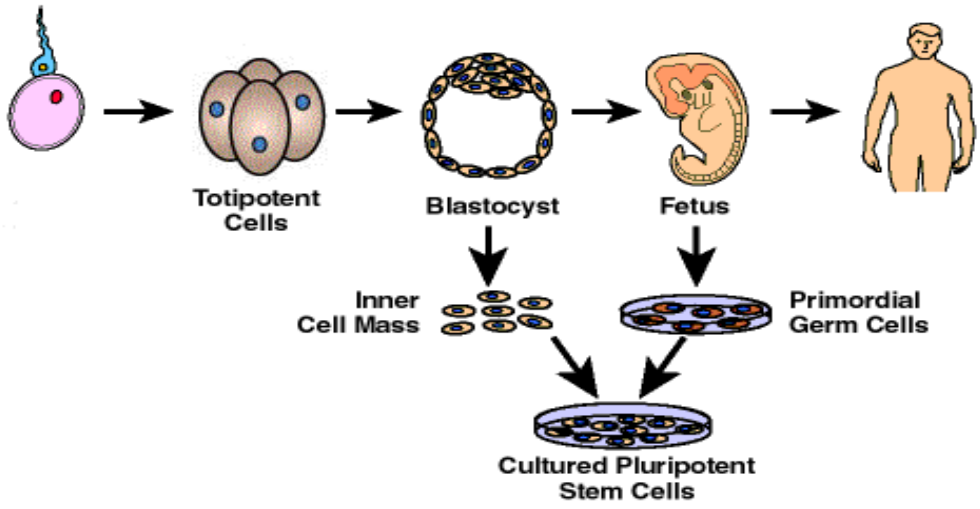
Pluripotent Stem Cells
From about day four in human development until about day twenty-two, the stem cells are classified as pluripotent. There ability to specialize into various specialized cells is called

[4] Canadian Institutes of Health Research, "Human Stem Cell Research: Opportunities for Health and Ethical Perspectives", 2001.
[5] *Ibid.*
[6] *Ibid.*
[7] "Stem Cells: A Primer", National Institutes of Health, May 2000.
[8] *Ibid.* Figure I.

pluripotency. Pluripotent stem cells can arguably be derived from three main sources. The first method involves extracting the inner cell mass from blastocyst stage embryo. These embryos are often "excess" embryos from in vitro fertilization clinics, which were originally created for reproduction, not research. The second method involves taking pluripotent stem cells from aborted fetus's bodily regions that would have developed into genital testes or ovaries.[9] The third method, parthenogenisis is a new technology that will be discussed in its own section below.



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As pluripotent stem cells continually undergo further specialization to the point that they have a specific function, they become part of a new category: multipotent.

Multipotent Stem Cells

The third distinct stem cell stage, multipotent stem cells can exist after about day twenty-two and can be found in a variety of adult tissue. Although multipotent stem cells have not yet been discovered for all tissue types the prospects are encouraging. Until recently, these specialized stem cells were not believed to be changeable into different specialized cells. However, in animals, it has been shown that one line of cells already thought to be specialized was able to develop into other types of specialized cells. For instance, a mouse's neural stem cells were placed into the bone marrow, and they in turn seemed to produce a variety of blood stem cells. There have been other similar experiments to support this.[11]

Stem cells are categorized by more characteristics than just their ability to specialize. They are also categorized by their age of development into two groups, embryonic stem cells and adult stem cells.

Embryonic Stem Cells

There are three main sources of embryonic stem cells: Fertilization, Cloning, and Parthenogenesis.

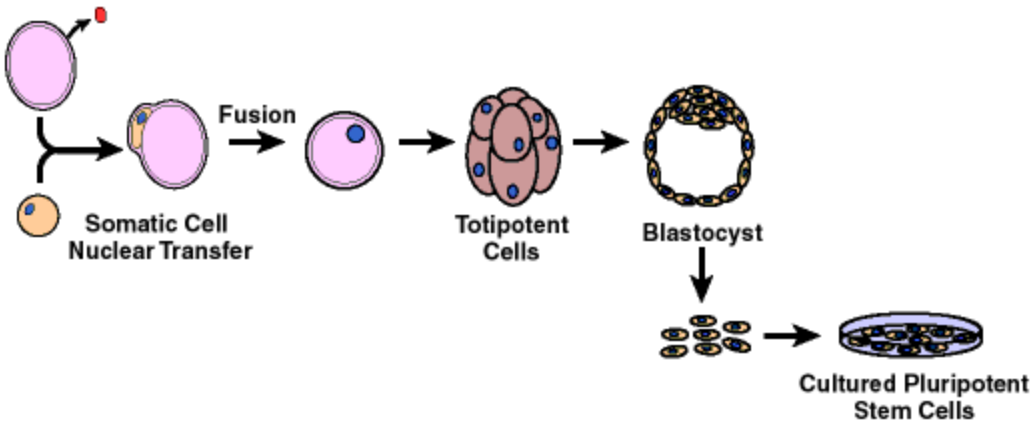
Fertilization

[9] "Stem Cells: A Primer", National Institutes of Health, May 2000.
[10] Figure II, "Stem Cells: A Primer", National Institutes of Health, May 2000.
[11] "Stem Cells: A Primer", National Institutes of Health, May 2000.

A sperm fertilizes an egg. This egg now contains genetic material from both the mother and father. The cells of a normal embryo each contain 23 pairs of chromosomes, one set from each parent. This embryo develops into a blastocyst. Stem cells from the embryo are extracted and can form other specialized cells, such as nerve cells, blood cells, etc.; the stem cells are pluripotent. Hosts will probably reject these specialized cells unrelated to the donator after transplantation.[12]

Cloning

In cloning, an egg's genetic material is removed and replaced with the chromosomes of an adult cell. This too can develop into a blastocyst. A cloned embryo is almost a perfect genetic twin of an existing person. Stem cells can be removed from the embryo to form specialized cells that are a perfect match the cell donor's and will be less likely to be rejected.[13]



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Parthenogenesis

The term "parthenogenesis" comes from the Greek words for "virgin birth."[15] In parthenogenesis an egg is electrically or chemically stimulated to create an embryo. The egg is basically tricked into forming an embryo. The blastocyst that develops is called a "parthenote" embryo. It contains a double set of the mother's chromosomes. Because it lacks paternal genes, it cannot form a fetus. Stem cells removed from the parthenote might be well matched to the donor, but this suggests limitations to the usefulness of such cells for males.[16] Although Dr. Cibelli, of Advanced Cell Technology, suggests that it is theoretically possible to make a parthenote embryo from male sperm.[17]

Adult Stem Cells

There are some specific difficulties at present with isolation and purification of adult stem cell research. First, adult stem cells have not been isolated for all body tissues. Second, the stem cells

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[12] Antonio Regalado, "Stem Cells Without Cloning", Wall Street Journal, Section B1, February 1, 2002.
[13] *Ibid.*
[14] Figure III, "Stem Cells: A Primer", National Institutes of Health, May 2000.
[15] *Ibid.*
[16] *Ibid.*
[17] *Ibid.*

that are isolated are often only found in minute numbers, which seem to decrease with age. Third, some evidence suggests that adult stem cells may not have the same proliferation capacity as embryonic stem cells. Also note, adult stem cells may contain mutations in the DNA due to radiation, toxins, or simple replication error.[18]

THE POLITICAL CONTEXT OF STEM CELL RESEARCH

It makes little sense to do an extensive policy analysis including recommendations for policy without first examining the political climate that the recommended policies will encounter. Policy analysis should always recommend a policy proposal that at least as the potential to be adopted through a vigorous debate.

Prior to President George W. Bush's policy announcement in August 2001, domestic stem cell research was privately funded. Largely under the protections of private enterprise, research concerned few states and went largely unnoticed on the national radar, until now. Massachusetts's Advanced Cell Technology Co. openly clones humans.[1] California's Geron Corp. in Menlo Park is the only company in the world to successfully create purely human stem cell lines.[1] The scientific, political, and moral special interests would be satisfied only with a national policy decision.

The national debate over stem cell research policy has crossed two presidential administrations. In 1994, a panel of government advisors recommended the Executive Office allow the creation of embryos for research under certain, specific circumstances. Quietly and with little fanfare, President Bill Clinton denied the measure although he had publicly endorsed the approach as having "potentially staggering benefits."[19] Instead he appointed a bioethics commission to examine all possible solutions to the growing stem cell research debate. The commission recommended that while there was no good reason to create an embryo solely for research, an ample supply of embryos already slated for destruction was ready and available for such science.[20]

In 1999, the Clinton Administration decided that taxpayer dollars could be used to fund research into human embryonic stem cells.[21] During the last years of the Administration, President Clinton planned to quietly support stem cell research and instructed the panel to draft guidelines for federal grants. In the end, the guidelines the Clinton Administration created lay dormant until the subsequent presidential administration. Incoming President Bush promptly suspended the guidelines in favor of a full review of the cutting edge issue.

Since 1996, the United States government has generally banned federal funding of research that harms, damages, or destroys human embryos. President Bush was faced with the politically and morally volatile decision whether to reverse or maintain the Clinton Administration's policy of allowing federal money to pay for research on stem cells from surplus embryos – as long as those cells were extracted through private funds.[22]

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[18] "Stem Cells: A Primer", National Institutes of Health, May 2000.
[19] Levine, Jeff. "New Guidelines to permit Stem Cell Research." WebMD. August 23, 2001.
[20] Weiss, Rick. "Scientists Use Embryos Made Only For Research." Washington Post. July 11, 2001. Page A25.
[21] Martin, Sean. "Stem Cell Rages on Capitol Hill." WebMd Medical News.. July 17, 2001
[22] McQueen, Anjetta. "Parents Hope Embryo Kids Prevent Stem Cell Opposition." Los Angeles Times. July 17, 2001.

In his 2000 Presidential Campaign, presidential candidate George W. Bush promised to oppose any bioethical measures funding research on embryonic stem cell lines. Once in the White House, political pressure from national, state, and special interests caused him to reconsider his previous stance. Competing political interests placed President Bush in an awkward position.

Rumored to be impressed with scientific data but very anxious over unanticipated ethical precedents, President Bush focused on examining two fundamental questions:[23]

1.) Are these frozen embryos human life, and therefore, something precious to be protected?
2.) If they are going to be destroyed anyway, should they be used for a greater good, for research that has the potential to save and improve other lives?[24]

President Bush made his feelings known on August 9, 2001 in a televised address. The following is a summary of the proposed policy President Bush presented to the American public:

> "As a result of private research, more than 60 genetically diverse stem cell lines already exist." "I have concluded that we should allow federal funds to be used for research on these existing stem cell lines…where the life and death situation has already been made." This allows us to explore the promise and potential of stem cell research "without crossing a fundamental moral line by providing taxpayer funding that would sanction or encourage further destruction of human embryos that have at least the potential for life."[25]

"This is a decision that will have far-reaching implications for our nation 20-30 years from now and beyond," said White House spokesman Scott McClellan. Dr. Larry Goldstein, from the Howard Hughes Medical Center, publicly warned that if Bush fails to adopt funding "it would be very unfortunate. It would indicate he was willing to put a very narrow set of interests ahead of a broad set of interests."[26] Goldstein summarized what supporters fear: without federal resources, American stem cell research would slow and sputter to a halt as the world flew past us on the way to scientific progress.

Reverend Pat Mahoney disagreed. As a spokesperson of the Vatican, Mahoney weighed in heavily against the funding. "If [President Bush] agrees to public funding, he is not pro-life. He is writing his own script for being a one-term president" as the "betrayal" would endanger Republican control of the United States House by discouraging pro-lifer voter turn out in the next elections. The conservative Family Research Council added in August that if the federal government funds stem cell research, "we will say that it is permissible to kill so long as we intend to bring good from it. The new modus operandi for medicine will be 'kill to cure.'"[27]

Unorthodox Congressional Politics:

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[23] Connolly, Ceci. "Conservatives Pressure For Stem Cell Funds Builds." Washington Post. July 2, 2001. Page A1.
[24] President George W. Bush. "Remarks on Stem Cell Research." August 9, 2001. Transcript of the National Address/CNN.
[25] President George W. Bush. Senate Testimony footnote. August 9, 2001
[26] Martin, Sean. "Bush's Stem Cell Decision: What Will It Mean?" WebMD Medical News. August 9, 2001.
[27] Martin, Sean. "Bush's Stem Cell Decision: What Will It Mean?" WebMD Medical News. August 9, 2001.

Gauging Congressional support or opposition for stem cell research still troubles the most sophisticated political analysts and confused the Bush Administration. For the majority of the Congress, the issue is highly personal and debates center on emotions, not politics. Legislators even hotly contended the types of language to use in just debating the terms on the Congressional floor.[28]

The Congressional debate over whether or not to fund embryonic stem-cell research with federal dollars has split the capital in an unusual way. Key players for funding research rally behind unlikely proponent Utah Senator Orin Hatch, a staunch anti-abortionist senator who believes stem cell research "facilitates [and improves existing] life" and is consistent with pro-life and Christian values.[29] Secretary of the Department of Health and Human Services Tommy Thompson also lobbied the President extensively in favor of stem cell research. Republican Senator Arlen Spencer sent President Bush a letter in which he stated that "research on embryonic stem cells could result in treatments or cures for millions of Americans suffering a variety illnesses…You have the lives of millions of our – and your—constituents in your hands."[30] GOP leader Senator Trent Lott sees "great potential" for research cautiously funded with federal monies. On July 20, 2001 over 61 Senators sent President Bush a letter pushing for funding for embryonic studies.

Senator Sam Brownback led the charge against federal funding of this controversial research. Brownback rallied the undecided and staunch critics to lobby newly elected President Bush, with the sentiment "[w]e simply do not need to do any research which relies on the destruction of human beings." Fellow opponents include House Speaker Dennis Hastert, Minority Whip Tom Delay, and Representatives Dick Armey and Jay Dickey agreed, "stem cell research is nothing more than dismembering a human being."[31] Indiana Representative Mark Souder chaired the House Stem Cell hearing and stressed legislators "must not ignore or rationalize the tremendous moral questions posed by destroying living human embryos."[32]

New Jersey Representative Chris Smith displayed the three "adopted embryos" of Lucinda and John Borden – Hannah, Luke, and Mark, before one Congressional hearing. Smith noted these three children resulted from embryonic implant and argued that if President bush approved federal money for research, more of the tiny embryos would be destroyed for science instead of adopted by infertile couples. Mr. Borden held up his children in front of the lawmakers and asked, "Which one of my children would you choose to kill?"[33]

From this din, the Senate's lone medical doctor and a close Bush Administration ally, Tennessee Senator Bill Frist called for a limited approach to the issue. Frist testified repeatedly at Senate hearings for limited support for embryonic research under strict and impregnable guidelines.

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[28] Silver, Lee. "Watch What You Are Calling An Embryo." Washington Post. August 19, 2001. Page B4. "Words like 'destruction,' 'creation,' 'embryo,' and even 'life' and 'death' are ambiguous" definitions in the Congressional debate. Informed scientists and philosophers "understand this ambiguity to be a reflection of the complexity of living things. Meanwhile, both advocates and opponents of stem cell research are using that ambiguity to their best advantage…Is a one-week old human embryo alive? The answer is clearly "yes" if we use a cellular or vegetative definition. And it is just as clearly "no" if we use the definition of sentience.

[29] Connolly, Ceci. "Conservatives Pressure For Stem Cell Funds Builds." Washington Post. July 2, 2001. Page A1.

[30] Martin, Sean. "Bush's Stem Cell Decision: What Will It Mean?" WebMD Medical News. August 9, 2001.

[31] Levine, Jeff. "New Guidelines to Permit Stem Cell Research." WebMD. August 23, 2001.

[32] Martin, Sean. "Stem Cell Debate Rages on Capitol Hill." WebMD Medical News. July 17, 2001.

[33] *Ibid*.

"Research using the more versatile embryonic stem cells has greater potential than research limited to adult stem cells." Scientists should decide on a limit on the number of cell lines that could receive federal funding, because "[y]ou don't need unlimited cell lines."[34] Finally, Frist said taxpayer dollars should not be spent for the actual extraction of stem cells from embryos, the act that results in their destruction. [35]

WHERE WE ARE TODAY

The resulting Bush Administration policy closely reflects the sentiment of Senator Frist. In reaching a compromise, President Bush made neither extreme happy, but did reach a compromise based on Congressional, medical, and religious influences. Rocky roads still lie ahead. Many challenges and bumps face the implementation of the Bush policy on stem cell research.

[34] Martin, Sean. "Stem Cell Pressure Builds on Bush." WebMD Medical News. July 18, 2001.

[35] In a Senate Testimony Fact Sheet (8/9/01), realized Senator Frist's policy suggestions.

a.) Federal funding of medical research on these existing stem cell lines will promote the sanctity of life" without undermining it "and will allow scientists to explore the potential of this research to benefit the lives of millions of people who suffer from life destroying diseases.

b.) Federal funds will only be used for research on existing stem cell lines that were derived: (1) with the informed consent of the donors; (2) from excess embryos created solely for reproductive purposes; and (3) without any financial inducements to the donors.

c.) No federal funds will be used for: (1) the derivation or use of stem cell lines derived from newly destroyed embryos; (2) the creation of any human embryos for research purposes; or (3) the cloning of human embryos for any purpose. This decision relates only to the use of federal funds for research on existing stem cell lines derived in accordance with the criteria set forth above.[35]

CHAPTER II - THE ISSUES OF STEM CELL RESEARCH POLICY

There are three main issues affecting the formulation of a stem cell research policy. First, public health is central to this stem cell research debate because the purpose for this research is the benefit the America's public health. Second, since this is research that requires high investment costs, it is important to consider the economic and business environment for which this funding is derived. Third and finally, the issue of the morality of a policy on stem cell research must be thoroughly examined.

A. PUBLIC HEALTH

As living organisms age, their cells degenerate. With this degeneration come illnesses and diseases that plague those organisms. The United States considers these illnesses and diseases matters of public health and therefore it places treatment of these diseases a priority for the public. Stem cell research is a part of the public effort to find and support regenerative medicines that make life better for an aging population. The domestic public health is driven by some key organizations. In the broadest since, these organizations are the Department of Health and Human Services (HHS), the Food and Drug Administration (FDA) and the general medical community. These organizations are the key public health players in the stem cell research debate.

The principal organization of American public health is the Department of Health and Human Services (HHS), directed by Secretary Tommy Thompson. A division of HHS, the National Institute of Health (NIH), is doing much of the public health advocacy on behalf of stem cell research. The NIH is the principal funding mechanism for the federal government's granting process for stem cell research. Advocates of embryonic stem cell research maintain that the public health can best be served by having this research coordinated by public granting processes. The structure that the Department of Health and Human Services provides for the distribution of government grants allows for the best results to follow from these funds.

Stem cell research shows great public health promise for this nation's pharmaceutical industry. The biotechnology industry views stem cells as the "pharmaceuticals of tomorrow." The FDA is the final check for drugs that could be developed through tests on stem cells. This would not end the need for testing on animals and human tests but it may streamline the testing processes. This agency regulates pharmaceuticals and therefore holds a tangential relationship to the effects of stem cell research policy.

While not exactly an organization, the general medical community can get very organized over public matters that directly deal with health issues. The medical community has looked upon the Bush decision of August 9, 2001 as a mixed blessing. The medical community is supportive of federal money and support of research on stem cells that come with the Bush policy. However, it also sees the limitation of grants for research on only the existing stem cell lines as detrimental to the long-term development of stem cell research and regenerative therapies.

Federal grants open the door for more stem cell research. This increased research is enabled by the federal dollar's access to the multitude of researchers at public institutions. Before public funding, select scientists and doctors associated with private biotechnology companies accomplished all of the research on stem cells. By limiting the number of cell lines that are available, the Bush Administration may have limited the access that researchers have to the promising few cell lines. Furthermore, the genetic diversity within those authorized cell lines may not be adequate to cover the diversity of the population as a whole when the therapies

resultant from this research is applied. In these ways, medical researchers may have been simultaneously enabled and limited in their scientific pursuits by the current Bush policy.

Potential for Stem Cell Research

Stem cell research has the potential to provide treatments for Alzheimer's Disease, Arthritis, Crohn's Disease, Diabetes (particularly Juvenile Diabetes), Lou Gehrig's Disease (ALS), Parkinson's Disease, and spinal cord injuries as well as the big three matters of Heart Disease, Cancer, and Stroke. Though this list is not all encompassing, it allows the reader to recognize the possible benefits of stem cell research on almost every type of malady and injury to the body.

Public Health Issues	Number of Americans Affected
Alzheimer's Disease	4,000,000
Arthritis (Osteo and Rheumatoid)	15,800,000 and 2,900,000 respectively
Crohn's Disease	400,000
Diabetes	16,000,000 diagnosed, 5,400,000 undiagnosed
Lou Gehrig's Disease (ALS)	30,000
Parkinson's Disease	1,000,000
Spinal Cord Injuries	183,000 – 230,000
Cancer	8,900,000
Heart Disease	12,000,000 approximately
Stroke	750,000

The versatility of stem cell research becomes obvious after looking at the breadth and diversity of diseases for which the medical applications of stem cell therapies holds promise. In being this versatile, medical contributions to humanity are of such great potential that the medical community is energetically supporting stem cell research and therapy advancement. Regenerative therapy at the cellular level may be a benefit to so many diseases and so many people.

Public Health Challenges Facing the Bush Decision

First and most importantly, the scientific community is concerned about the quantity and quality of the embryonic stem cells authorized for federal funding under President Bush's decision. Scientists fear that by identifying specific existing stocks of cell lines and halting any examination or research on an ideal additional line poses serious constraints for the development of new medical treatments for diseases. In fact, scientists were startled by the targeted number 60 as the scientific community knew of approximately 15 lines suitable for such delicate research. Speculation has circulated since Bush's decision that the many of the existing lines "do not exist, are of poor quality, or are under such tight commercial control as to make them unattractive to researches hoping to study and perhaps profit from them."[36]

One supplemental argument gaining momentum concerning the quality of the available and authorized stem cells revolves around the base of cells the stem cell lines have been 'grown on.' "Most or all of the human embryonic stem cell colonies approved for research funding…have been mixed in the laboratory with mouse cells, which may create substantial hurdles for scientists trying to turn the colonies into treatments for Parkinson's Disease, spinal cord injuries and other ailments."[37] The basic technique for strengthening budding stem cells is to grow them atop

[36] Connolly, Cecil, Justin Gillis, and Rick Weiss. "Viability of Stem Cell Plan Doubted." Washington Post. August 20, 2001. Page A1.

[37] Justin Gillis and Connolly, Cecil. "Stem Cell Research Faces FDA Hurdle." Washington Post. August 24, 2001. Page A1.

embryonic stem cells, a practice so common that the mouse cells are referred to as "feeder cells."[38] While the feeder cells fortify the human stem cells for future testing purposes, the most successful stem cell lines, the same lines authorized by the Bush Administration's policy, may have picked up mouse viruses as a result of growing in direct contact with mouse cells.

As a result, the lines authorized by the Bush policy may automatically fall under FDA regulations as "xenotransplants" or transplants of animal tissues for human purposes. FDA guidelines are stringent. Private companies, either domestic or foreign, interested in utilizing federal funds for stem research may ultimately be dissuaded not by the public accessibility of results but because of the "large burden" FDA regulations impose.[39] Companies such as Australia's BresaGen Inc. feel that the scientific community will soon develop stem cells grown only on human feeder cell bases but that these lines will be ineligible for American grants as they were developed after the August 9, 2001 deadline for federal US funding. Only one company, Geron Corp. in California has successfully grown strong pure human cell lines but is currently uninterested in federal monies.

Either way, the quality of the available and authorized stem cells may be unfit for long term stem cell funding. Besides, most private veteran research companies "believe that new embryonic stem cell lines will need to be developed in the long run to replace existing lines that become compromised by age, and to address concerns about culture with animal cells and serum could result in health risks for humans."[40]

The second public health challenge is the question of the adequacy of the consent process used to obtain the cells could ultimately affect the availability of stem cell-based therapies. While the Bush Administration claims to have examined the documents of each cell line authorized, the quality and condition of each cell line was not.

Third, is the issue of genetic diversity. If research produces therapies or a solution to the world's debilitating diseases, it will prove critical "to find a good immunological match between the implanted cells and the recipient to try to stave off rejection…Such matching is easier within racial and ethnic groups that are more closely related." If federally funded research continues to be limited to the authorized cell lines, potential cures could end up being most useful to a narrow sliver of the world's population (Caucasian and Asian ethnicities.) The Washington Post surveyed ten labs with approved lines. The survey concluded "as many as 49 of the lines are from white couples" while approximately "15 of the Asian-based lines harvested at Clinics in Singapore and India are of South and East parentage."[41] Scientists argue this genetic homogeneity has huge medical consequences for creating therapies applicable to a genetically diverse population.

Fourth, policy analysts and researchers are worried laboratories have not obtained adequate consent from embryo donors which may result in disqualification. Analysts in the Bush administration admitted to looking at the consent forms to make sure there was "informed

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[38] *Ibid.*.

[39] Senior VP Allan Robins, BresaGen Inc. Australia. Justin Gillis and Connolly, Cecil. "Stem Cell Research Faces FDA Hurdle." Washington Post. August 24, 2001. Page A1.

[40] Dr. Bert Vogelstein, Johns Hopkins Univ. and Chair of the National Academy of Sciences stem cell committee. Rick Weis. "Broader Stem Cell Research Backed; Key Science Group Differs With Bush." Washington Post. September 11, 2001. Page A1.

[41] Jon Entine and Sally Satel. "Inserting Race Into the Stem Cell Debate." September 9, 2001. Page B1.

consent" but didn't analyze them.[42] "Too often we have learned that procedures used in other parts of the world in [stem cell] research with human subjects do not measure up to the ethical standards we embrace in this country," according to the AAAS.[43] In short, if some of the consent forms or standards are inadequate, scientists in America seeking access to these lines and their federal funds would be left with even fewer numbers of cell lines than previously thought.

Fifth, American researchers are concerned about the access they will have to the 60 cell lines. Approximately a dozen companies and labs around the world control the lines. Such labs and companies may retain the potentially lucrative commercial rights to future discoveries.

Sixth and finally, one of the main concerns in the medical industry in America is a possible "brain drain" out of the United States if regulations are too strict on medical researchers. The problem is that talented researchers may leave a highly regulated research environment for nations with medical research-friendly governments. This would be counter to the "brain influx" from around the world of many talented health care professionals who have helped make the American medical system one of the most innovative in the world. Given a tougher policy on stem cell research and human cloning, there may be significant numbers of medical researchers and doctors who choose to set up there businesses oversees to accomplish their research. The most logical recipient for this "brain drain" is England. England has a much more relaxed governmental policy on human cloning and stem cell research. The English government also supports research on stem cells through governmental grants. Therefore, it is possible that the influx of medical professionals will slow and some of America's top medical professionals will move overseas. This will be a significant loss to the aggregate quality and capacity of the public health of the United States.

To say the least, the stem cell issue is complex when viewed through the lens of public health. It is important to recognize that one could never conceptualize and delineate all of the arguments and ramifications of stem cell research and its applications to our nation's public health. The nation's public health is simply too big and complex. Stem cell research does have at least two major ramifications to American public health. First, it may be highly beneficial to those millions of Americans who suffer greatly from the above diseases and others not mentioned. Medical application of stem cell technologies could provide answers for those diseases. Second and indirectly, stem cell technologies may help tens of millions of Americans who care for individuals with the above diseases. Health concerns are not just those of the individuals suffering with health problems. Health concerns are also an issue for primary and secondary caregivers, usually the family. Public health is one of the principal concerns for society. It is for these reasons that many advocate for increased investment in stem cell research.

B. PUBLIC AND PRIVATE INVESTMENT IN STEM CELL RESEARCH

Medical research is dependent upon streams of financing to for its support. Where this funding and investment should best come from presents its own important issue.

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[42] Skirboll, Lana. Director of Science Policy and Bush Administration cohort. Connolly, Cecil, Justin Gillis, and Rick Weiss. "Viability of Stem Cell Plan Doubted." Washington Post. August 20, 2001. Page A1.

[43] Connolly, Cecil, Justin Gillis, and Rick Weiss. "Viability of Stem Cell Plan Doubted." Washington Post. August 20, 2001. Page A1.

Federal Funding for Fetal Tissue Research and Transplantation

In 1974, Congress placed a moratorium on federally funded research on living human fetuses. The following year, the department of Health and Human Services (HHS) imposed a *de facto* moratorium the funding of human embryo research. This moratorium resulted from HHS regulations requiring all research applications involving in-vitro fertilization to be reviewed by an HHS-appointed Ethical Advisory Board (EAB) before federal funding could be allocated.[44]

"In vitro fertilization (IVF)*"* was defined as "any fertilization of human ova which occurs outside the body of a female, either through mixture of donor human sperm and ova or by any other means" id. (adding s46.203(g)). Although the preamble to the regulation implementing the EAB requirement stated explicitly that research on human embryos created through IVF was not intended to be included with the scope of regulation, id at 33527 (discussing the "nonimplanted product" of IVF), HHS nevertheless took the position that human embryo research was within the scope of IVF research and therefore subject to EAB review.[45] The EAB was convened between 1978 and 1980 and concluded that IVF was ethically acceptable providing certain safeguards were followed. However, no action was taken based on this recommendation, and no EABs were chartered after 1980. Consequently, NIH did not fund any IVF or embryos research protocols.

After considering the report, the HHS promulgated regulations governing federally funded research involving pregnant women, fetuses and "cells, tissue or organs excised from a dead fetus."[46] HHS lifted the moratorium on federally funded research on living human fetuses.[47] HHS regulations provided that "activities involving the dead fetus, macerated fetal material, or cells, tissue, or organs excised from a dead fetus shall be conducted only in accordance with any applicable state or local laws regarding such activities" [48] The commission report referred to organs, tissues, and cells from a dead fetus collectively as "fetal tissues," although the HHS regulations included them under the general heading of dead fetus and fetal material.[49]

HHS allowed the use of living and dead (subject to state and local laws) fetuses for research. However, neither the preamble to the regulations, nor the report of the commission considered by the HHS in promulgating the regulations, limited those "activities " involving a dead fetus to any particular type of research such as basic research or therapeutic research.

In November 1989, the Secretary of HHS continued the moratorium on federal funding of research in which human fetal tissue from induced abortions is transplanted into human recipients. This did not prohibit the "funding of such research in the private sector...[or] Federal support of therapeutic transplantation research [50] that uses fetal tissues from spontaneous abortions or ectpoic pregnancies" [51] It also did not prohibit the use of federal funding of fetal cell and tissues for research that did not involve transplantations into human recipients. During the

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[44] 40 Fed Reg 33526, 33529 (Aug 8, 1975) (adding 45 CFR s46.204(d).
[45] 59 Fed Reg 45293 (Sept.1, 1994).
[46] 40 Fed Reg 33526, 33530 (aug 8 1975) (establishing Subpart B of 45 CFR Part 46)
[47] *ibid*.
[48] 40 Fed Reg 33530 (aug 8 1975) ibid. (codified at 45 CFR s46.210) (1998).
[49] 40 Fed Reg 33530 (s46.210), 33532 (definition of dead fetus)
[50] National Institute of Health, *Human Fetal Tissues Research supported by the NIH in Fiscal Year 1990,* 1-4 (1992); Helen M Maroney, "Bioethical Catch 22: The Moratorium on Federal Funding of Fetal Tissues Transplantation Research and the NIH Revitalization Amendments." *9 J. contemp. Health L. and Pl'y* 485,487 n.11 (1991) (citing NIH document).
[51] *Finding Medical Cures: The Promise of Fetal Tissues Implantation Research, Hearing on S.1902 Before the Senate Comm. On labor and Human Resources*, 102d Cong., 1st Sess. 4 (1991) (statement of Ass Sec for Health James O Mason)

moratorium, the NIH continued to fund research using fetal tissues and cells from a variety of purposes, including use in testing vaccines and virus research.

In 1993 Congress acted in the areas of human embryo research and human fetal tissues transplantation. Congress enacted the National Institutes of Health Revitalization Act of 1993[52] which:

1. Authorizes the Secretary of HHS to allocate federal funds for "research on the transplantation of human fetal tissues for therapeutic purposes," regardless of whether the tissues were obtained pursuant to an induced abortion."[53]
2. Defines "human fetal tissue" as "tissues or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion, or after a stillbirth."[54]
3. Specifies that fetal tissues may be used for transplantation research only if informed consent is obtained from the woman donating the tissue[55] and from the researcher.[56]
4. Prohibits the solicitation, or acceptance of fetal tissues for transplantation into a specific individual (i.e. directed donation) under certain circumstances.
5. Codifies the nullification of the 1988 moratorium on human fetal tissue transplantation research.[57] It is allowed for therapeutic drugs and treatment.
6. Limits the sale of human fetal tissue.[58]

Federal Funding of Stem Cells Derived From Human Embryos:
The Omnibus Consolidated and Emergency Supplemental Appropriations Act for Fiscal Year 1999[59] restricted use of federal funds for human embryo research from:

1. The creation of a human embryo or embryos for research purposes; or
2. Research in which a human embryo or embryos are destroyed, discarded or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in uteri under 45 CFR 46.208(a)(2) and section 498(b) of the Public Health Service Act (42 USC 289g(b)).[60]

However, the General Counsel concluded that federal funding for research using pluripotent stem cells derived from embryos would not violate federal law because the statute defines embryos as "organisms" and stem cells are not organisms and therefore are not embryos. The term "human

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[52] Pub. L No. 103-43, Title I, ss111,112,121(b)(1), 107 Stat. 122,129,131,133 (1993) (codified at 42 USC ss289g,289g-1, 198g-2 [Supp. 1997]).
[53] 42 USC s289g1(a) (Supp. 1997)
[54] Id. Ss289g-1(g) and 289g-2(d)(1) (emphasis added). In May 1998 (45 CFR s46.203(f) (1998)), a "dead fetus" was defined as a fetus *ex utero* which exhibits neither a heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached).
[55] The woman providing the tissue must state in writing that (1) she is donating the fetal tissues for research on the transplantation of human fetal tissues for therapeutic purposes , (2) the foundation us being made without any restriction regarding the identity of individuals who may be recipients of the transplantation of the tissue, and (3) she has not been informed of the identity of the recipient. 42 USC s289g-1(b)(1) (Supp.1997) . The attending physician involved in obtaining the tissue also must make certain declarations in writing. Id s289g-1 (b)(2).
[56] See D10 (of analysis from Marks handout footnote 27
[57] Memorandum from the President to the Secretary of Health and Human Services, January 22, 1993 (reprinted in 58 Fed Reg 7457 [feb. 5, 1993]
[58] Pub. L. No. 103-43, s121©, 107 Stat. 122,133 (1993) (codified at 42 USC 289g note); 59 Fed Reg. 28276 (June 1, 1994) (rescinding 45 CFR 46.204(d)).
[59] Pub. L. No. 105-277, 112 Stat. 2681 (1998)
[60] Pub. L. No. 105-277,Div.A. s101(f), Title V, s511(a), 112 Stat. 2681-386. Division A, s101(f) of te bill contains appropriations for the Departments of Labor, Health and Human Services, Education and related agencies.

embryo" is defined as "any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act (1998), that is derived by fertilization, parthenogenesis, cloning or any other means form one or more human gametes or human diploid cells."[61]

Federal funding is not prohibited for research using pluripotent stem cells derived from nonliving fetuses, provided applicable state and local legal requirements are satisfied. In addition, federal funding is not prohibited for research using pluripotent stem cells derived from living fetuses.[62] The recent Bush policy on August 9, 2001 appropriates federal funding for research on the existing embryonic stem cell lines listed in the NIH Registry. Adult stem cell research is federally funded and consistent with the Public Health Act. In August 2001, federal funds were specifically made available for research using human embryonic stem cell lines so long as they meet the following Bush policy criteria:

- Derivation process (including the destruction of embryos) must have been initiated prior to August 9, 2001 0900 hours.
- The stem cells must have been derived from an embryo that was created for reproductive purposes and was no longer needed.
- Informed consent must have been obtained for the donation of the embryo and that donation must not have involved financial inducements.

Private v. Public Funding: Economic and Business Implications of Federal Funding

Many argue that more permanent funds are needed to increase the number of embryonic stem cell lines. Without government funding**,** it will be difficult to continue raising the large amounts of money needed to further the research within the private sector.[63] This may limit overall scientific progress as small companies that hold patents on stem cell lines are unlikely to do broad-ranging, high risk, and higher cost studies. Successful commercial enterprises are reluctant to show much interest in funding expensive and risky scientific experiments that may not pay off for decades.

Research may be further slowed by the fact that the private research teams will be far less likely to share data discoveries than the public sector. Moreover, that instead of broad access and collaboration in the scientific community, stem cell breakthroughs will be proprietary products owned solely by these private biotechnology companies. Results may then be available only at astronomical costs to a narrow public, and if cost is not covered by private health insurance, the taxpayer will have to cover the rest. "The Medicare budget will therefore take another beating."[64]

Maria Freire, Director of the Office of the United States Technology Transfer appeared on behalf of the National Institutes of Health before the Senate Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies. The goal of these agencies, she said "is to promote economic development, enhance U.S. competitiveness and benefit the public by encouraging the commercialization of technologies developed with federal funding to elect to retain title to their inventions. They also impose certain obligations: promoting utilization,

[61] Pub. L. No. 105-277,Div.A. s101(f), Title V, s511(b)

[62] *Analysis of Federal Laws Pertaining to Funding of Human Pluripotent Stem Cell Research* Commissioned Paper Ellen J. Flannery and Gail H. Javitt (ask Mark for the rest of the details)).

[63] The Washington Post **January** 18, 2002, Friday, Final Edition **SECTION** A Pg. A14 **HEADLINE:** Center Shifts **Stem Cell** Approach;

[64] September 10, 2001, The American Prospect COMMENT; Pg. 2, 981 words, The Great Obfuscator, BY ROBERT KUTTNER

encouraging commercialization and ensuring public availability of these [resulting] technologies."[65]

Freire pressed for federal funds for embryonic research under the guidelines of these acts. Continuing "to contribute to the global leadership of the U.S. biomedical enterprise" with federal funds reinforces the United States as the archetype for "governments around the world [to] emulate these laws in the hopes of promoting economic development in their own nations. Domestically, "the only way to maximize the benefit to the public is to ensure that both research use and the potential for commercial development are preserved. Experience over the last 20 years has shown that to maximize public health benefit, the balance between exclusivity and access must be carefully maintained, and research uses of new technologies must be preserved. These concepts form the basis for the licensing policies of the NIH, as well as for the proposed guidelines for our grantees mentioned above."[66]

Public funding and its attached regulations may also reduce the likelihood of an "egg and embryo black market." Currently recipients pay all medical fees (injections, doctor visits, counseling, medical exams, etc.), but egg donors receive payment for their participation in a donor cycle. The sum varies depending on where you live and how viable a candidate you are, but compensation from respectable clinics and accredited programs currently ranges between about $2500 and $5000 per cycle.[67] The work was usually funded with private money, not government funds. However this practice has stopped due to political pressure.

On the other hand, public sector research, development and production may be too inefficient for such a delicate scientific pursuit. It often results in government grants that are misallocated and essentially wasted. As an example, misallocation of government grants has been found among a number of public universities. Keeping the public sector out of the medical funding business may stimulate private sector research. Private sector firms have a bottom–line and their costs are upfront whereas with the government, the costs are disguised in the form of taxes. In addition, as the public sector is not often result-oriented, time and costs/money are often underestimated by 40%. This would benefit the patient, as private sector research and therapeutic products may be of higher quality and more cost-effective.

C. MORALITY AND STEM CELL RESEARCH

Terms of morality vary from person to person. As a pluralistic democracy, the United States government is in the untenable position of trying to decide what the moral course for the nation should be concerning stem cell research. There is no way to completely satisfy every opinion on the subject but as a society we should deal with tough issues before and within our deliberative processes.

Today, scientists believe that stem cell research and derived therapies may have many benefits to society. But all things have a price. Many questions should be addressed to determine if the moral cost to society will be to high if the research is done in a way that violates our fundamental

[65] Maria Freire. US Senate Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies. Statement on National Institutes of Health. August 1, 2001.
[66] *Ibid.*
[67] The Jones Institute (a division of Eastern Virginia Medical School) was extracting eggs from women who were paid $ 1,500 to $ 2,000 each and had signed informed-consent documents. The eggs were inseminated with donor sperm and eventually destroyed to get the stem cells that lie within.

beliefs about the inviolate dignity of human life. To determine these "moral costs" there are four moral questions that we address.

The first moral question asks, "What is the value of a human life?" There is integrity in the uniqueness of human life. Every life is precious and should be treated with respect and dignity. Every human is unique and important either in the eyes of its Creator or as its own intrinsic being. It is not surprising that nearly every religion, faith, or creed embraces the notion of the dignity of human life. It is equally unsurprising that people vary widely in their understanding of what human life is and how it should be protected.

The second moral question asks, "When does human life begin?" This question is the crux of the embryonic stem cell research debate. Completely different answers posited by different religions create a difficult situation for the government in the stem cell research debate. This question is central in determining what sources of stem cells are acceptable to society.

Most, but certainly not all, Christian faiths including, Catholic, Protestant, and Orthodox, recognize human life as beginning when an egg is fertilized by a sperm regardless of whether the fertilization takes place *in vivo* or *in vitro.*

Most Mormons, Jews, and Muslims believe that a human life begins sometime after fertilization. Mormons believe that only when the embryo attaches to the mothers womb is the human spirit joined with human flesh and a resulting full human being is created. This process in normally viewed to be on the 14th day after conception. Jewish theology has generally held for over 3,500 years that until an embryo reaches 40 days old it is not considered a full human being. At 40 days the embryo undergoes a "quickening" which is the time when God bestows a soul upon the body and the embryo becomes a full human being. Muslims, while having a much more varied tradition, generally hold similar views to the Jewish faith and place ensoulment at 120 days. Many argue from no particular religious view that the beginning of human life starts anywhere from conception all the way through when a baby exits a mother's womb. Credible scientific arguments can be made for almost all of these views. Two of the more compelling arguments relevant to stem cell research and the source of stem cells are explored below.

First, human life begins at conception. When the sperm fertilizes the egg it creates a single cell that, under a natural course of events, will develop into an adult human being. The fetus has a separate blood type, a different genetic code, and depending on the stage of the pregnancy a separate heart beat from the mother's.

Second, human life begins when the fetus becomes viable outside of the mother's womb. If the fetus cannot survive without the mother, than it is still part of the mother. At this stage of development, the fetus is not human life but rather a development within the body of the human life of the mother.

The third moral question asks, "What is a quality life?" If humanity has notions of a quality life, then it has a minimum stage of health to which it is morally obligated to try to help people. That would then mandate research on therapies that would allow people to reach that minimum quality of life. However, some of these people that would be considered to have illnesses that do not allow them to experience a "quality life" have learned to cope with their health situation and live as happily as anyone else who may be considered normal.

Stemming from the above three questions, the fourth moral question asks, "how does America deal with societal differences over morality?" Strident differences over moral issues have always

been a part of the American experience. Consider the debates over independence, slavery, succession, poverty, and civil rights. These issues must be approached maturely and directly. If America is going to resolve these differences over moral issues she must do it through collective inquiry and respectful discourse.

Is research on stem cells acceptable if the life or death decision about the source of the stem cells (embryo or fetus) has already been made? Many argue that if the source is already going to be or already is destroyed, than it is better that the source be used to further human life than for it to be wasted. This argument separates the possibly morally wrong act of destroying a source from the presumed moral good of doing research on the source to help the living. As a utilitarian argument or as part of a cost-benefit analysis this is very persuasive.

Sources of stem cells are at the center of these moral questions. They are morally contested because of differences in how they are created and for what purposes they are created or destroyed.

CHAPTER III - EXAMINING THE SOURCES OF STEM CELLS

Our policy recommendation turns on the origins of the cell lines in question. Where the stem cell lines are derived dramatically changes our policy. The source is the keystone for what we advocate should be the American policy on this controversial issue.

There are nine key sources of stem cells for stem cell research, which we have placed within six categories according to how they are derived.

CURRENT EMBRYONIC STEM CELL LINES[68]

These are stem cell lines that met the following conditions before 9:00 p.m. August 9, 2001:

(1) The derivation process (which commences with the removal of the inner cell mass from the blastocyst) had already been initiated,

(2) The embryo from which the stem cell line was derived no longer had the possibility of development as a human being,

(3) The stem cells was derived from an embryo created for reproductive purposes,

(4) The embryo was no longer needed for these purposes,

(5) Informed consent was obtained for the donation of the embryo and,

(6) No financial inducements were provided for donation of the embryo.

There are currently 78 lines listed in the NIH registry. (Please see Appendix VII for more details.)

ADULT

These are stem cells derived from adult tissue and cells such as the liver, brain, etc. As in a later section, there are some specific difficulties at present with adult stem cell research.

EMBRYONIC

Fetal tissue and material from an abortion to save a mothers' life.

Abortions to save a mothers' life are those recommended by the health care provider to protect the mother's physical or mental health. Thus, an abortion carried out to save the mother's life although requiring the deliberate termination of a pregnancy, involves limited choice.

Fetal tissue and material from elective abortions.

We prefer to place all other abortions that are not carried out to save a mothers' life within this category. These abortions involving the deliberate termination of a pregnancy are initiated by personal choice. Abortions induced by the drug mifepristone, or in the cases of a rape/incest would therefore fall within this category. Most elective abortions take place between 8 and 12 weeks of gestation.[69]

Fetal tissue and material from miscarriages.

The health communities including HHS refer to this as a spontaneous abortion. It is estimated that up to 50% of all fertilized eggs die and are lost (aborted) spontaneously, usually before the

[68] Taken directly from http://escr.nih.gov/

[69] http://www.drkoop.com/conditions/ency/article.asp?id=1512

woman knows she is pregnant. Among known pregnancies, the rate of spontaneous abortion is approximately 10% and usually occurs between the 7th and 12th weeks of pregnancy.

In this policy paper we use the term 'tissue and material from miscarriages' to distinguish this source from the entangling abortion debate because most miscarriages are caused by a fetal death due to fetal growth abnormalities not caused by the mother.[70] For this reason, we also include fetal tissue and material from ectopic pregnancies[71] (where the fertilized egg implants in tissue outside of the uterus and the placenta and fetus begins to develop there), premature births i.e. where the birth occurs before 37 weeks of gestation (the full-term gestation being 37 to 42 weeks)[72] and, stillbirths (the birth of a dead fetus) in our treatment of the above category.

"Spare" embryos from reproductive *in vitro* fertilization.
In this case, an egg is fertilized by a sperm for the purpose of assisting reproduction.

LAB CREATION
These embryos are created through *in vitro* fertilization practices for the sole purpose of conducting research.

CLONING
Cloning involves removing and replacing an egg's genetic material with the chromosomes of an adult cell. The key thing for this policy paper is that embryos are created (by way of cloning) and used for reproduction and/or therapy. There are several cloning techniques currently used by private sector firms. This includes somatic cell nuclear transfer whereby a cell nucleus is transferred from a somatic cell (a cell of the body other than egg or sperm) into an egg from which the nucleus has been removed.[73] The federal government does not fund this activity but allows it to carry on in the private sector. Some states have placed a permanent or temporary ban on either reproductive or therapeutic cloning, or both. For more details please see table in appendix no. 3.

PARTHENOGENESIS
Here, an egg is electrically or chemically stimulated/tricked into forming an embryo for purposes of research.

Criteria for This Examination
In deciding the most responsible option for the use of federal funds, three criteria must be met:

First, **does this source destroy human life?**
The United States federal government can only cautiously enter into the contentious aspects in the point of life debate. It is currently impossible for the federal government to place a date on when life begins. Federal monies and resources should only be used for scientific pursuits when it is clear that research does not tamper with, impede, or destroy human life. It can however support research on subject matter that is clearly not life. Federal monies carry the weight of public endorsement, if not by the volume of the grant, then by its symbolic gesture.

[70] http://www.drkoop.com/conditions/ency/article/001488.htm

[72] http://www.drkoop.com/conditions/ency/article.asp?id=1562. Approximately 10 percent of all births in the U.S. occur before 37 weeks gestation.
[73] http://www.nih.gov/news/stemcell/primer.htm

Second, **could this source demonstrate an improvement to domestic public health?**
The Preface to the United States Constitution directs the federal union to provide for the "General Welfare" of the American People. The United States government should support that research that may potentially provide therapies to America's most debilitating diseases. Millions of Americans suffer from degenerative illnesses. It is the duty of the federal government to further advance studies that plausibly could remedy so much suffering. Should a study indicate potential improvements to domestic public health, they should be eligible for federal support. Intricate cellular research holds much promise but few guarantees. Research and development by necessity includes educated risks. If researchers demonstrate likely results, the government may take calculated risks and invest in potentially long-term solutions at short-term costs. Proposals to receive federal funding should include a plan for development with reasonable probability that the results are technically feasible and sustainable.

Third, **does this source comport with existing statutory guidelines?**
An Executive policy must comply with previous legislative action. Executive actions must take care not to violate preexisting Congressional laws, regulations and guidelines. Any fiscal venture initiated by one branch to the other ought to adhere to preset steps when in search for appropriated funding as laid out in Article 1 of the U.S. Constitution.

Governmental Options
Because the sources of stem cells are generally more controversial than the general issue of stem cell research, we have come up with three basic approaches that the government can take in regards to these sources.

Governmental Approach:

1. Ban - Ban source for both public and private research.
2. Not Fund - Allow the source for the private sector but appropriate NO federal funds on research on stem cells derived from source.
3. Fund - Allow the source for the private sector AND appropriate federal funds for research on stem cells derived from source.

Application of Criteria
By applying criteria to the each potential source of stem cells, the appropriate governmental approach should follow that analysis. This analysis, unfortunately, is not a perfect science. On seven of the nine sources, the method worked perfectly. However, two of the questions are too intricately linked to issues remaining for social dialogue to determine governmental action through this analysis.

Source 1: **Lines recognized under President Bush's current plan**
The existing cell lines authorized under President Bush's August 2001 policy are not a source of stem cell: they are a stem cell. Therefore, our criteria cannot apply. We recommend funding these existing lines.

Source 2: **Adults or afterbirth**
Research performed on adult stem cells is uncontroversial and meets all of our criteria. It is technically feasible, morally sound, legal, and medically promising. We recommend funding research and development of new therapies from this source.

Source 3: **Fetal material derived from miscarriages**

Funding miscarriages does not present a moral dilemma. Therefore, it is acceptable to invest some federal support on research materials that do not disrupt human life given the natural demise of the fetus. Miscarriages provide good materials for research on stem cell therapies.

Source 4: **Embryos created through Parthenogenesis**

While this process holds potential, existing Congressional legislation classifies this technique as a full human embryo. Therefore, while we encourage private enterprises in exploring this procedure, we do not feel prudent funding this procedure until a later juncture when statutes and future evidence of parthenogenesis's technical feasibility mature.

Source 5: **Fetal material derived from abortions that were necessary to save the mother's life**

Abortion materials, regardless of its incentives, are not scientifically lucrative enough in research potential to warrant federal monies. Materials from abortions do not demonstrate enough potential improvements to domestic health to weather the fervor accompanying any financial support. It is domestically awkward politically and unsound economically to fund research performed on these materials at this time given domestic technological, economic, and political realities.

Source 6: **Embryos created specifically for research**

We have chosen to regulate this source with a government-enforced ban on public and private research. Because of our first criterion, we believe the procedure of fertilizing eggs with sperm purely for scientific research is antithetical with sound moral judgment and against the spirit of human life.

Source 7: **Cloned embryos**

There is a dignity in human individual's uniqueness. Any scientific practice that duplicates a person for scientific research is in violation of that dignity. To recreate an already unique human life for scientific pursuits compromises a fundamental principle in our collective existence. To pursue a scientific process at such a cost is immoral and should therefore be banned.

Source 8: **Fetal material derived from elective abortions**

Fetal materials from elective abortions utilized as a source for stem cell research fails to garner neither unanimous support in our group nor a general consensus in America generally. Funding research on materials from this source uncomfortably places the federal government in close proximity to the abortion question. This is an abortion issue. The contentious nature of this issue propels us to abstain from this matter as it relates to stem cell policy.

Source 9: **Embryos left over from fertility procedures**

Representing American society, our group of five policy analysts could not reach consensus, much like American society in general. Supporters advocate funding unwanted embryos left over from in vitro fertilization procedures as they are already slated for destruction and already funded for other types of medical research. The likelihood of high quality research materials from this source is better than any other source available for stem cell research. Opponents contend that these embryos are alive as they are at the earliest stages of human life. To destroy it, or create an incentive to destroy life, even for research purposes violates our first criterion in that it ends the life of that embryo. It is therefore appropriate not to take a collective, formal position.

CHAPTER IV – RECOMMENDATIONS AND IMPLEMENTATION

We do not endeavor to provide a single solution to this controversial and complex issue, but instead, to acknowledge impasses where they exist and make recommendations that are in the public interest when possible. The arena of stem cell research is messy. All advocates from different positions claim morality. Scientific progress is uncertain but may be overwhelmingly beneficial. Federal funding laws are ambiguous. Here are our recommendations.

FUND - Registered Lines as Set Forth in the Bush Policy

We recommend funding research on the already registered lines through fiscal year 2004. This will provide the opportunity to evaluate the benefits of stem cell research to public health. At the end of this funding period, the scientific progress of the research should be evaluated before more grants are authorized.

Implementation:

The NIH currently reviews all grant applications for stem cell research to ensure that they meet statutory guidelines. This procedure is quite slow, with first-time applicants having applied before February 1st 2002. Pending acceptance to federal grants, we recommend working with the grant recipients to acknowledge and accept a built in sunset funding clause as well as Congressional and Executive reviews of their work.

FUND – Research on Adult Stem Cells

Adult stem cells are beneficial to therapeutic research in their capacity to divide and regenerate the organs from which they were taken. In addition, use of these mature stem cells for research, is already federally funded and also flourishes within the private sector. We therefore recommend continued federal funding and support of private sector research.

Implementation:

Increase federal funding on adult stem cell lines. This source should be a focus of the administration's energy and rhetoric on the stem cell research issue.

FUND – Stem Cell Research on Miscarried Material

We recommend funding the use of miscarried material for stem cell research. This is advisable because it does not destroy existing life and simultaneously provides adequate research material. In addition, the National Health Revitalization Act already legalizes and provides federal funding for the use of fetal tissue and cells for research and transplantations.

Implementation:

Funds should be earmarked specifically for this research increasing at the rate of inflation. Appropriate regulations must be followed in regards to this miscarried material.

NOT FUND/ALLOW – Parthenogenesis Created Embryos

We recommend reclassifying embryos created through 'parthenogenesis' technology. The Omnibus Consolidation and Emergency Supplemental Act (1999) classified these embryos as "human embryos." This misclassification was a result of misunderstood scientific data. Therefore these embryos should not be classified as "human."

Implementation:

Implementing this recommendation requires a lobbying effort to reclassify by statute and recognize these "embryos" as chemically altered eggs. The earlier this reclassification is accomplished, the more options for funding the government will have in the future.

NOT FUND/ALLOW – Fetal Tissue From Abortions to Save a Mother's Life
Research performed on fetal tissue extracted from abortions recommended to save a mother's life should not be federally funded given its close proximity to the elective abortion debate. However, we recommend allowing research to continue on this material though it has surpassed the twenty-second day for ideal embryonic materials.

Implementation:
Allow private biotechnology companies to continue existing research practices. Establish a monitoring system within the National Institute of Health to update the President and Congressional Committees on the scientific progress from research performed on this material.

BAN – Human Cloning for the Purpose of Stem Cell Research
Human cloning violates the integrity of human life in a way similar to international lab created embryos mentioned above. Integrity of life is lost when the uniqueness of a human individual is disregarded and purposefully a laboratory copy is created of that individual. This practice must be banned as it applied to stem cell research.

Implementation:
This recommendation can best be implemented through full support for S.1899, a bill currently in the United States Senate that supports a general prohibition on human cloning as applied to human embryos. This bill is more encompassing than just a ban on cloned human embryos for stem cell research. It therefore includes within it the ban that we recommend as applied to stem cell research.

BAN – Lab Creation of Embryos for Stem Cell Research
Lab creation of embryos for stem cell research destroys the integrity of human life. By this we mean, that the practice encourages the creation of embryos only for the purposes of research resulting in their ultimate destruction. To allow these practices to continue would be incongruous with a moral nation that values not just human life itself, but its meaning and purpose. Thus, this nation must ban the practice of creating embryos purposefully for stem cell research.

Implementation:
The administration must support the drafting and Congressional passage of a bill on lab creation of human embryos expressly for the purpose of research.

DEFER – On Using Electively Aborted Fetal Material
The government should not take a position that either encourages or discourages abortion given the deep divide in America. Concerns exist about creating incentives for abortion. We therefore duly note that abortion is the controversy that inhibits substantial action on embryonic stem cell research. As Congress and the Executive branches are aware, the abortion controversy has debilitating spillover affects on stem cell research policy.

Implementation:
It should be publicized that the abortion controversy creates these impasses in regards to important governmental policy on stem cell research. Leaders across the nation must cease to be cowardly and make a concerted effort to intellectually discuss point of life matters. This discussion is well overdue as is true leadership on this matter.

DEFER – On Spare Embryos Left From IVF Procedures
Similar to the abortion issue, IVF policy is too charged of an issue to recommend a formal position. Until there is a larger dialogue on the ethical application of in vitro fertilization and a

formal policy that governs this technology, there cannot be a policy on IVF as applied to stem cell research.

Implementation:

The Administration should make clear that once again stem cell research policy is held up by failures to address other policy matters. In this case, it must be made clear that IVF procedures should be examined to determine what is ethical and what is not.

Stem cell research is not its own policy. It is closely linked with many of the other bioethics policies that must be incorporated into a national bioethics plan. It is important to understand that America is currently in a serious discussion on the point of life. Final decisions on these maters should not be made solely by presidential orders or through court decisions, but should be handled within legislative and social dialogues. These debates should be opened to all interested within the community, including the academic, religious, young and old, and scientific. Much of this will in fact begin at the state level. As an example, the Kansas Legislature has directed its Attorney General to bring a case to the Kansas Supreme Court to determine when life begins. A grassroots discussion of this topic should not be put aside during other domestic and international distractions.

We have focused on stem cell research but many of these issues have broader implications for society. Until the United States makes a concerted effort to make a decision or take a stance on aborted fetuses and the use of IVF embryos currently unused, we cannot address further issues. It is important for us to create public value and prescribe where possible, the moral course and position for a world leading nation like ours.

APPENDIX I -- GLOSSARY OF TERMS

Activation—the signals sent within the acolyte cell that a sperm has fertilized the oocyte, or in the case of cloning, the molecular mimicry of the sperm's activity to initiate development.

Adult Stem Cells—stem cells that dwell in the adult body and are far less versatile than embryonic stem cells. Each type generates replacement cells for the particular tissue in which it is found. Scientists are trying to see if adult stem cells can be reprogrammed to produce cells beyond their normal range.

Allogenic—biological materials such as genes, proteins, cells, tissues, or organs used for transplantation and derived from another donor individual of the same species as the recipient.

Apheresis—any procedure in which blood is withdrawn from a donor, a portion (plasma, leukocytes, platelets, etc.) is separated and retained and the remainder is re-transfused into the donor. It includes leukapheresis, plateletpheresis, plasmapheresis, etc.

Assisted Reproductive Technology (ART)—fertility treatments that involve a laboratory handling eggs or embryos, such as in vitro fertilization.

Autologous—biological materials such as cells, tissues, or organs used for transplantation and derived from the recipient himself.

Autologous Regenerative Medicine—transplantation of cells, tissues, or organs derived from and genetically essentially identical to the recipient himself.

Blastocyst—a hollow sphere of some 250 cells that develop four to five days after an egg is fertilized. Inside is a clump of about 30 cells, the inner cell mass, from which the embryo develops. When removed and grown in a laboratory dish, cells from the inner cell mass are called embryonic stem cells. They can be changed while being cultured.

Bone Marrow—a highly vascular, modified connective tissue found in the long bones and certain flat bones of vertebrates that is the origin of blood cells.

Cell Cycle—the life cycle of a cell, usually divided into the phase when DNA is replicated (S phase), the phase when the cell actually divides into two cells (M phase), the two intervening gap phases (G_1 and G_2) and a non-dividing state called "quiescence" (G_0).

Cellular Aging—most cells in the human body can replicate only a finite number of times and then cease dividing in what is called cell aging, or cell senescence.

Chimera—an animal made of cells from what would normally be two separate animals each with unique DNA.

Chromosome— nucleic acid protein structures in the nucleus of a cell, which contains DNA, the carrier of hereditary information. Human cells have 46 chromosomes.

Cleavage—the process of cell division in the very early embryo before it becomes a blastocyst.

Clone—an organism having the same nuclear genes as another organism.

Cloning—creating a genetically identical organism, through any of several techniques. Dolly the sheep, the first mammal to be cloned, was created by inserting DNA from the nucleus of a sheep mammary gland cell into an egg cell emptied of its own nuclear DNA.

Cryostorage—storage in frozen form.

Cytoplasm—cells are often thought of being composed of a small entity called the nucleus containing the DNA that resides within a larger "sack" of molecules called the cytoplasm within which many cellular processes occur.

Deoxyribonucleic Acid (DNA)—the blueprint of life composed of four "letters" A, C, T, and G that in their unique ordering make a molecular code for the organization of life.

Differentiation—the process in which a stem cell generates a cell with a specialized function. The process begins when certain genes are activated and others silenced, causing the bland, shapeless stem cell to change into some other type of cell, such as heart, tissue, liver, or muscle.

Embryo—the earliest stage of development from the single cell to implantation in the uterus.

Embryonic Germ Cells—embryonic cells that are set aside and protected from maturing. They migrate through the fetus to the ovary or testes, where they form the egg and sperm cells. If removed from the fetus and grown in culture, they behave much like embryonic stem cells.

Embryonic Stem Cells—derived from the inner cell mass of a blastocyst, a 4 to 5-day old embryo.

Enucleation—the removal of the nucleus from a cell. Because the egg cells often used in cloning are in a special stage called MII oocytes and don't actually have a nucleus, but rather have free chromosomes, the term is used loosely for the removal of the nuclear DNA.

Fibroblast—a cell commonly grown in the laboratory because of the ease with which they can be cultured and made to proliferate.

Gamete—a reproductive cell, egg or sperm.

Gene—a small region of the strand of DNA that often provides the instructions for a single protein molecule. It is the basic unit of heredity.

Genetic Programming—the precise engineering of the genome of animals.

Genomics—the science of identifying the sequence of DNA in various species, and subsequent processing of that information.

Germline—the lineage of cells that connect the generations. The sperm and the egg are examples of germline cells.

Immortalization—while human cells generally have a finite capacity to divide, they can occasionally be made to divide without limit, usually by restoring telomeres through the protein telomerase. Cells that divide without limit are said to be immortal. The process of transforming a mortal cell to immortality is immortalization.

Implantation—the process in which the embryo becomes attached to the inside of the uterus, usually at 7 to 10 days in humans.

In Vitro—done outside the body.

In Vivo—done within the living body.

Leukapheresis— apheresis procedure applied to remove normal or abnormal white blood cells.

Meiosis—the formation of germ cells where the chromosome number is reduced in half.

Mitosis—the process of cell division where the DNA is replicated and one cell becomes two complete cells.

Mutation—a change in a gene, leading in some cases to deformity or disease.

Nuclear Transfer—a general term for the process of cloning where the genetic information from a body cell is transferred to an egg cell whose DNA is removed.

Nucleus—the core of a cell that contains the DNA.

Oocytes—the diploid egg cell before meiosis is complete.

Parthenogenesis—reproduction in which the egg develops into an embryo without fertilization. Parthenogenesis does not occur in mammals, but scientists can use chemicals or electricity to stimulate the eggs of certain animals into dividing as if they had been fertilized. One company has started experiments with human eggs.

Plasma—the liquid portion of blood, excluding the cellular elements but including the proteins.

Plasmapheresis— apheresis procedure applied to remove plasma.

Platelets—cell fragments in blood, which are involved in blood clotting.

Pluripotent—a stem cell that can become numerous cell types.

Primordial Germ Cells—totipotent stem cells, such as embryonic stem cells, embryonic germcells and other cells capable of forming any cell type in the body.

Primordial Stem Cells—a totipotent cell that comes from a pre-implantation embryo. Because it is undifferentiated, it has the potential of transforming into all cell types.

Promoter—the region of DNA near a gene that prompts the gene to be "on" or "off".

Quiescence—the resting phase of the cell cycle.

Recombinant DNA Technology—the technique that allows the cutting and splicing of DNA in a precise manner allowing the engineering of DNA sequence.

Regenerative Medicine—repairing the body by harnessing its own repair mechanisms (stem cells and signaling proteins) to renew damaged tissues and organs.

Somatic Cell—a body cell, as opposed to a germ line cell.

Stem Cells—non-specialized cells that have the capacity to self-renew and to differentiate into more mature cells.

Superovulation—the stimulation of the ovary to release more than the normal number of egg cells.

Telomerase—the linear ends of the DNA molecule of most species. In the case of mammals, the ends are composed of the sequence "TTAGGG" repeated thousands of times. Telomeres are a "clock" of cellular aging, shortening over time in many cell types.

Therapeutic Cloning—the new idea of repairing patients with their own cells, making a skin cell, say, turn into heart cells to repair the heart. This would be accomplished by inserting the nucleus of a patient's skin cell into a donated human egg cell without its own nucleus. The egg cell would reprogram the skin cell nucleus back into its totipotent state. After the egg had become a 5-day-old embryo, embryonic stem cells would be cultured and changed into heart cells for injection into the patient.

Totipotent—a stem cell that can become all cell types.

Telomere—the linear ends of the DNA molecule of most species. In the case of mammals, the ends are composed of the sequence "TTAGGG" repeated thousands of times. Telomeres are a "clock" of cellular aging, shortening over time in many cell types.

Transgenesis—the stable introduction of modified genes or genes from another animal or species into an animal's genome.

Xenotransplantation—the transfer of cells or tissues from one species to another.

APPENDIX II -- KEY DOMESTIC BIOTECH PLAYERS

Geron Corporation, is a relatively small biopharmaceutical firm located in Menlo Park, California, which focuses on discovering, developing and commercializing therapeutic and diagnostic products for applications in oncology and regenerative medicine, and research tools for drug discovery.[74] According to CNN analyst reports, it is currently a strong buy on the stock market.[75] Geron's product development programs are based upon three patented core technologies: telomerase, human embryonic stem cells and nuclear transfer.[76] It was the first firm to mobilize the potential of stem cell research here in the US. The firm funded the University of Wisconsin's research (led by Dr. Gearhart) that isolated human embryonic stem cells derived from the tissue of aborted fetuses, embryos and frozen eggs that had been discarded from fertility clinics after parents had already had the children and decide that they no long wanted the embryos. Geron has provided 7 of the 78 embryonic stem cells lines[77] for public sector research.

Another key player is BresaGen[78]. This is an Australian biotechnology company which has offices and laboratories in Georgia USA and is represented by three divisions; Protein Pharmaceuticals, Cell Therapy and Reproductive Biotechnology. BresaGen's Cell Therapy division has three major programs including human stem cell based in Athens, GA, USA. This division aims to be the first to bring a package of proprietary cells and proprietary delivery and imaging technology to the market. This 'would enable the company to standardize and establish the procedure amongst clinicians, and thereby make it difficult for new entrants into the market and furthermore, give BresaGen a long-term dominant position in the market.[79]' BresaGen has 4 lines in the NIH embryonic stem cell registry.[80]

The third key player is Advanced Cell Technology[81] in Worcester, Massachusetts. This company is involved in the research and development of Nuclear Transfer technologies for human therapeutics and animal cloning. This firm in collaboration with researchers from Wake Forest University School of Medicine, have recently been in the spotlight for developing a large variety of specialized cell types — including heart and brain cells — from embryonic monkey stem cells through parthenogenesis.[82] In one experiment, a high proportion became brain cells that produce a chemical called dopamine, the type of cell that is damaged by Parkinson's disease. Although these embryos have not survived for long, a few have reached the blastocyst stage, which consists of about 100 cells. These are sufficient for researchers to extract some of the inner cells and create a long-lived line of stem cells, capable of being transformed into many different types of tissue.[83]

A fourth key player is WiCell a nonprofit organization set up under Wisconsin Alumni Research Foundation (WARF). This organization currently has 5 embryonic stem cell lines in the NIH

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[74] http://www.geron.com/
[75] CNN Money http://money.cnn.com/news/companies/firstcall/GERN.html
[76] http://dir.yahoo.com/Business_and_Economy/Business_to_Business/Scientific/Biology/Biotechnology/Geron_Corporation/
[77] As of March 29, 2002 see http://escr.nih.gov/
[78] http://www.bresagen.com.au/
[79] http://www.bresagen.com.au/cell.asp
[80] As of March 29, 2002 see http://escr.nih.gov/
[81] http://www.advancedcell.com/
[82] Wake Forest University Baptist Medical Centre *Researchers Develop Primate Stem Cells from Unfertilized Embryo* 01/31/2002 http://www.wfubmc.edu/news_sys/fullstory.php?articleid=1661
[83] Carey, John and Licking, Ellen *The Stem-Cell Debate Just Got Thornier* February 1, 2002 commentary Business Week online http://www.businessweek.com/bwdaily/dnflash/feb2002/nf2002021_8062.htm

registry[84]. Non-profit researchers can pay $5,000 (U.S.) or $6,000 to purchase one embryonic stem cell line. For those seeking to commercialize their discoveries (i.e. make a product or therapy from a discovery using Wisconsin Stem Cells) a commercial license is required. However, the investigator or researcher who makes the discoveries is free to patent and publish the discoveries.

The last key player is CyThera Inc. a private biotechnology company in San Diego, California. This firm focuses on developing cell replacement therapies and a technology platform that have the potential to treat a wide range of human degenerative diseases including liver disease, Parkinson's disease, macular degeneration, and stroke. The company's initial focus will be pancreatic islet transplantation for the treatment of diabetes. Accordingly, CyThera's first product will be allogenic (donor) cell replacement therapy (a cell transplant product produced from human embryonic stem cells) to treat severe diabetics and immune suppressed diabetic patients.[85] CyThera has 9 lines available on the NIH registry.

[84] As of March 29, 2002 see http://escr.nih.gov/
[85] http://www.cytheraco.com/

APPENDIX III -- HUMAN CLONING DESCRIPTION

Somatic cell nuclear transfer is yet another possible means to produce pluripotent stem cells. Scientists have performed studies using animal cells in which the nucleus is removed from the animal egg. Then, under delicate conditions, a somatic cell is placed next to the altered egg and the two are fused. The resultant cell is believed to be capable of forming a blastocyst, which in theory would produce pluripotent cells in its inner cell mass. Any method of forming a human blastocyst will in theory have the potential to be a source of pluripotent stem cells.[86]

Stem cell biology has come full circle, however, with one of the two groups that cultured the first human embryonic stem cells. In 1998 reporting on the isolation of the most promising type of human stem cell yet: embryoid body-derived cells, or EBDs. This may be a viable alternative to pluripotent stem cells. EBDs appear to be in a "ground state," retaining the potential to specialize into nerve, blood, muscle, or more, yet retaining chromosomal and cell cycle normalcy—a long sought combination. EBDs must be isolated and cultured. They can also be frozen, cloned, and genetically manipulated.[87]

This is done by taking early embryoid bodies (from cell culture) and dissociating them into single cells on a plate, then exposing them to differing media (serum-based versus growth factor-based) and attachment surfaces (plastic, bovine collagen, or human extracellular matrix extract) that has been reported to be nurturing for neuronal, hematopoietic, or other cell types. The single cells are then taken and cloned out, so that one cell yields one cell line. The clonal lines have gene expression profiles for early differentiation.

This experiment was the next logical step to take, because pluripotent (ES) stem cells have difficulty being transplanted into anything because of the issue of tumor formation. These cell lines were derived with the intent to have a gene expression pattern that says that they are part of a lineage. Sure enough, these cells do, and they have a finite lifespan. They go through 70 to 80 passages, and then the cell lines expire. In essence, scientists are on the pathway toward cell specialization, but not to cancer. EBD cells implanted into mice lacking immune systems did not cause cancer.

These cells are fairly uniform in morphology, although they do express a variety of genes. There has been expression of neural or hematopoietic or endodermal marker genes. All the cells shared a common gene expression profile pattern. The meaning of this is unknown, but maybe this is like it is in vivo. It may mean that a cell must do this to begin differentiating, and then instructions from the environment—depending on whether they are put in an embryo, fetus, or adult—determine the fate of the cell and direct further development. This may make sense in light of all the stem cells that are being found in the adult. This is somewhat speculative.

Neural markers form first. This may be because neural tissue is one of the first to form in the embryo, and it is one of the easiest to form. But these may be more general types of markers than thought. It may be premature to talk about lineage-restricted markers (in light of recent demonstrations that bone marrow cells can migrate to and differentiate as brain, muscle, or liver cells). It will be interesting to go back into the embryo to see if cells in normal development have the array of markers seen in EBD cells, and to show that it is not iatrogenic, not an artifact.

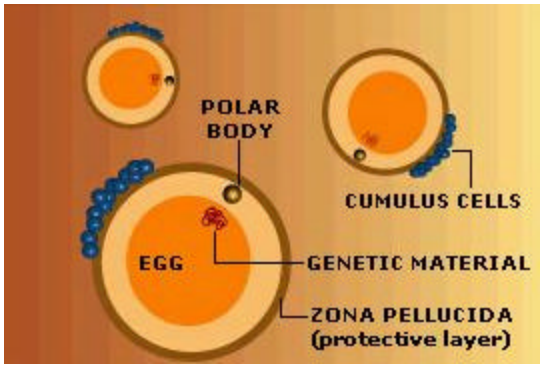
These cell lines are already being used in many transplant paradigms in the mouse. For example, a spinal cord injury model is created by viral destruction of motor neurons. The EBD cells are infused, and they migrate and form neurons. They seem to function. The animals begin to be able to bear weight on their limbs and to move their limbs. There have also been hematopoietic and

[86] "Stem Cells: A Primer", National Institutes of Health, May 2000.

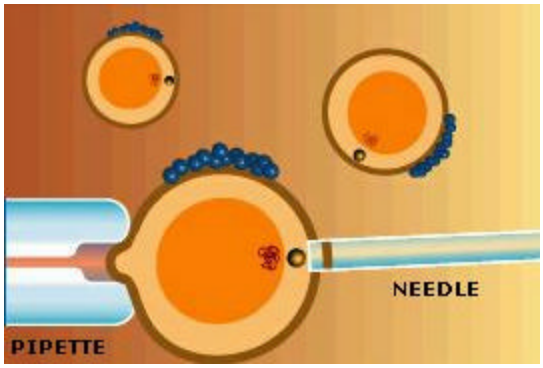
[87] R. Lewis, "New Workhorses of Stem Cell Technology", The Scientist, 15[2]:17, Jan. 22, 2001.

glucose responses. EBDs are much easier to culture and maintain than pluripotent embryonic stem cells, and therefore should require less embryonic or fetal material.[88]

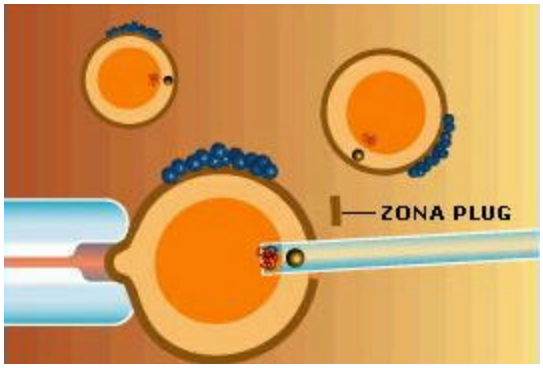
Human Cloning Diagram



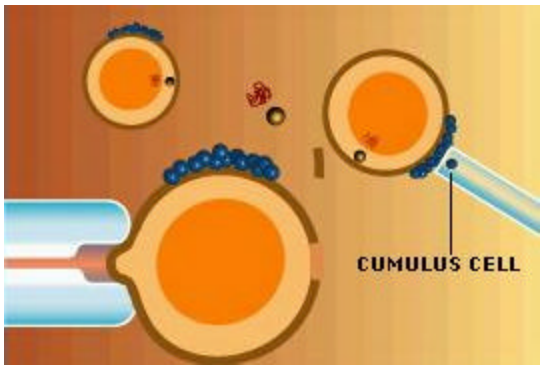
1 Eggs are coaxed to mature in a culture dish. Each has a remnant egg cell called the polar body and cumulus cells from the ovary clinging to it.



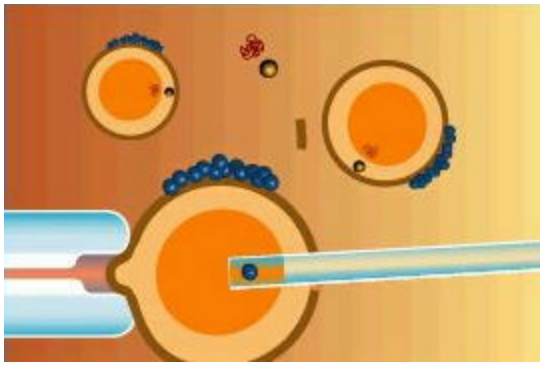
2 While an egg is held still with a pipette, a needle is used to drill through the zona pellucida, removing a plug.



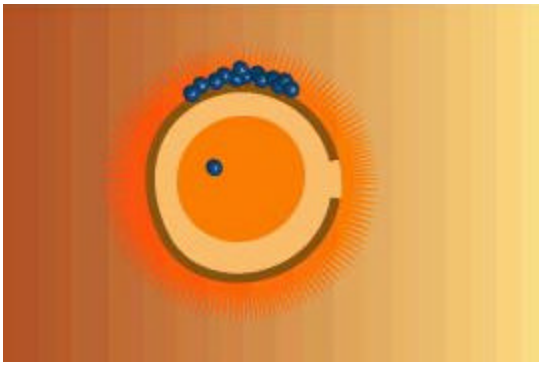
3 After ejecting the zona plug, the needle is inserted back in the egg through the hole to withdraw and discard the polar body and the egg's genetic material.



4 A cumulus cell from another egg is taken up into the needle. Cells called fibroblasts (or their nuclei) can also be used in this step.



5 The cumulus cell is injected deep into the egg that



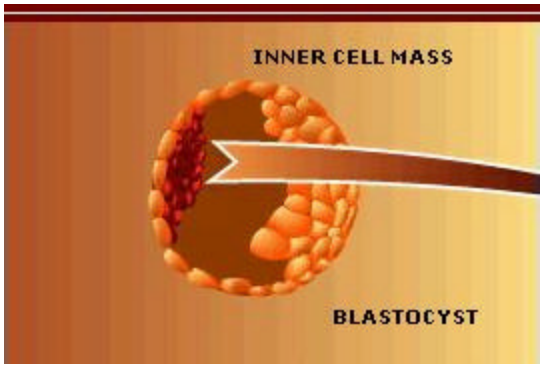
6 The injected egg is exposed to a mixture of

[88] R. Lewis, "New Workhorses of Stem Cell Technology", The Scientist, 15[2]:17, Jan. 22, 2001.

has been stripped of its genetic material.

chemicals and growth factors designed to activate it to divide.

7



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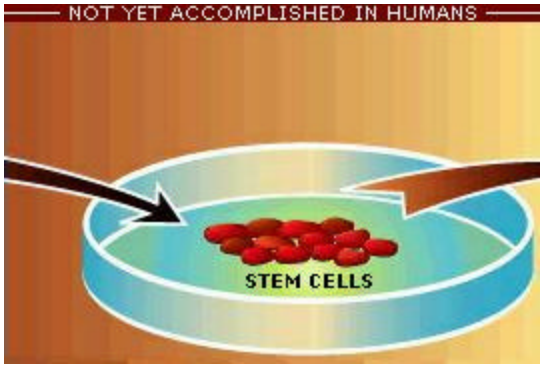
After roughly 24 hours, the activated egg begins dividing. The cells contain genetic material only from the injected cumulus cell.

By the fourth or fifth day, a hollow ball of roughly 100 cells has formed. It holds a clump of cells called the inner cell mass that contains stem cells.



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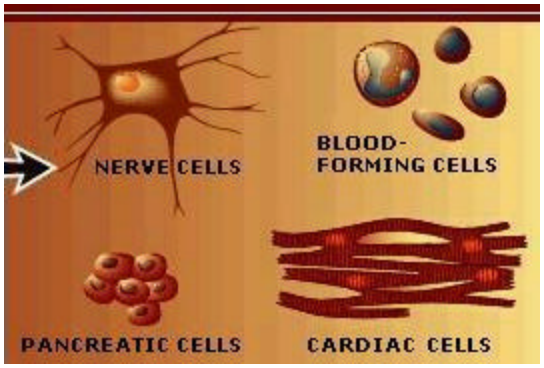

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The blastocyst is broken open, and the inner cell mass is grown in a culture dish to yield stem cells.

The stem cells, in turn, can be coaxed to grow into a variety of cells that might one day be injected into patients.[89]

[89] "Therapeutic Cloning: How It's Done", *http://www.sciam.com,* Scientific American, 2001.

APPENDIX IV -- STATE LAWS EXPLICITLY PROHIBITING HUMAN CLONING[90]

STATE LAWS EXPLICITLY PROHIBITING HUMAN CLONING				
State	**Year Enacted**	**Law Prohibits**		**Duration**
		Reproductive Cloning	Therapeutic Cloning	
California	1997	**X**		expires 2003
Louisiana	1999	**X**	*****	expires 2003
Michigan	1998	**X**	**X**	permanent
Rhode Island	1998	**X**	*****	expires 2003
Virginia	2001	**X**	**X**	permanent
*A separate state law governing embryo research could be interpreted to prohibit therapeutic cloning.				

[90] The Guttmacher Report of Public Policy *Not Waiting for Congress to Act, Some States Move to Ban Human Cloning* Volume 5, Number 1, February 2002
http://www.guttmacher.org/pubs/journals/gr050113.html

APPENDIX V -- <u>OUTLINE OF PRESIDENT BUSH'S POLICY</u>

In an attempt to educate the public and back up his decision, President George W. Bush outlined the issue for the nation in his August 9, 2001 speech:

1.) "Scientists believe further research using stem cells offers great promise that could help improve the lives of those who suffer from many terrible diseases…They believe stem cells derived from embryos have unique potential."
2.) "You should also know that stem cells can be derived from sources other than embryos – from adult cells, from umbilical cords that are discarded after babies are born, from human placenta…Many patients suffering from a range of diseases are already being helped with treatments developed from adult stem cells."
3.) "However, most scientists, at least today, believe that research on embryonic stem cells offer the most promise because these cells have the potential to develop in all of the tissues of the body."
4.) "Scientists further believe that rapid progress in this research will come only with federal funds. Federal dollars help attract the best and brightest scientists. They ensure new discoveries are widely shared at the largest number of research facilities and that the research is directed toward the greatest public good."
5.) "The United States has a long and proud record of leading the world advances in science and medicine that improve human life. And the United States has a long and proud record of upholding the highest standards of ethics as we expand the limits of science and knowledge."
6.) "Research on embryonic stem cells raises profound ethical questions, because extracting the stem cell destroys the embryo, and thus destroys its potential for life."
7.) "At its core, this issue forces us to confront fundamental questions about the beginnings of life and the ends of science. It lies at a difficult moral intersection, juxtaposing the need to protect life in all its phases with the prospect of saving and improving life in all its stages."
8.) "In recent weeks, we learned that scientists have created human embryos in test tubes solely to experiment on them. This is deeply troubling, and a warning sign that should prompt all of us to think through these issues very carefully."
9.) "Embryonic stem cell research is at the leading edge of a series of moral hazards." (Includes cloning.)
10.) "I strongly oppose human cloning, as do most Americans…I also believe human life if a sacred gift from our Creator. I worry about a culture that devalues life, and believe as your President I have an important obligation to foster and encourage respect for life in America…no one can be more certain that the science will live up to the hope it has generated."
11.) "As a result of private research, more than 60 genetically diverse stem cell lines already exist. They were created from embryos that have already been destroyed, and they have the ability to regenerate themselves indefinitely, creating ongoing opportunities for research. I have concluded that we should allow federal funds to be used for research on these existing stem cell lines, where the life and death decision has already been made…This allows us to explore the promise of stem cell research without crossing a fundamental moral line, by providing taxpayer funding that would sanction or encourage further destruction of human embryos that have at least the potential for life."

"I will also name a President's new Council on Bioethics [of leading scientists, doctors, ethicists, lawyers, and theologians and Chaired by Dr. Leon Kass (Univ. of Chicago)] to monitor stem cell research, to recommend appropriate guidelines and regulations, and to consider all of the medical and ethical ramifications of biomedical innovation."

APPENDIX VI -- NIH EMBRYOINIC STEM CELL REGISTRY.[91]

Name	Number
BresaGen, Inc., Athens, Georgia	4
CyThera, Inc., San Diego, California	9
ES Cell International, Melbourne, Australia	6
Geron Corporation, Menlo Park, California	7
Göteborg University, Göteborg, Sweden	19
Karolinska Institute, Stockholm, Sweden	6
Maria Biotech Co. Ltd. – Maria Infertility Hospital Medical Institute, Seoul, Korea	3
MizMedi Hospital – Seoul National University, Seoul, Korea	1
National Centre for Biological Sciences/ Tata Institute of Fundamental Research, Bangalore, India	3
Pochon CHA University, Seoul, Korea	2
Reliance Life Sciences, Mumbai, India	7
Technion University, Haifa, Israel	4
University of California, San Francisco, California	2
Wisconsin Alumni Research Foundation, Madison, Wisconsin	5

[91] http://escr.nih.gov/ As of March 29, 2002 there are now 78 lines in total. There are 14 new lines since President Bush's announcement in 2001. These include 7 from Geron, US, 1 more from Karolinska, Sweden and 6 from 3 different organizations in Seoul, Korea. 22 lines are from US firms that is BresaGen, Geron, Cythera, WARF, UCSF

APPENDIX VII -- BIBLIOGRAPHY

Antonio Regalado, "Stem Cells Without Cloning," *The Wall Street Journal*, Section B1, February 1, 2002.

Canadian Institutes of Health Research, "Human Stem Cell Research: Opportunities for Health And Ethical Perspectives," 2001.

Carol Morello, **"**Center Shifts Stem Cell Approach; Va. Institute Will Stop Creating Human Embryos for Research," *Washington Post*, January 18, 2002, Page A14.

Cecil Connolly, "Conservatives Pressure For Stem Cell Funds Builds," *The Washington Post*, July 2, 2001, Page A1.

Cecil Connolly, Justin Gillis, and Rick Weiss, "Viability of Stem Cell Plan Doubted," *The Washington Post*, August 20, 2001, Page A1.

Ellen J. Flannery and Gail H. Javitt, "Analysis of Federal Laws Pertaining To Funding Of Human Pluripotent Stem Cell Research," Volume II: Commissioned Papers (January 2000), in *National Bioethics Advisory Commission 1998–1999 Biennial Report.* http://bioethics.georgetown.edu/nbac/pubs/Biennial98-99.pdf

Geron Corporation, "Human Embryonic Stem Cells: Source for Replacement Tissues," http://www.geron.com/02.02_hesc.html2001.

James O. Mason, Assistant Secretary for Health, statement before The Senate Committee On labor And Human Resources, *Finding Medical Cures: The Promise Of Fetal Tissues Implantation Research*, Hearing on S.1902 102d Cong., 1st Sess. 4 (1991).

Jeff Levine, "New Guidelines to Permit Stem Cell Research," *WebMD*, August 23, 2001. Dr. Paul Berg of Stanford University during a debate with stem cell opponents on August 19, 2001.

John Carey and Ellen Licking, "The Stem-Cell Debate Just Got Thornier," *Business Week Online*, http://www.businessweek.com/bwdaily/dnflash/feb2002/nf2002021_8062.htm February 1, 2002.

John Carey and Ellen Licking, "Commentary: The Stem-Cell Debate Just Got Thornier," *Business Week Online*, http://www.businessweek.com/magazine/content/02_06/b3769070.htm February 11, 2002.

Jon Entine and Sally Satel, "Inserting Race Into the Stem Cell Debate," *The Washington Post*, September 9, 2001. Page B1.

Justin Gillis and Connolly, Cecil. "Stem Cell Research Faces FDA Hurdle," *The Washington Post*, August 24, 2001, Page A1.

Robert Klupacs, Cecil Connolly, Justin Gillis, and Rick Weiss, "Viability of Stem Cell Plan Doubted," *Washington Post*, August 20, 2001, Page A1.

Jeff Levine, "New Guidelines to permit Stem Cell Research," *WebMD*, August 23, 2001.

Justin Gillis and Cecil Connolly, "Stem Cell Research Faces FDA Hurdle," *The Washington Post*,

August 24, 2001, Page A1.

Lee Silver, "Watch What You Are Calling An Embryo," *The Washington Post,* August 19, 2001, Page B4.

Maria Freire, US Senate Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies Statement on National Institutes of Health, August 1, 2001.

McQueen, Anjetta. "Parents Hope Embryo Kids Prevent Stem Cell Opposition," *The Los Angeles Times,* July 17, 2001.

Memorandum from the President to the Secretary of Health and Human Services, January 22, 1993 (reprinted in 58 Fed Reg 7457 [feb. 5, 1993].

National Institute of Health, *Human Fetal Tissues Research Supported By The NIH in Fiscal Year 1990,* 1-4 (1992); Helen M Maroney, "Bioethical Catch 22: The Moratorium On Federal Funding Of Fetal Tissues Transplantation Research And The NIH Revitalization Amendments." *9 J. Contemp. Health L. and Pl'y*, 485,487 n.11 (1991) (citing NIH document).

National Institutes of Health, "Stem Cells: A Primer," May 2000 http://www.nih.gov

National Institutes of Health Research Initiatives /Programs Of Interest
http://www4.od.nih.gov/officeofbudget/FundingResearchAreas.htm

President George W. Bush, Senate Testimony footnote, August 9, 2001.

President George W. Bush. "Remarks On Stem Cell Research," August 9, 2001. Transcript of the National Address/CNN.

Pub. L No. 103-43, Title I, ss111,112,121(b)(1), 107 Stat. 122,129,131,133 (1993) (codified at 42 USC ss289g,289g-1, 198g-2 [Supp. 1997]).

Pub. L. No. 103-43, s121 (c) Stat. 122,133 (1993) (codified at 42 USC 289g note); 59 Fed Reg. 28276 (June 1, 1994) (rescinding 45 CFR 46.204(d)).

Pub. L. No. 103-43, s121©, 107 Stat. 122,133 (1993) (codified at 42 USC 289g note); 59 Fed Reg. 28276 (June 1, 1994) (rescinding 45 CFR 46.204(d)).

Pub. L. No. 105-277, 112 Stat. 2681 (1998).

Pub. L. No. 105-277,Div.A. s101(f), Title V, s511(a), 112 Stat. 2681-386. Division A, s101(f) of the bill contains appropriations for the Departments of Labor, Health and Human Services, Education and related agencies.

Pub. L. No. 105-277,Div.A. s101(f), Title V, s511(b).

R. Lewis, "New Workhorses Of Stem Cell Technology," *The Scientist,* 15 [2]:17, (January 22, 2001) sponsored by Senator Specter.

R. Southwick, "95 Lawmakers Ask Bush To Allow Federal Aid For Stem-Cell Studies," T*he Chronicle of Higher Education,* Mar 30, 2001.

Rick Weiss, "Scientists Use Embryos Made Only For Research," *The Washington Post,* July 11, 2001, Page A25.

Rick Weis, "Broader Stem Cell Research Backed; Key Science Group Differs With Bush," *The Washington Post*, September 11, 2001, Page A01.

Robert Goldberg, "Two Thumbs Up," *National Review Online*, August 10, 2001.

Robert Kuttner, "The Great Obfuscator," *The American Prospect,* September 10, 2001, Pg. 2.

Scientific American, "Therapeutic Cloning: How It's Done," 2001. http://www.sciam.com

Sean Martin, "Bush's Stem Cell Decision: What Will It Mean?" *WebMD Medical News,* August 9, 2001.

Sean Martin, "Stem Cell Debate Rages On Capitol Hill." *WebMD Medical News,* July 17, 2001.

Sean Martin, "Stem Cell Pressure Builds On Bush." *WebMD Medical News,* July 18, 2001.

Steve Connor, "Britain Set To Become A 'Magnet' For Top US Scientists," *Independent News,* February 15, 2002. http://news.independent.co.uk/world/science_medical/story.jsp?story=120057

The LabRat.com review on Geron http://www.thelabrat.com/review/geron120399.shtml

The Chronicle of Higher Education, The Clinton Administration Cleared The Way For The Use Of Federal Funds In The Controversial Field, Vol. 47, Issue 2 (Sep 8, 2000), p A38.

The Chronicle of Higher Education, Volume:47, Issue:36 (May 18, 2001), P.A30.

The White House, *Fact Sheet: Embryonic Stem Cell Research,* August 9, 2001.

US Senate Fact Sheet. Senate Subcommittee Hearing on Health and Human Services. August 9, 2001.

William B. Schwartz, "Advances In Medical Technology Are Causing A Crisis In Health Care In America" in *Health Care In America: Opposing Viewpoints,* Carol Wekesser ed., (San Diego, CA: Greenhaven Press, 1994).

39 Fed Reg. 18914 (May 30, 1974) (establishing 45 CFR Part 46); 40 Fed Reg 11854 (Mar. 13, 1975) (amending and readopting Part 46).

40 Fed Reg 33526 (aug 8 1975) ibid.

40 Fed Reg 33526, 33530 (aug 8 1975) (establishing Subpart B of 45 CFR Part 46).

40 Fed Reg 33530 (aug 8 1975) ibid. (codified at 45 CFR s46.210) (1998).

40 Fed Reg 33530 (s46.210), 33532 (definition of dead fetus).

40 Fed Reg 33526, 33529 (Aug 8, 1975) (adding 45 CFR s46.204(d).

42 USC s289g1(a) (Supp. 1997).

59 Fed Reg 45293 (Sept.1, 1994).

APPENDIX VIII -- ABOUT THE AUTHORS/ACKNOWLEDGEMENTS

Lance Iverson focused on the implications of stem cell research on American public health. He will graduate with a Master of Public Policy degree from Pepperdine University in 2002. Lance received a Bachelor of Arts degree from the University of Minnesota in 1998 with a major in Political Science and a minor in Criminal Justice, Law, and Deviance.

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