EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20502

June 25, 1999

MEMORANDUM FOR HARRIET S. RABB
MARCY WILDER
HHS OFFICE OF THE GENERAL COUNSEL

FROM: RACHEL E. LEVINSON REL
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
EXECUTIVE OFFICE OF THE PRESIDENT

SUBJECT: NIH Funding Guidelines for Stem Cell Research

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Thank you for the opportunity to comment on the guidelines at this point in their development. It would be very helpful if you could let me know as soon as you get a publication date from the *Federal Register*. Please let me know if I may be of further assistance.

cc: Chris Jennings
Devorah Adler
Arthur Bienenstock
Jeff Smith
Holly Gwin
Cliff Gabriel
Joanne Tornow

Date: _____

FAX

Health Division

Office of Management and Budget
Executive Office of the President
Washington, DC 20503

To: DEVORAH
Fax: 65557

From: MATT

Number of Pages (excluding cover): 2

Subject: INTERNET DRUGS

Voice Numbers:

Health Division (Front Office)	202/395-4922
Health & Human Services Unit	202/395-4925
Health Programs & Services Branch	202/395-4926
Health Financing Branch	202/395-4930

Fax Numbers:

Health Division (Front Office)	202/395-3910
Health Division (Room 7001)	202/395-7840
Health Division (Room 7002)	202/395-5648

Tuesday, June ~~22, 1999~~

CQ DAILY MONITOR

The Morning News Briefing, Updated Continuously on www.CQ.com/news

Democrats' Ploy Plows Into Agriculture Bill

Spending measure set aside after attempt to attach health care proposal; Amendment to State Department authorization nets day's only recorded vote

HILL NEWS

Democrats in the Senate dusted off last year's procedural playbook Monday, and made good on threats to attempt to attach patients' bill of rights (S 6) to the fiscal 2000 agriculture appropriations bill (S 1233).

Byron L. Dorgan, D-N.D., who presented S 6 as an amendment to the agriculture spending measure, was the first of a possible parade of Senate Democrats to try to stall legislation on the floor until a vote is guaranteed on the managed care bill.

Last year, Democrats repeatedly attempted to attach managed care legislation to other bills to force Republicans to vote on it.

Should a managed care bill come to the floor, the Democrats want approximately 20 amendments allowed per side. Republicans consider that amount unreasonable, and maintain that four to six amendments should be plenty.

Majority Leader Trent Lott, Miss., declared on the floor that Republicans would be "ready to go" when a "reasonable time agreement" can be reached with Democrats.

Lott next moved to block the Democrats by introducing as a counter-amendment a Republican managed care substitute (S 326). He then squashed the Democratic move by setting the agriculture bill aside, and moved to the next item on the week's agenda: the State Department reauthorization bill (S 886),

continued on page 3

Congress Wonders: Who's Minding the Internet Store?

House Commerce leaders to Probe FDA on potential for Abuse of on-line drug sales

THE PULSE OF CONGRESS

As Congress grows increasingly concerned about burgeoning Internet sales of prescription drugs, a House subcommittee plans to hold hearings on the issue next month.

"This has been on our radar screen for some time," said Fred Upton, R-Mich., chairman of the Commerce Subcommittee on Oversight. "It's clear that there's been some abuse."

While prescription drug sales generally are regulated by state law, the Internet moves the issue into the federal arena. But lawmakers say no one is aggressively monitoring the situation, and it is not clear which federal bureaucracy will take charge: the Justice Department, the Federal Trade Commission or the Food and Drug Administration (FDA).

Commerce Committee leaders are frustrated by the lack of communication from the executive branch about what the Clinton administration plans to do about Internet drug sales.

On June 14, Chairman Thomas J. Bliley Jr., R-Va.; ranking Democrat John D. Dingell, Mich.,

continued on page 5

TODAY AT A GLANCE

House Floor: Three bills are scheduled for action under suspension of the rules, along with a measure (HR 659) that calls for preservation programs with respect to historic battlefields. *(Convenes at 12:30 p.m.; no recorded votes until after 2 p.m.)*

Senate Floor: Consideration will resume on the State Department reauthorization measure (S 886), with a final vote anticipated on the measure; a cloture vote is scheduled on legislation (HR 975) that would impose quotas on steel imports; and debate will continue on the agriculture appropriations bill (S 1233). *(Convenes at 9:30 a.m.; first vote at 12:15 p.m.)*

Appropriations Work: Two Senate Appropriations panels will mark up the Treasury-Postal and Interior spending bills.

Budget Overhaul: House Appropriations will mark up a bill (HR 853) that would implement a number of changes aimed at streamlining the federal federal budget process.

Treasury Nomination: Senate Finance will vote on the nomination of Lawrence Summers as Treasury secretary and take up several trade measures that would ease some restrictions for Central American, Caribbean and sub-Saharan African countries.

Suspected Terrorists: A House Judiciary subcommittee is scheduled to mark up three bills, including legislation (HR 2184) calling for the deportation of aliens associated with terrorist groups or who have aided terrorist activity.

Policy Meetings: Senate Democrats and Republicans will hold their regular weekly policy luncheons; presidential contender George W. Bush will be the featured speaker at the Republican gathering.

(The complete Daybook begins on p. 7)

INSIDE ..... Tuesday

...son, Mich., and Ron Klink ... the Oversight Subcommittee ... Democrat, wrote to FDA ... Commissioner Jane E. Henney, ... demand that she provide them with information about what her agency and others are up to ...

"Presently, it remains unclear which federal agencies or departments are in charge, or what the responsibilities are for each agency," the lawmakers wrote.

They also complained that FDA staff would not brief committee staff on their activities yet — although they promised to do so later. "In light of the overall seriousness of this matter and the growing volume of Internet sites advertising and selling prescription drugs to the public, such a delay is unacceptable," the letter said.

The Commerce leaders demanded volumes of material from the FDA, ranging from all records relating to Internet drug regulation to information on a variety of Internet sites selling drugs and what, if anything, the FDA has done to substantiate the claims made by the companies. And they want it all by June 25.

— Elizabeth A. Palmer

Senate Unlikely to Act Before July 4th Recess on FAA Bill

House Transportation Chairman Bud Shuster, R-Pa., has won another round in his fight to fence off aviation funding, but an even bigger challenge lies ahead: the Senate.

Shuster last week garnered 316 House votes for his five-year, $59.5 billion Federal Aviation Administration (FAA) authorization bill (HR 1000), which carries the fence-off language. He ran roughshod over a powerful coalition of opponents, including Appropriations Chairman C.W. Bill Young, R-Fla.; Budget Chairman John R. Kasich, R-Ohio; Ways and Means Chairman Bill Archer, R-Texas; and Majority Whip Tom DeLay, Texas.

But the Senate is another matter.

"It's going to be a wild shootout between the House and the S... in ...

...recess. Senate leaders do not want to schedule the bill until Commerce, Science and Transportation Chairman John McCain, R-Ariz., and John W. Warner, R-Va., resolve a dispute about adding daily flights at Ronald Reagan Washington National Airport. That won't be easy. Warner resisted the new slots during consideration of the bill last year. Eventually, he agreed to an extra 24 flights per day. During full committee markup in February, McCain increased the number to 48.

The current, temporary FAA authorization is due to expire Aug. 6. As the process moves into July, pressure will build for another short-term extension. Senate aides already are saying there is not enough time to complete a conference before the deadline.

Shuster fought the last such extension vigorously, relenting only when House leaders gave him a guaranteed date for floor debate on HR 1000.

Because of term limits for committee chairman enacted by the House GOP as part of the "Contract With America" in 1995, Shuster will step down as full committee chairman at the end of 2000. A few more short-term extensions effectively would run out the clock on his tenure as chairman.

Aides on the Senate side think time is on their side, and as the August deadline draws closer, they will only gain leverage. "We don't have any problem waiting," said an aide to a senior Republican.

— Jeff Plungis

Quick Insights

• Not a Job for Upwardly Mobile

President Clinton shouldn't have too much trouble finding someone to step into Alice M. Rivlin's shoes as vice chairman of the Federal Reserve Board, but the nominee better have no delusions about the job. Alan S. Blinder, Rivlin's predecessor as vice chairman, notes that no Fed vice chairman has ever been named chairman. "There's no reason for a vice chairman to think he, or she in this case, would ever become chairman," Blinder said. Rivlin resigned to devote more time to her other job, chairman of the District of Columbia financial

People ON T

Elena Kagan has be... the U.S. Court of Appeal... of Columbia Circuit. Ka... ously clerked for the Su... Justice Thurgood Mars... from 1987 to 1988, most... as deputy assistant to t... domestic policy and de... the Domestic Policy Co... to 1999. Before that, she ... ciate counsel to the pres... to 1996. In 1993, she se... counsel to the Se... Committee during the ... hearings of Justice Ruth ...

From 1991 to 1995, ... the faculty of the ... Chicago Law School. B... was an associate at t... law firm Williams & ... 1989 to 1991.

Around the Ag...

★ **Sally Katzen** has ... ed by the president to b... tor of management at ... Management and Budge... currently the deputy as... nomic policy to the ... deputy director of ... Economic Council. Ka... service in the Clinton ... has included a stint as a ... the Office of Info... Regulatory Affairs at th... joining the administratio... a partner in the Washing... Wilmer, Cutler & Picker... specialized in regulatory ... issues.

Lobbyists A...

★ **Karen Frey** ... lic relations division of ... firm PriceWaterho... C... she will focus on the co... mation technology ... recently, Frey served ... public communicatio... American Electronics ... (AEA), a post she held f... year. AEA not nam...

Office of Policy
Food and Drug Administration
5600 Fishers Lane, HF-11
Rockville, MD 20857
Phone: (301) 827-3360
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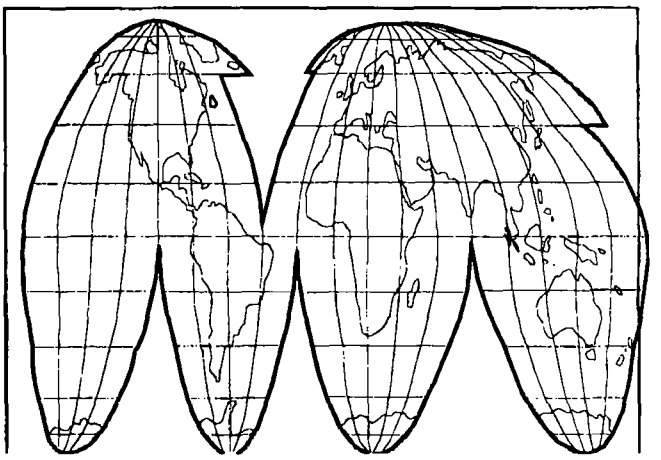

DATE: 6/30/99

TO: Devora Adler

FAX: (202) 456-5557

FROM: Jeffrey Shuren

NO. OF PAGES: (Including Cover Sheet) 3

COMMENTS:

DRAFT – May 28, 1999 (5:41PM)

EXECUTIVE ORDER TO ESTABLISH WORKING GROUP ON UNLAWFUL CONDUCT ON THE INTERNET

By the authority vested in me as President by the Constitution and the laws of the United States of America, including the . . ., it is hereby ordered as follows:

Section 1. Establishment and Purpose. There is hereby established a working group to address unlawful conduct that involves the use of the Internet ("Working Group"). The purpose of the Working Group shall be to prepare a report and recommendations concerning:

(a) The extent to which existing federal laws provide a sufficient basis for effective investigation and prosecution of unlawful conduct that involves the use of the Internet, such as the illegal sale of guns, explosives, controlled substances, and prescription drugs;

Elizabeth Ake

(b) The extent to which new technological tools, capabilities, resources, or legal authorities may be required for effective investigation and prosecution of unlawful conduct that involves the use of the Internet; and

(c) The potential for new or existing tools and capabilities to educate and empower parents, teachers, and others to prevent or to minimize the risks from unlawful conduct that involves the use of the Internet.

This review shall be undertaken in the context of current Administration Internet policy, which includes support for industry self-regulation where possible, technology-neutral laws and regulations, and an appreciation of the Internet as an important medium both domestically and internationally for commerce and free speech.

Section 2. Schedule. The Working Group shall complete its work to the greatest extent possible and present its report and recommendations to the President and Vice President within 120 days of the date of this order. Prior to such presentation, the report and recommendations shall be circulated through the Office of Management and Budget for review and comment by all appropriate federal agencies.

Section 3. Membership.

(a) The Working Group shall be composed of the following members:

(1) The Attorney General (who shall serve as Chair of the Working Group);
(2) The Director of the Office of Management and Budget;
(3) The Secretary of the Treasury;
(4) The Secretary of Commerce;
(5) The Secretary of Education;

(6) The Director of the Federal Bureau of Investigation;
(7) The Director of the Bureau of Alcohol, Tobacco and Firearms;
(8) The Administrator of the Drug Enforcement Administration;
(9) The Administrator of the Food and Drug Administration; and
(10) Other federal officials deemed appropriate by the Chair of the Working Group.

(b) The co-chairs of the Interagency Working Group on Electronic Commerce shall serve a liaison to and attend meetings of the Working Group. Members of the Working Group who are full-time federal officials may serve on the Working Group through designees.

Section 4. Administration. To the extent permitted by law and subject to the availability of appropriations, the Department of Justice shall provide the Working Group with funding, administrative services, facilities, staff, and other support services necessary for the performance of the functions of the Working Group.

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20502

June 25, 1999

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MARCY WILDER
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Holly Gwin
Cliff Gabriel
Joanne Tornow

DEPARTMENT OF HEALTH AND HUMAN SERVICES
THE GENERAL COUNSEL
PHONE: 202/690-7741
FAX: 202/690-7998

TO: CHRIS JENNINGS

DATE: 6/22/99

DEPARTMENT/OFFICE: DPC

PHONE: 202/ 456-5560

FAX: 202/ 456-5557

FROM: HARRIET S. RABB
GENERAL COUNSEL

COMMENTS:

PAGES INCLUDING COVER: 24

TO: Chris Jennings
Rachel Levinson

FROM: Harriet S. Rabb
Marcy Wilder
HHS Office of the General Counsel

SUBJECT: NIH Funding Guidelines for Stem Cell Research

DATE: June 22, 1999

Accompanying this note are the proposed NIH guidelines for federal funding of research using human pluripotent stem cells. You'll recall that the guidelines were developed by the Director of NIH's advisory group with input from NBAC.

NIH has put this set of guidelines into HHS clearance; we are simultaneously offering them to you for your reaction.

NIH proposes imminently to publish the guidelines in the Federal Register for comment.

Please get your thoughts to us (690-7741 or 690-6318) by COB Thursday, June 24.

Thanks.

(Billing Code 4140-01-P)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health

Draft National Institutes of Health Guidelines for Research Involving Human Pluripotent Stem Cells (June 1999)

SUMMARY: The National Institutes of Health (NIH) is requesting public comment on a document entitled "Draft National Institutes of Health Guidelines for Research Involving Human Pluripotent Stem Cells (June 1999." The purpose of these draft guidelines is to recommend procedures to ensure that Federally-funded research in this area is conducted in an ethical and legal manner. The NIH will not fund research using human pluripotent stem cells until final guidelines are published in the Federal Register and an oversight process is in place.

DATES: Written comments should be received by NIH by 60 days after the date of publication.

ADDRESSES: The NIH welcomes public comment on the Draft National Institutes of Health Guidelines for Research Involving Human Pluripotent Stem Cells (June ,1999), set forth below. Comments should be addressed to: Stem Cell Guidelines, NIH Office of Science Policy, 9000 Rockville Pike, Building 1, Room 218, Bethesda, MD 20892. Comments may also be sent by facsimile transmission to Stem Cell Guidelines, at (301) 402-0280, or by e-mail to: **WE NEED TO SET UP A SEPARATE MAILBOX OF THESE COMMENTS**

SUPPLEMENTARY INFORMATION: In November, 1998, two different groups of scientists reported the successful isolation and culturing of human pluripotent stem cells. These human pluripotent stem cells have an unlimited capacity to divide, and the ability to develop into most of the specialized cells or tissues in the human body.

This advance represents a major step forward in human biology and has generated much enthusiasm and interest among scientists and the public, particularly patients and their families. Because these cells can give rise to many different types of cells, such as muscle cells, nerve cells, heart cells, blood cells, and others, they are enormously important to science and hold great promise for advances in health care. For example, further research using human pluripotent stem cells may help scientists:

- Generate cells and tissue that could be used for transplantation. Human pluripotent stem cells may be stimulated to develop into many different specialized cells of the body, which may someday be used as replacement cells and tissue to treat many diseases and conditions including Parkinson's disease, spinal cord injury, stroke, burns, heart disease, diabetes, and arthritis.

- Improve our understanding of the complex events that occur during normal human development and also help us understand what goes wrong to cause diseases and conditions such as birth defects and cancer.

- Change the way we develop drugs and test them for safety and potential efficacy. New medications could be tested using human pluripotent stem cells, such as liver cells or skin

cells; only the drugs which are both safe and appear to have a beneficial effect would graduate to human testing.

These human pluripotent stem cells were isolated using two different methods. One group of scientists derived the pluripotent stem cells from early-stage embryos donated by people who were undergoing fertility treatment in an *in vitro* fertilization (IVF) clinic. Another group of scientists isolated the pluripotent stem cells from non-living fetuses obtained from pregnancies that had been terminated. In both cases, all of the individuals gave full informed consent for the embryos or fetal tissue to be used in research. Neither research project utilized federal funds. Because of the regenerative capacity of pluripotent stem cells, a single culture of human pluripotent stem cells could supply numerous other researchers.

Federal law currently prohibits the DHHS from funding human embryo research. In light of this legislative ban, the Director of the NIH sought a legal opinion from the DHHS Office of the General Counsel on whether DHHS funds may be used for research utilizing human pluripotent stem cells.

DHHS concluded that the Congressional prohibition on the use of DHHS funds for certain types of human embryo research does not apply to research utilizing human pluripotent stem cells because such cells are not embryos. The legal opinion also clarified that human pluripotent stem cells derived from non-living fetuses would fall within the legal definition of human fetal tissue and are, therefore, subject to certain Federal restrictions on the use of such tissue.

Thus, research using pluripotent stem cells derived from human embryos can be funded by DHHS. Research that generates and uses human pluripotent stem cells from non-living fetuses can also be

supported by DHHS, subject to existing law and regulation.

In view of the scientific and medical benefits that may result from research using human pluripotent stem cells, the NIH plans to fund research using these cells. It is essential that the Federal government play a role in funding and overseeing the conduct of this research, so that all scientists--both privately and federally funded--have the opportunity to pursue this important line of research. Federal funding will provide oversight and direction that would be lacking if this research were the sole province of privately funded industry and academe.

The NIH understands and respects the compelling ethical, legal, and social issues relevant tohuman pluripotent stem cell research and is sensitive to the need for stringent oversight of this research that goes beyond the traditional NIH scientific peer review process. In light of these issues, the NIH plans to move forward in a careful and deliberate way, prior to funding any research utilizing human pluripotent stem cells.

In an effort to ensure that any research utilizing human pluripotent stem cells is appropriately and carefully conducted, the NIH Director convened a Working Group of the Advisory Committee to the Director (ACD), NIH to advise the ACD on guidelines and oversight for research involving human pluripotent stem cells. Specifically, the NIH Director charged the Working Group with developing appropriate guidelines under which research involving the *derivation and use* of human pluripotent stem cells from *fetal tissue* and research involving the *use* of human pluripotent stem cells derived from early IVF *embryos in excess of clinical need* could proceed. In an effort to ensure that a broad spectrum of viewpoints are considered, the working group is

made up of individuals with varied expertise and experience, including basic and clinical scientists, ethicists, lawyers, clinicians, as well as patients and their family members. On April 8, 1999, the working group held a public meeting to discuss these guidelines. During the meeting, time was set aside for public comment; several groups came forward to speak, including the American Society of Cell Biology, the National Conference of Catholic Bishops; the Society for Developmental Biology, the Alliance for Aging Research and the House pro Life Caucus. The Executive Director of the National Bioethics Advisory Commission (NBAC) also presented comments reflecting the deliberations of the NBAC to date. The draft guidelines represent the results of these deliberations.

The text of the draft guidelines follows.

Draft National Institutes of Health Guidelines for Research Involving Human Pluripotent Stem Cells (June 1999)

I. Scope of Guidelines

These guidelines apply to research applications or proposals for National Institutes of Health (NIH) funding or support that involve the study of 1) human pluripotent stem cells derived (without NIH funding) from early human embryos, and 2) human pluripotent stem cells derived from human fetal tissue.

The DHHS is prohibited by appropriations law (P.L. 105-277, section 511,112 STAT. 2681-386) from using any appropriated funds "for the creation of a human embryo or human embryos for

research purposes or research in which a human embryo or embryos are destroyed, discarded or knowingly subjected to risk of injury or death...." The National Institutes of Health (NIH) asked the General Counsel of DHHS to clarify whether or not research *utilizing* human pluripotent stem cells is permissible under existing laws governing human embryo and fetal tissue research. After careful consideration, the DHHS concluded that because these cells are not embryos, current law does *not prohibit* DHHS funds to be used for research *utilizing* human pluripotent stem cells. The guidelines in this document identify the requirements that should be met before NIH funds can be used to support any research that utilizes human pluripotent stem cells. These guidelines also outline categories of this class of research that are ineligible for NIH funding.

II. Definitions for the Purposes of these Guidelines

Early embryo:

> The product of fertilization that has not implanted into a woman's uterus and has not yet reached the developmental stage when the mesoderm, one of the three major tissue types of the future fetus, begins to form. This defines the stage from fertilization until the appearance of the primitive streak at approximately 14 days.

Human pluripotent stem cells:

> Human cells that can divide for indefinite periods in culture without specializing; have the potential to develop into the three major primary tissue types; are isolated from early embryos or from fetal germ cells; and are not themselves embryos. Also known as human embryonic stem cell lines or human embryonic germ cell lines. More advanced

cells of more restricted potential derived from adult human tissues, such as human blood stem cells, are not included in this definition.

Totipotent cells:

Cells that can give rise to all the cell types found in an adult and embryo, including the trophoblast which forms the placenta. Such cells are able, without being combined with other cells, to give rise to a complete organism, including the extraembryonic tissues.

Attending Physician/Clinician:

Health care professional who cares for the woman who is seeking an abortion or the couple that is obtaining infertility treatment. This person may not be the "deriver", "supplier" or "investigator."

Obtainer:

Health care professional or other individual who, through interaction with a patient, obtains early human embryos or fetal tissue that become available as a result of medical care or treatment of the patient. This person may, or may not, be the "attending physician/clinician." This person may not be the "deriver", "supplier" or "investigator."

Deriver:

Individual who derives human pluripotent stem cells from early human embryos or human fetal tissue. This person may not be the "obtainer" or "attending physician/clinician." As long as the "deriver" does not use DHHS funds for equipment,

materials or salaries to derive pluripotent stem cells from human embryos, he/she may also be the "investigator."

Supplier:

Individual or organization who supplies human pluripotent stem cells to DHHS-supported investigators. For the purposes of Federally supported research, this person may not be the "obtainer" or "attending physician/clinician," but he/she may be the "deriver." This person may also be the "investigator," as long as he/she does not use DHHS funds for equipment, materials or salaries to derive pluripotent stem cells from human embryos.

Investigator:

Individual who conducts research *utilizing* human pluripotent stem cells. For the purposes of Federally supported research, this person may not be the "obtainer" or "attending physician/clinician." He/she may also be the "deriver," as long as he/she does not use DHHS funds for equipment, materials or salaries to derive pluripotent stem cells from human embryos.

III. Guidelines for Areas of Research with Human Pluripotent Stem Cells That Are Eligible For NIH Funding

A. Derivation and Utilization of Pluripotent Stem Cells From Human Fetal Tissue

Considerations for the Derivation and Use of Human Pluripotent Stem Cells Derived From Human Fetal Tissue

Unlike pluripotent stem cells derived from human embryos, Federal funds may be used to support research to derive pluripotent stem cells from human fetal tissue. However, the following rules should be followed. Pluripotent stem cells derived from human fetal tissue are considered human fetal tissue; therefore, the restrictions governing human fetal tissue research (42 U.S.G. 289g;45CFR46, Subpart B) have been incorporated into these guidelines. In addition, human pluripotent stem cells may not be used in therapeutic human fetal tissue transplantation research unless the investigator adheres to the human fetal tissue transplantation statutes (42 U.S.C. 289g-1, 289g-2(b)[1]).

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[1]42 U.S.G. 289g includes requirements that "human fetal tissue may be used only if the woman providing the tissue makes a statement, made in writing and signed by the woman, declaring that– (A) the woman donates the fetal tissue for use in research described in subsection (a); (B) the donation is made without any restriction regarding the identity of individuals who may be the recipients of transplantations of the tissue; and (C) the woman has not been informed of the identity of any such indivduals....In research carried out under subsection (a), human fetal tissue may be used only if the attending physician with respect to obtaining the tissue from the woman involved makes a statement, made in writing and signed by the physician, declaring that– (A) in the case of tissue obtained pursuant to an induced abortion– (I) the consent of the woman for the abortion was obtained prior to requesting or obtaining consent for a donation of the tissue for use in such research; (ii) no alteration of the timing, method, or procedures used to terminate the pregnancy was made solely for the purposes of obtaining the tissue; and (iii) the abortion was performed in accordance with applicable State law; (B) the tissue has been donated by the woman in accordance with paragraph (1); and (C) full disclosure has been provided to the woman with regard to– (I) such physician's interest, if any, in the research to be conducted with the tissue; and (ii) any known medical risks to the woman or risks to her privacy that might be associated with the donation of the tissue and that are in addition to risks of such type that are associated with the woman's medical care. (c) Informed Consent of researcher and donee–In research carried out under subsection (a), human fetal tissue may be used only if the individual with the principle responsibility for conducting the research involved makes a statement, made in writing and signed by the individual, declaring that the individual– (1) is aware that the tissue is human fetal tissue; (B) the tissue may have been obtained pursuant to a spontaneous or induced abortion of pursuant to a still-birth; (C) the tissue was donated for research purposes; (2) has provided such information to other individuals with responsibilities regarding the research; (3) will require, prior to obtaining the consent of an individual to be a recipient of a transplantation of the tissue, written acknowledgment of receipt of such information by such recipient, and (4) has had no part in any decisions as to the timing, method, or procedures used to terminate the pregnancy made solely for the purposes of the research.

Restrictions Governing Human Fetal Tissue Research

Activities involving human fetal tissue shall be conducted only in accordance with any applicable Federal, State or local laws regarding such activities.

There should be a clear separation between the patient/attending physician relationship and the procurement and use of tissue for research purposes. Decisions related to the abortion must be based solely on the needs and medical treatment of the patient, with no influence by the deriver, supplier or investigator on the medical treatment or the procedures used.

When tissue is obtained following an induced abortion, the attending physician should make a statement in writing declaring that:

- The consent of the woman for the abortion was obtained prior to requesting and receiving consent for a donation of the tissue for use in such research;

- No alterations of the timing, method, and procedures used to terminate the pregnancy were made solely for the purposes of obtaining the tissue;

- No inducements, monetary or otherwise, were offered to terminate the pregnancy for purposes of the activity.

It is unlawful for any person to knowingly acquire, receive, or otherwise transfer any human fetal

tissue for valuable consideration if the transfer affects interstate commerce[2] (42 U.S.C. 289g-2(a)).

Informed Consent

- Informed consent must be obtained from the woman donating the tissue.

- Protocols and informed consent documents for the donation of fetal tissue to be used to derive pluripotent stem cells from human fetal tissue must be approved by an IRB, as defined by the Common Rule (45 CFR part 46) or FDA regulations (21 CFR Parts 50 and 56). Investigators planning to utilize human pluripotent stem cells should obtain documentation of IRB approval.

- Laboratories from which derived stem cells are obtained should have written policies in place regarding the protection of privacy and confidentiality.

- The informed consent document should contain:

  - A statement that the fetal tissue will be used to derive human pluripotent stem cells for research.

[2]This has been interpreted to mean that it is unlawful for any person to sell, purchase, receive, or otherwise transfer human fetal tissue for profit over and above reasonable payments associated with the transportation, transplantation, processing, preservation, quality control, or storage of human fetal tissue, if the transfer affects interstate commerce.

- Information regarding the general type of human pluripotent stem cell research that will likely be conducted with the derived cells.

- A statement that the human pluripotent stem cells will be derived and used following established guidelines, and that the cells may be used, at some future time, for transplantation research.

- Disclosure of the possibility that the donated material may have commercial potential in the future, and a statement that the donor will not receive financial or any other benefits from any such commercial development in the future.

- Disclosure that the tissue and the derived cells may be used for future research, the specific nature of which is not known at the present time.

- Information on the extent to which privacy and confidentiality will be maintained.

- A statement that identifiers will be stripped immediately from all fetal tissue used to derive human pluripotent stem cells.

- A statement that donors will not get any information back regarding any subsequent testing on the tissue or derived human pluripotent stem cells.

- A statement that derived cells and/or cell lines (without any information that would

identify the donor or the fetus) may be kept for many years.

- A statement that, at all levels, the tissue and cells will be handled respectfully, as is appropriate for human tissue used in research, and that the tissue and cells will be disposed of in a manner appropriate to human pathological material.

- The responsibility for ensuring that full and informed consent was obtained for the use of fetal tissue for research lies with the deriver. The burden of demonstrating that the consent process was voluntary and free of coercion rests with the deriver.

B. The Utilization of Human Pluripotent Stem Cells That Were Derived From Early Human Embryos

Studies *utilizing* early human embryo-derived pluripotent stem cells may be conducted using DHHS funds, if the cells were derived from early human embryos that were in excess of clinical need and if the derivation is not carried out with DHHS funding.

Considerations for Research Utilizing Human Pluripotent Stem Cells That Were Derived From Early Human Embryos

The derivation of pluripotent stem cells from early human embryos can currently only be done in private laboratories that do not receive DHHS funding. To be eligible for DHHS funding of research utilizing human pluripotent stem cells derived from early human embryos, an

investigator should obtain the cells only from suppliers who follow these practices:

- Human pluripotent stem cells may be derived only from embryos that were created specifically for infertility treatment and are in excess of clinical need of the donating couple. Investigators planning to utilize pluripotent stem cells derived in the private sector from early human embryos should obtain documentation from the deriver or supplier that the embryos were created for infertility treatment.

- When early human embryos are donated by couples in infertility programs, the infertility clinic and/or its affiliated laboratory must have written practices in place to ensure that there is no undue incentive or even subtle pressure to donate. The voluntary nature of such donations is essential, and under no circumstances should individuals who do not wish to donate their embryos ever feel pressured to do so. Discounted infertility treatment in exchange for consent to donate for research is considered a financial incentive and is prohibited.

- Consent may be obtained from the parents only after it has been established that the embryos in question are in excess of clinical need of the donating couple. For this reason, and to allow potential donors time between the creation of the embryos for infertility treatment and the decision to donate, only frozen early human embryos should be used to derive human pluripotent stem cells. Furthermore there should be a clear separation between the patient/attending physician relationship and the deriver as well as the investigator. The embryo should be created only for purposes of infertility treatment, with

no influence by the deriver or the investigator on the treatment or procedures used. Investigators who plan to utilize pluripotent stem cells derived in the private sector from early human embryos should obtain documentation from the deriver/supplier of the cells that the couple was approached in this way and that only frozen embryos, no longer needed for infertility treatment, were used.

- Laboratories from which derived stem cells are obtained should have written policies in place regarding the protection of privacy and confidentiality.

Informed Consent

- Investigators planning to utilize human pluripotent stem cells derived in the private sector from early human embryos should obtain documentation from the deriver/supplier of the cells that informed consent was obtained from both parents. The burden of demonstrating that the consent process was informed, voluntary and free of coercion rests with the deriver of the human pluripotent stem cells. To avoid possible conflicts of interest, the attending physician and the deriver of the human pluripotent stem cells should never be one and the same person.

- Protocols and informed consent documents for the derivation of pluripotent stem cells from early human embryos must be approved by an IRB, as defined by the Common Rule or FDA regulations. Investigators planning to utilize human pluripotent stem cells should obtain documentation of IRB approval.

- Laboratories from which derived stem cells are obtained should have written policies in place regarding the protection of privacy and confidentiality.

- The informed consent process, therefore, should disclose to the potential donors information that a reasonable individual would consider pertinent in making the decision whether or not to donate their embryos for research purposes. Informed consent should contain:

  - A statement that the early embryo will be used to derive human pluripotent stem cells for research.

  - Information regarding the general type of human pluripotent stem cell research that will likely be conducted with the derived cells.

  - A statement that the human pluripotent stem cells will be derived and used following established guidelines, and that the cells may be used, at some future time, for transplantation research.

  - Disclosure of the possibility that the donated material may have commercial potential in the future, and a statement that the donor will not receive financial or any other benefits from any such commercial development in the future.

  - Disclosure that the tissue and the derived cells may be used for future research, the

nature of which is not known at the present time.

- Information on the extent to which privacy and confidentiality will be maintained.

- A statement that identifiers will be stripped immediately from all embryos used to derive human pluripotent stem cells.

- A statement that donors will not get any information back regarding any subsequent testing on the embryo or the derived human pluripotent cells.

- A statement that derived cells and/or cell lines (without any information that would identify the donors or the embryo) may be kept for many years.

- A statement that, at all levels, the embryos and cells will be handled respectfully, as is appropriate for human tissue used in research, and that the embryos and cells will be disposed of in a manner appropriate to human pathological material.

C. Equitable Selection and Distribution of Benefits and Burdens

To ensure that the benefits and risks involved in human pluripotent stem cell research are equitably distributed, no one group or subgroup of patients should be the sole or primary source for fetal or embryonic tissue, nor should any group or subgroup be systematically excluded.

IV. Areas of Research Involving Human Pluripotent Stem Cells That Are Ineligible For NIH Funding[3]

- The derivation of pluripotent stem cells from early human embryos (after implantation, embryos are legally considered fetuses and are governed by different laws and regulations (see Section III (A) of these guidelines).

- Studies in which human pluripotent stem cells are, in any way, used to create or contribute to a human embryo. This includes studies in which human pluripotent stem cells are combined with a normal early human or animal embryo to create a human or human-animal chimera.

- Research in which human pluripotent stem cells are used for human reproductive cloning

- Research utilizing pluripotent stem cells that were derived from human embryos created for research purposes, rather than for infertility treatment.

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[3]Areas of research ineligible for NIH funding are based on these Guidelines, the President's December 2, 1994 Directive, the March 1997 Directive on human cloning, and PUBLIC LAW 105-277, SECTION 511. None of the funds made available in Public Law 105-277 can be used for:

- the creation of a human embryo or embryos for research purposes
- 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 utero under 45CFR46(a)(2) and section 498 of the Public Health Service Act (42 U.S.C. 289g(b)). Human embryo or embryos are defined in the statute to "include any organism, not protected as a human subject under 45CFR46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning or any other means from one or more human gametes or human diploid cells."

V. Pertinent Federal Regulations

In addition to these guidelines, investigators should also consult 45 CFR 46 (Protecting Human Subjects) for general requirements that apply to research involving human subjects, 42 U.S.C. 289g-1 & 2 for regulations regarding research involving human fetal tissue, and Public Law 105-277 prohibiting DHHS funding for research involving human embryos.

VI. State and Local Laws

Research should be in compliance with relevant State, local, and other Federal laws.

VII. Oversight

- Requests to the NIH for the funding of research utilizing human pluripotent stem cells must document that the human pluripotent stem cells have been derived pursuant to these Guidelines.

- Such requests would be submitted by: 1) grantees who are already funded and who want to use existing funds for work with human pluripotent stem cells; 2) grantees requesting an administrative supplement to conduct human pluripotent stem cell research; and 3) grantees who submit new applications for research utilizing human pluripotent stem cells.

- All applications shall be first reviewed for scientific merit by: 1) an initial review group, in

the case of new applications; or 2) by IC staff in the case of requests to use existing funds or applications for an administrative supplement.

- The NIH will establish a Human Pluripotent Stem Cell Review Group (HPSCRG). This review group will be responsible for ensuring compliance with the NIH Guidelines for Research Utilizing Human Pluripotent Stem Cells. The group will meet in public session only when a newly derived line of human pluripotent stem cells that has not been reviewed previously is proposed in the funding request.

- The NIH may provide means for the HPSCRG to investigate the authenticity of the documents, build in the option for direct discussion with the applicant, discussion with the IRB chair, site visits to grantee institutions, or presentations to the committee.

- The NIH will inform investigators of the timing of the HPSCRG review process and any potential delays that may result from the review process.

- The HPSCRG will publish a yearly report which will include: 1) the number of applications reviewed; 2) the titles of those applications or supplements funded; 3) a review of any research advances that have resulted from funded grants.

- The HPSCRG will also serve as a resource for recommending to the Director, NIH any revisions to the NIH HPSC Guidelines.

[ ]

Dated:

_____

Ruth L. Kirschstein, M.D.

Deputy Director, NIH

FAX TRANSMISSION

U.S. Department of Health and Human Services
Office of the Secretary

DATE: 6/4/99

TO: Chris Jennings.

FAX: 456-5557. **PHONE:** _____

FROM: Lorrie McHugh.

Press Office, OASPA
Phone: (202) 690-6343
Fax: (202) 690-6247

TOTAL NUMBER OF PAGES TRANSMITTED: 3.

COMMENTS:

Chris-

The following press release will be issued today embargoed for Monday. NIH will encourage reporters to clarify in their stories that these stem cells are NOT the embryonic stem cells that have created media & other attention.

Thanks,
Lorrie.

DRAFT NIH NEWS RELEASE

NATIONAL INSTITUTES OF HEALTH

National Institute of
Neurological Disorders and Stroke

Embargoed for release:
Monday, June 7, 1999, 5:00 p.m. EDT

For more information, contact:
Natalie Larsen or Margo Warren
301-496-5751

Transplanted Neural Stem Cells Spread Throughout the Abnormal Brain, Reduce Disease Symptoms

For years, researchers have probed the mysteries of neural stem cells — immature cells that can differentiate into all the cell types that make up the brain — with the idea that they might be useful for treating brain disorders such as Parkinson's disease. Important new research now suggests that these cells may be effective in treating a much broader array of brain diseases than previously anticipated, including Alzheimer's disease and many childhood brain disorders.

The new study, led by Evan Snyder, M.D., Ph.D., of Children's Hospital and Harvard Medical School in Boston, provides the first evidence that neural stem cells can be used to repair damage from brain disorders such as adrenoleukodystrophy and multiple sclerosis, where cell dysfunction is "global" or spread throughout the brain. Investigators previously believed that the promise of these cells was limited to disorders such as Parkinson's disease in which damage is restricted to defined areas of the brain. While preliminary, the new findings raise exciting possibilities for future therapies. The study was funded in part by the National Institute of Neurological Disorders and Stroke (NINDS) and appears in the June 8, 1999, issue of the *Proceedings of the National Academy of Sciences (PNAS)*.[1]

<Quote from Dr. Fischbach>

In the new study, Dr. Snyder and his colleagues injected cultured neural stem cells into the brain ventricles of newborn mice from a mutant strain that develops severe tremors by 2 to 3 weeks of age. The tremor develops because the mice lack a key protein needed to make myelin, the insulating coating that surrounds nerve fibers. The lack of normal myelin in these mice mimics the defect seen in many human demyelinating disorders, such as multiple sclerosis and a group of childhood disorders called leukodystrophies. The researchers found that most of the transplanted cells migrated throughout the brain and matured into normal-looking oligodendrocytes, the brain cells that produce myelin. These oligodendrocytes produced a significant amount of the missing protein and began to cover nearby nerve fibers with myelin just as normal oligodendrocytes would. Moreover, tremors disappeared almost completely in 60 percent of the tested mice that received the transplants.

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[1] Yandava, Booma D.; Billinghurst, Lori L.; and Snyder, Evan Y. "'Global'" cell replacement is feasible via neural stem cell transplantation: Evidence from the dysmyelinated *shiverer* mouse brain." *Proceedings of the National Academy of Sciences*, Vol. 96, No. 12, June 8, 1999, pp. XXX - XXX.

Intriguingly, the neural stem cells transplanted into the brains of the mutant mice were much more likely to form oligodendrocytes than were neural stem cells transplanted into the brains of normal mice. This suggests that the neural stem cells somehow sense that an oligodendrocyte-produced factor is missing in the mutant mice and attempt to compensate for the problem. A similar study previously found that neural stem cells transplanted into mice missing a particular type of neuron tended to form that neural cell type more frequently than expected. If confirmed, this ability to compensate for missing cell types could make neural stem cells a much more effective therapy than researchers anticipated.

While this study looked only at a model of demyelinating disease, Dr. Snyder believes it is plausible that neural stem cells will react to cues from the brains of animals or humans affected with other diseases and compensate for the defects associated with those diseases as well. It may also be possible to genetically engineer neural stem cells so that they not only replace lost cells throughout the brain – as is seen in Alzheimer's disease – but also produce proteins that correct whatever problem made the original brain cells die. "Sometimes the original cells are overly sensitive to stress from toxins, viral infections, or other problems, because of missing or damaged genes. If so, transplanted cells with normal genes could withstand the stress," says Dr. Snyder. "Researchers also can engineer neural stem cells to withstand, neutralize, or even protect other cells against a toxin or other threat."

While neural stem cell research is very promising, researchers still need to show that human neural stem cells behave like their mouse counterparts, says Dr. Snyder. They also need to learn whether the benefits shown in young animals extend to older animals and whether transplanted cells can overcome ongoing degenerative disease processes so that they do not become new victims of that degeneration. Follow-up research is also needed to better understand how transplanted cells are directed to grow throughout the brain and compensate for missing brain proteins

Dr. Snyder is now testing neural stem cells in animal models for many other disorders, including perinatal asphyxia (which can lead to cerebral palsy), Krabbe's disease (a demyelinating disorder), and stroke. If all goes well, these studies could eventually lead to clinical trials. However, it is too early to say which human disorders might be the first to be targeted with neural stem cell therapy, and it will take years of careful clinical tests before researchers can show conclusively whether the stem cells work in human disease.

The NINDS is the nation's premier supporter of research on the brain and nervous system. It is part of the National Institutes of Health located in Bethesda, Maryland, and will celebrate its 50th anniversary in the year 2000.

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This release will be posted on EurekAlert! at http://www.eurekalert.org and on the NINDS home page at http://www.ninds.nih.gov/whtnwhp.htm

Copies of the paper are available to reporters from the PNAS news office at ph: 202-334-2138, or email: pnasnews@nas.edu.

THE WHITE HOUSE

WASHINGTON

November 14, 1998

Dr. Harold Shapiro
Chair
National Bioethics Advisory Commission
Suite 3C01
6100 Executive Boulevard
Bethesda, Maryland 20892-7508

Dear Dr. Shapiro:

This week's report of the creation of an embryonic stem cell that is part human and part cow raises the most serious of ethical, medical, and legal concerns. I am deeply troubled by this news of experiments involving the mingling of human and non-human species. I am therefore requesting that the National Bioethics Advisory Commission consider the implications of such research at your meeting next week, and to report back to me as soon as possible.

I recognize, however, that other kinds of stem cell research raise different ethical issues, while promising significant medical benefits. Four years ago, I issued a ban on the use of federal funds to create human embryos solely for research purposes; the ban was later broadened by Congress to prohibit any embryo research in the public sector. At that time, the benefits of human stem cell research were hypothetical, while the ethical concerns were immediate. Although the ethical issues have not diminished, it now appears that this research may have real potential for treating such devastating illnesses as cancer, heart disease, diabetes, and Parkinson's disease. With this in mind, I am also requesting that the Commission undertake a thorough review of the issues associated with such human stem cell research, balancing all ethical and medical considerations.

I look forward to receiving your reports on these important issues.

Sincerely,

Bill Clinton

National Institutes of Health
Department of Health and Human Services
March 30, 1999

FACT SHEET ON STEM CELL RESEARCH

The Department of Health and Human Services (DHHS) has concluded that current law permits federal funds to be used for research utilizing human pluripotent stem cells. The National Institutes of Health (NIH) plans to move forward in a careful and deliberate fashion to develop rigorous guidelines that address the special ethical, legal, and social issues relevant to this research. The NIH will not fund research using human pluripotent stem cells until guidelines are developed and widely disseminated to the research community and an oversight process is in place.

The Promise of Stem Cell Research

Scientists have recently isolated and successfully cultured human pluripotent stem cells[1]. These human pluripotent stem cells have an unlimited capacity to divide, and the ability to develop into most of the specialized cells or tissues in the body.

This advance represents a major step forward in human biology and has generated much enthusiasm and interest among scientists and the public, particularly patients and their families. Because these cells can give rise to many different types of cells, such as muscle cells, nerve cells, heart cells, blood cells, and others, they are enormously important to science and hold great promise for advances in health care. For example, further research using pluripotent stem cells may help us:

- Generate cells and tissue that could be used for transplantation. Pluripotent stem cells may be stimulated to develop into many different specialized cells of the body, which may someday be used as replacement cells and tissue to treat many diseases and conditions including Parkinson's disease, spinal cord injury, stroke, burns, heart disease, diabetes, and arthritis.

- Improve our understanding of the complex events that occur during normal human development and also help us understand what goes wrong to cause diseases and conditions such as birth defects and cancer.

- Change the way we develop drugs and test them for safety and potential efficacy. New medications could be tested using human pluripotent stem cells, such as liver cells or skin cells; only the drugs which are both safe and appear to have a beneficial effect would graduate to human testing.

Legal Issues

These human pluripotent stem cells were isolated using two different methods. One group of

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[1]Michael Shamblott, et al, Derivation of pluripotent stem cells from cultured human primordial germ cells. PNAS, 95: 13726-13731, Nov. 1998.

James Thomson, et al, Embryonic stem cell lines derived from human blastocysts. Science, 282: 1145-1147, Nov. 6, 1998.

scientists derived the pluripotent stem cells from early-stage embryos donated by people who were undergoing fertility treatment in an *in vitro* fertilization (IVF) clinic. Another group of scientists isolated the pluripotent stem cells from non-living fetuses obtained from pregnancies that had been terminated. In both cases, all of the individuals gave full informed consent for the embryos or fetal tissue to be used in research. Neither research project utilized federal funds. Because of the regenerative capacity of pluripotent stem cells, a single culture of human pluripotent stem cells could supply numerous other researchers.

Federal law currently prohibits the DHHS from funding human embryo research. In light of this legislative ban, the Director of the NIH sought a legal opinion from the DHHS Office of the General Counsel on whether DHHS funds may be used for research utilizing human pluripotent stem cells.

After a thorough analysis of the law, DHHS concluded that the congressional prohibition on the use of DHHS funds for certain types of human embryo research does not apply to research utilizing human pluripotent stem cells because such cells are not embryos. The legal opinion also clarified that human pluripotent stem cells derived from non-living fetuses would fall within the legal definition of human fetal tissue and are, therefore, subject to certain Federal restrictions on the use of such tissue.

Thus, research using pluripotent stem cells derived from human embryos can be funded by DHHS. Research that generates and uses pluripotent stem cells from non-living fetuses can also be supported by DHHS, subject to existing law and regulation.

NIH Support

In view of the scientific and medical benefits that may result from research using pluripotent stem cells, the NIH plans to fund research using these cells. It is essential that the Federal government play a role in funding and overseeing the conduct of this research, so that all scientists--both privately and federally funded--have the opportunity to pursue this important line of research. Federal funding will provide oversight and direction that would be lacking if this research were the sole province of industry and academe.

The NIH understands and respects the compelling ethical, legal, and social issues relevant to pluripotent stem cell research and is sensitive to the need for stringent oversight of this research that goes beyond the traditional NIH scientific peer review process. In light of these issues, the NIH plans to move forward in a careful and deliberate way, prior to funding any research utilizing pluripotent stem cells.

In an effort to ensure that any research utilizing human pluripotent stem cells is appropriately and carefully conducted, the NIH will convene a Working Group of the Advisory Committee to the Director (ACD), NIH to advise the ACD on guidelines and oversight for research involving human pluripotent stem cells, at the Bethesda Marriott, 5151 Pooks Hill Road, Bethesda, Maryland 20814, on April 8, 1999. The meeting will begin at approximately 9:00 a.m. and end at approximately 5:30 p.m. The goal of the Working Group is to provide advice to the ACD about the scientific, ethical, legal, and social issues relevant to guidelines for the conduct of research utilizing human pluripotent stem cells. The working group will meet in public session and will be composed of scientists, patients and/or their families, ethicists, clinicians and

lawyers. They will be asked to consider advice from the National Bioethics Advisory Commission (NBAC), the public, and the Congress. Once developed, guidelines for research utilizing human pluripotent stem cells will be published in the Federal Register for public comment. Until both the guidelines and the oversight process are in place, interested investigators have been notified, via the NIH web site, NIH program staff, and the Deputy Director for Intramural Research that they cannot use DHHS funds to conduct research using human pluripotent stem cells.

Congress of the United States

Washington, DC 20515

February 11, 1999

The Honorable Donna E. Shalala
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Madam Secretary:

Last month the General Counsel at HHS, Harriet Rabb, issued a memorandum to Dr. Harold Varmus, Director of the National Institutes of Health (NIH), supporting the claim that taxpayer funds may be used for research on stem cells taken from living human embryos. Shortly thereafter, and using the Rabb memo as a basis, Dr. Varmus announced that NIH will reverse current federal policy and begin funding research which relies on the mutilation and destruction of human embryos.

We wish to express to you, in the strongest possible terms, our objection to Ms. Rabb's memo and to Dr. Varmus's decision. Any NIH action to initiate funding of such research would violate both the letter and spirit of the federal law banning federal support for research in which human embryos are harmed or destroyed.[1] Rather than providing guidance on how best to implement the law that Congress passed and the President signed, the memorandum appears to be a carefully worded effort to justify transgressing that law.

In her memorandum Ms. Rabb makes significant errors on the way to her conclusion that it would be permissible for NIH to fund research using stem cells harvested from human embryos. We call upon you to correct the General Counsel's interpretation and to reverse Dr. Varmus's decision.

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[1] Since January 1996, Congress has included in the annual Labor, Health and Human Services, Education Appropriations Act a section prohibiting funding for this type of research. Section 511 of the most recently enacted research funding bill, Public Law 105-277, provides (in part) that--

> (a) None of the funds made available in this Act may be used for--
> (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 utero under CFR 46.208(a)(2) and section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)).

The Honorable Donna E. Shalala
February 11, 1999

At the start of her analysis, the General Counsel unilaterally narrows the meaning of "research in which a human embryo or embryos are destroyed" and states that it prohibits only direct federal funding of the specific act of destroying the embryo. In this way she limits the scope of the law passed by Congress. While the *act* of destroying or injuring an embryo would certainly be ineligible for Federal funding, the law has a broader application. It also bars the use of tax dollars to fund research which follows or depends upon the destruction of or injury to a human embryo.

Congress could have structured paragraph (2) of subsection (a) of the law like paragraph (1) and simply prohibited the use of funds for the destruction or discarding of human embryos. We did not do that, and by established rules of statutory construction, HHS may not construe the law's provision on "research in which" embryos are destroyed as narrowly as its provision on the creation of embryos.[2] Instead, we prohibited the funding of research projects in which the lethal dissection or harmful manipulation of living human embryos is a necessary prerequisite, including projects where the material used in the experiments is obtained by destruction of an embryo that would not otherwise be done (or not otherwise done in the same way). In congressional testimony, Dr. Varmus has confirmed that it is impossible to obtain stem cells from embryos for these experiments without destroying the embryos.

The Rabb memo also ignores the policy reflected in current law on fetal tissue transplantation research using tissue from intentionally aborted children. While that law is itself open to criticism, it at least bans the use of fetal tissue in federally funded research if abortion was induced for the purpose of providing the tissue. Under current law, federal funds may not be used for fetal tissue transplantation experiments following an abortion if the timing and method of the abortion were altered solely for the purpose of providing usable tissue for research. Yet, in the embryonic stem cell research which NIH proposes to fund, the timing, method and procedures for destroying the embryonic child would be determined solely by the federally funded researcher's need for usable stem cells.

Finally, both Ms. Rabb's memorandum and Dr. Varmus's testimony before a Senate subcommittee present a new definition of "human embryo" that would undermine both the congressional rider on embryo research, and the President's own 1994 directive against using federal funds to create human embryos for research purposes. They now say that an entity is an "embryo" only if one can show that it is capable, if implanted in the womb, of becoming a born "human being." This narrow definition has no support whatsoever in federal law.

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[2]When a law has two parallel clauses, one of which is deliberately written in broader terms than the other, it may not be interpreted to have the same meaning as the narrower clause. See *Russello v. United States*, 464 U.S. 16, 23 (1983), and cases cited therein.

Nevertheless, researchers are already offering to use damaged human embryos in their destructive research, or even to engineer lethal defects in advance into the embryos they create for such research, in order to take advantage of this Administration cover and ignore the congressional and presidential directives altogether.

For more than 20 years, Federal laws and regulations have protected the human embryo and fetus from harmful experimentation at the hands of the Federal government -- regardless of whether the embryo is "perfect" or damaged, wanted or unwanted, intended for abortion or intended for live birth. This area of law has provided a bulwark against government's misuse and exploitation of human beings in the name of medical progress. It would be a travesty for this Administration to attempt to unravel this accepted ethical standard.

We urge you to review this issue carefully, and to put a stop to a proceeding which so clearly does violence to the meaning and intent of Federal law.

Sincerely,

JAY DICKEY, M.C.

SPENCER BACHUS, M.C.

HENRY J. HYDE, M.C.

RON PACKARD, M.C.

JOE BARTON, M.C.

DAN BURTON, M.C.

DUNCAN HUNTER, M.C.

W.J. (BILLY) TAUZIN, M.C.

The Honorable Donna E. Shalala
February 11, 1999

JOSEPH R. PITTS, M.C.

GARY G. MILLER, M.C.

RON LEWIS, M.C.

TODD TIAHRT, M.C.

ROBERT B. ADERHOLT, M.C.

CHIP PICKERING, M.C.

PETER T. KING, M.C.

JOHN SHIMKUS, M.C.

JIM RYUN, M.C.

STEPHEN E. BUYER, M.C.

BOB SCHAFFER, M.C.

RON PAUL, M.C.

PETER HOEKSTRA, M.C.

PETE SESSIONS, M.C.

The Honorable Donna E. Shalala
February 11, 1999

JOHN T. DOOLITTLE, M.C.

JOHN J. HOSTETTLER, M.C.

DAVID M. McINTOSH, M.C.

RICK HILL, M.C.

HELEN CHENOWETH, M.C.

JAMES A. BARCIA, M.C.

CHARLES T. CANADY, M.C.

CHRISTOPHER H. SMITH, M.C.

NICK J. RAHALL II, M.C.

STEVE LARGENT, M.C.

RICHARD K. ARMEY, M.C.
Majority Leader

RONNIE SHOWS, M.C.

TOM A. COBURN, M.C.

LINCOLN DIAZ-BALART, M.C.

The Honorable Donna E. Shalala
February 11, 1999

CHRIS JOHN, M.C.

KEVIN BRADY, M.C.

ASA HUTCHINSON, M.C

PHIL ENGLISH, M.C.

PAUL RYAN, M.C.

TOM TANCREDO, M.C.

ROBERT W. NEY, M.C.

JIM TALENT, M.C.

JACK METCALF, M.C.

DONALD A. MANZULLO, M.C.

JIM DeMINT, M.C.

DAVE WELDON, M.C.

RAY LaHOOD, M.C.

TOM LATHAM, M.C.

The Honorable Donna E. Shalala
February 11, 1999

ROY BLUNT, M.C.

SUE MYRICK, M.C.

CHARLES H. TAYLOR, M.C.

PHILIP M. CRANE, M.C.

ED WHITFIELD, M.C.

STEVE CHABOT, M.C.

MICHAEL P. FORBES, M.C.

MARK E. SOUDER, M.C.

JOHN E. PETERSON, M.C.

TOM DeLAY, M.C.
Majority Whip

RICHARD H. BAKER, M.C.

BOB BARR, M.C.

MIKE McINTYRE, M.C.

VIRGIL H. GOODE, Jr., M.C.

The Honorable Donna E. Shalala
February 11, 1999

DAVID D. PHELPS, M.C.

LINDSAY O. GRAHAM, M.C.

IKE SKELTON, M.C.

ERNEST J. ISTOOK, Jr., M.C.

SOLOMON P. ORTIZ, M.C.

J.C. WATTS, Jr., M.C.
Republican Conference Chairman

THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

FEB 23 1999

The Honorable Jay Dickey
U.S. House of Representatives
2453 Rayburn House Office Building
Washington, DC 20515

Dear Mr. Dickey:

Thank you for your letter dated February 11, 1999, concerning the recent announcement by the Director of the National Institutes of Health (NIH) regarding federal funding for research utilizing human pluripotent stem cells. As you know, this research has the potential to lead to great progress in our treatment of debilitating and deadly diseases, our understanding of human development and our ability to develop and test new drugs. Stem cell research is richly promising, yet raises important ethical issues. Therefore, Dr. Varmus and his colleagues at the National Institutes of Health (NIH) will proceed with great caution to ensure that the highest standards are set before moving forward in this area.

In keeping with the important ethical concerns that must be considered, the NIH plans to proceed in a careful and deliberate fashion to develop rigorous guidelines. A working group of the Advisory Committee to the Director of NIH will develop guidelines for the conduct of research using pluripotent stem cells and will recommend an oversight mechanism for protocol review. The National Bioethics Advisory Commission is studying these issues and will provide us with advice that -- together with counsel from outside experts, Congress and other interested parties -- will help ensure appropriate oversight.

First and foremost, these guidelines will ensure that any research funded in this area is consistent with the prohibition on federal funding for human embryo research contained in section 511 of the HHS appropriations law. Since this prohibition was first enacted in 1996, the Department of Health and Human Services (HHS) has conscientiously adhered to its strictures. For example, we have included the restriction on the use of funds in the NIH Grants Policy Statement and have issued notices reminding NIH intramural staff and the extramural research community that they must observe the prohibition. When necessary, we have not and will not hesitate to take appropriate enforcement action. I am firmly committed to our continued adherence to the law.

Your letter makes specific inquiries regarding a legal memorandum on this subject from the HHS General Counsel. You suggest that the legal analysis is problematic because it relies on a new definition of human embryo that would undermine the Congressional prohibition. In fact, the memorandum relies on the definition provided in the statute itself. The statute defines human embryo as "any organism ... that is derived ... from one or more human gametes or diploid cells."

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The legal memorandum, relying on the scientific definition of the word "organism", concludes that the stem cells at issue are not organisms and therefore cannot be considered human embryos under section 511 of the HHS appropriations law.

The prohibition on federal funding for human embryo research bars the expenditure of federal funds for the creation of a human embryo for research purposes or for research in which a human embryo is destroyed, discarded or knowingly subject to greater than minimal risk. You suggest that this provision should be read to also bar federal funding for research which follows or depends upon the destruction of or injury to a human embryo. The plain language of the statute supports the opinion issued by the General Counsel. The law applies by its terms to research in which "a human embryo or embryos are destroyed, discarded" or subjected to more than minimal risk, and not to research preceding or following such research projects. Moreover, I have been advised that there is nothing in the legislative history to suggest that the provision was intended to prohibit funding for research in which embryos -- organisms -- are not involved.

I have reviewed our Department's position and am reassured that proceeding cautiously with research on existing pluripotent stem cell lines is both legal and appropriate. Further, it will allow the NIH to foster world-class research on stem cells, assure appropriate oversight, and bring together the finest minds and facilities to further medical and scientific advances. Allow me to assure you that the NIH understands and respects the deep convictions of people in the research, academic and religious communities, and in Congress, and intends to seek the advice and comment of those communities as we move ahead. I look forward to working with you to ensure that the legal and ethical issues involved in this extremely promising area of research are addressed.

Sincerely,

Donna E. Shalala

United States Senate

WASHINGTON, DC 20510

February 12, 1999

The Honorable Donna E. Shalala
The Department of Health and Human Services
200 Independence Avenue, SW
Washington, D.C. 20201

SPECIAL

Dear Secretary Shalala:

We are deeply concerned with what appears to be a unilateral attempt on your part to effectively undermine congressional intent, by circumventing the current federal funding ban on embryo research.

Of particular concern to us is testimony Dr. Varmus gave on January 26, 1999, during a hearing before the Appropriations Subcommittee on Labor, Health and Human Services and Education. During Dr. Varmus' testimony he stated, "Dr. Thomson and his co-workers derived pluripotent stem cells from the blastocyst stage of an early embryo — the embryos used were donated by couples who were receiving infertility treatment; this derivation of stem cells from the embryo does fall under the ban on Federal funding." The contention being made is that once the stem cells are derived, federal funding of research which directly relies on such destruction is acceptable. We disagree.

Also of concern to us is Dr. Varmus' response to a statement by some researchers that human pluripotent stem cells may come together in culture to begin developing as an embryo. If this does occur, then NIH would be directly violating the congressionally imposed ban by funding embryonic stem cell research. Dr. Varmus stated that he was unsure if it does occur, and that it would be "grossly unethical" to try to find out because that would involve implantation. If the director of the National Institutes of Health is unsure, then the proper course of action would be to take no action. Better to err on the side of preserving congressional intent than destroying it.

Congress never intended for the National Institutes of Health to give incentives for the killing of human embryos for the purpose of stem cell research. We are very interested in any further insight you might provide on this issue and look forward to hearing from you soon.

Sincerely,

Sam Brownback Don Nickles

99 FEB 17 AM 9:53

168409

Jon Kyl
JON KYL

Bob Smith

Jesse Helms

Michael B. Enzi
MICHAEL B. ENZI

John Ashcroft

SPECIAL

02-17-99-0011

THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

MAR 2 1999

The Honorable Don Nickles
United States Senate
133 Hart Senate Office Building
Washington, DC 20510

Dear Senator Nickles:

Thank you for your letter dated February 11, 1999, concerning the recent announcement by the Director of the National Institutes of Health (NIH) regarding federal funding for research utilizing human pluripotent stem cells. As you know, this research has the potential to lead to great progress in our treatment of debilitating and deadly diseases, our understanding of human development and our ability to develop and test new drugs. Stem cell research is richly promising, yet raises important ethical issues. Therefore, Dr. Varmus and his colleagues at the National Institutes of Health (NIH) will proceed with great caution to ensure that the highest standards are set before moving forward in this area.

In keeping with the significant ethical concerns that must be considered, the NIH plans to proceed in a careful and deliberate fashion to develop rigorous guidelines. A working group of the Advisory Committee to the Director of NIH will develop guidelines for the conduct of research using pluripotent stem cells and will recommend an oversight mechanism for protocol review. The National Bioethics Advisory Commission is studying these issues and will provide us with advice that -- together with counsel from outside experts, Congress and the public -- will help ensure appropriate oversight.

First and foremost, these guidelines will ensure that any research funded in this area is consistent with the prohibition on federal funding for human embryo research contained in section 511 of the HHS appropriations law. Since this prohibition was first enacted in 1996, the Department of Health and Human Services (HHS) has conscientiously adhered to its strictures. For example, we have included the restriction on the use of funds in the NIH Grants Policy Statement and have issued notices reminding NIH intramural staff and the extramural research community that they must observe the prohibition. When necessary, we have not and will not hesitate to take appropriate enforcement action. I am firmly committed to our continued adherence to this law.

You have asked whether pluripotent stem cells may come together in culture to begin developing as an embryo. The scientific knowledge base about pluripotent stem cells comes from years of experience in animal research. Mouse pluripotent stem cells grown in a petri dish can give rise to specialized cells and tissues which sometimes form an aggregated structure, similar to certain tumors of the ovary and testis, termed an "embryoid body." These mouse embryoid bodies, however, are not embryos. Similarly, in one report on the derivation of human pluripotent stem cells, researchers observed that the human pluripotent stem cells can form embryoid bodies that are similar in structure to mouse embryoid bodies, which, as noted above, are not embryos.

168409

I have reviewed our Department's position and am reassured that proceeding cautiously with research on existing pluripotent stem cell lines is both legal and appropriate. Further, it will allow the NIH to foster world-class research on stem cells, assure appropriate oversight of such research, and bring together the finest minds and facilities to further medical and scientific advances. I assure you that the NIH understands and respects the deep convictions of people in the academic, religious and bioethics communities, and in Congress, and intends to seek the advice and comment of those communities as we move ahead. I look forward to working with you to ensure that the legal and ethical issues involved in this extremely promising area of research are addressed.

Sincerely,

Donna E. Shalala

Congress of the United States

Washington, DC 20515

SPECIAL

March 15, 1999

99 MAR 16 PM 4:32

The Honorable Donna E. Shalala
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Madam Secretary:

Thank you for responding so quickly to our February 11 letter concerning federal funding of research in which human embryos are destroyed. Unfortunately, your letter was not responsive to our concerns but only raises further questions.

Consequently, we once again are compelled to point out that well-established rules of statutory construction have been ignored by the HHS General Counsel's memorandum reinterpreting current law on embryo research. The Supreme Court of the United States, as we noted in our earlier correspondence, has ruled that two parallel clauses of a law may not be interpreted in the same way if Congress expresses one provision narrowly and the other broadly. Had Congress intended only to ban the use of funds for the specific act of destroying or discarding embryos, Congress would have done that. Instead, Congress prohibited funding of "research in which" embryos are destroyed or discarded. For this reason, your contention that "the plain language of the statute supports the opinion issued by the General Counsel" remains unconvincing.

In fact, your conclusion that the ban was not intended to cover "research preceding or following" such destruction contradicts NIH's own policy and practice ever since the funding ban was first enacted. In 1997, for example, researcher Mark Hughes was found to be in violation of this law and dismissed from NIH. His violation was that he had used NIH-funded equipment to analyze genetic material obtained from human embryos. NIH funds were used in research which followed the harvesting of a cell from an embryo; in cases where a genetic defect was found, the analysis may also have preceded the discarding of an embryo. There was never any indication that the NIH equipment was used to destroy embryos. Yet in testimony before the House Commerce Subcommittee on Oversight and Investigations on June 19, 1997, NIH Director Harold Varmus agreed that the ban had been violated -- and he assured Congress that NIH had taken "several steps to further diminish the risk of subsequent violations." Now HHS proposes that these types of violations become the norm.

We would also point out that the context in which the funding ban was enacted supports NIH's enforcement of the law from its enactment in January 1996 until Dr. Varmus's announcement in January 1999. Congress passed the law in response to a 1994 report from the NIH Human Embryo Research Panel. The panel recommended taxpayer support of "research involving the development of embryonic stem cells" as part of its recommendations on funding of

"various areas of research involving the ex utero preimplantation human embryo." The panel treated embryonic stem cell research as a form of embryo research because it knew that the cells would have to be obtained by destroying embryos. When Congress rejected the recommendations of the NIH panel by enacting the current funding ban, it did not make any exceptions. It rejected this form of experimentation as well.

In this context, it is remarkable that your February 23 letter proposes the Advisory Committee to the Director of NIH as the body that will ensure respect for ethical and legal standards in this research. This committee unanimously endorsed the original recommendations of the Human Embryo Research Panel -- including proposals for special creation of embryos for research purposes that were immediately rejected by President Clinton. This same committee openly planned a lobbying campaign to prevent Congress from enacting the ethical protections that remain in law today. Thus we are more concerned than ever that HHS's current course is less a good-faith interpretation of the law than an attempted end-run by those who have always opposed the law.

With regard to the definition of human embryo[1], we are not troubled at all by HHS's use of a scientific definition of the word "organism." As the HHS General Counsel rightly states, an "organism" includes any "individual constituted to carry out all life functions," including a one-celled individual. Rather, we are troubled by the paragraph in which she completely ignores this definition and states that "a human embryo, as that term is virtually universally understood, has the potential to develop in the normal course of events into a living human being." Ms. Rabb declares on behalf the Department, with an appeal to no authority in science or law, that virtually no one considers a human embryo to actually be a living human being. This position simply contradicts the definitions which Ms. Rabb used a few lines before this in her memo to establish that a human embryo is an organism, and, as such, is an "individual constituted to carry out all life functions" of a human being. In other words, an embryo is a human being.

Ms. Rabb's statement that certain cells "do not have the capacity to develop into a human being, even if transferred to a uterus" leaves a doubt in our mind as to the point in biological development when Ms. Rabb considers a "human being" to come into existence, or whether she considers any child before birth to be a "human being." This is not an insignificant point. If the potential or capability of something "to develop... into a living human being" is the standard used to determine whether an organism is a human embryo, and HHS does not consider a "human being" to exist before live birth, then the entire law on embryo research, as well as President Clinton's directive against special creation of research embryos, is undermined. Scientists have already offered to conduct their destructive experiments on damaged embryos not expected to survive to live birth, or to engineer lethal defects into embryos in advance, so that the human embryos they create for purposes of destructive research will not legally be "embryos" at all.

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[1] Current law provides that, "For purposes of this section, the term 'human embryo or embryos' include any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells."

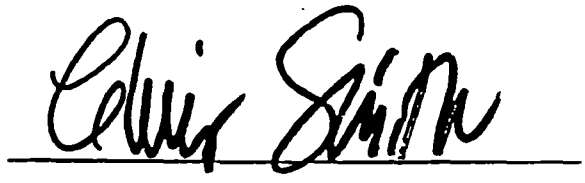
This new and arbitrary use of the term "human being" also contradicts the entire history of federal regulations on human experimentation which, since 1975, have treated the child in the womb at every stage of development as a "human subject" to be protected from harmful research. In commissioning studies of ethical issues in genetics, Congress has urged respect for "the essential equality of all human beings, born and unborn" (42 USC §300v-1). Clearly, in science and law, a human embryo has no need to "develop into" a human being because it already is a human being. The fact that a particular embryo may ultimately have a longer or shorter life span is irrelevant in this regard. It would be akin to HHS claiming that a seriously ill infant is not really an infant because he or she most likely will not "develop into" a live adult.

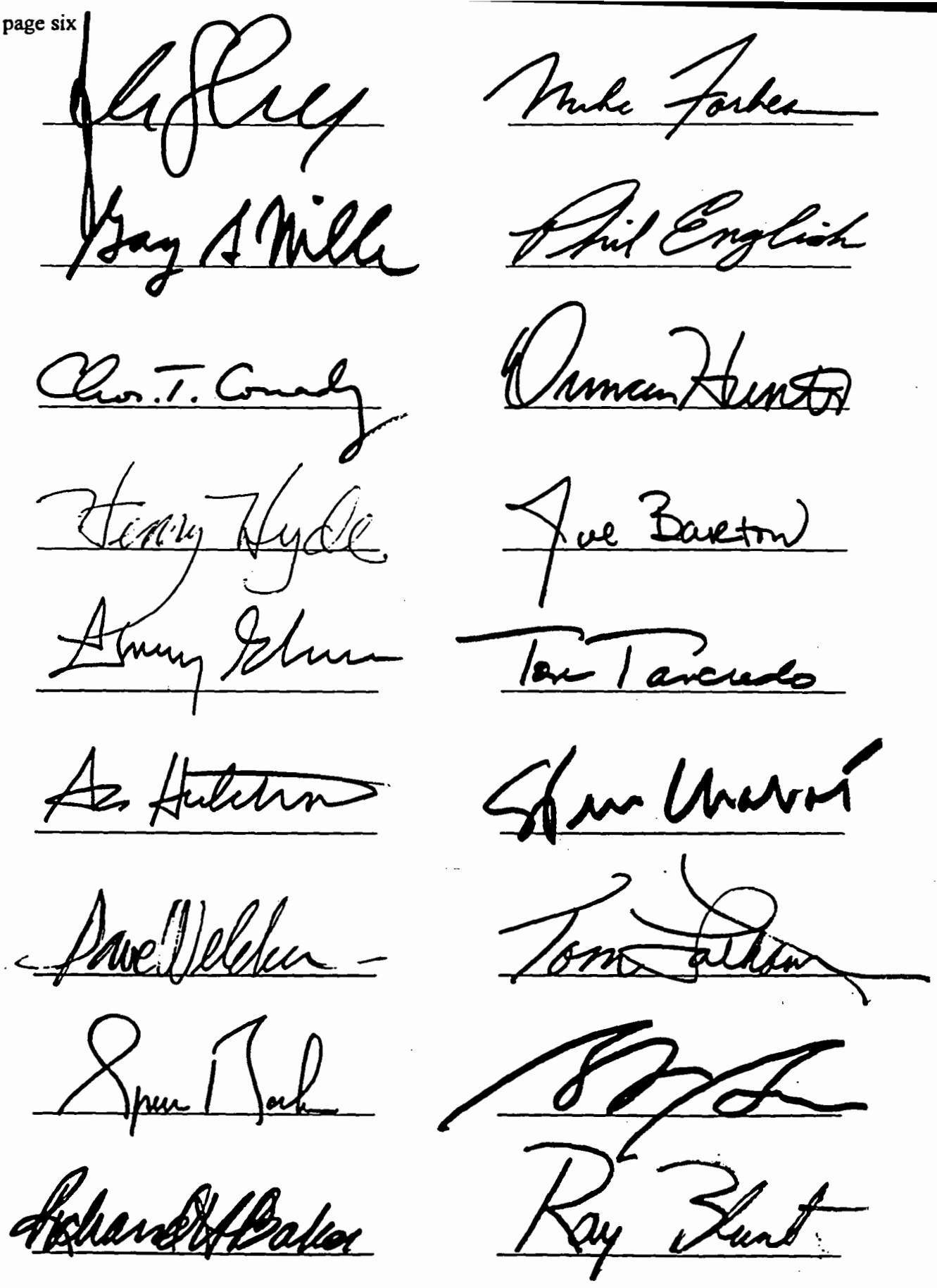
Even if HHS's arbitrary definition were valid, the General Counsel's statement that pluripotent stem cells "do not have the capacity to develop into a human being, even if transferred to a uterus" is open to question. On January 26, Dr. Varmus testified that he does not know whether these stem cells may sometimes recongregate in culture to begin developing as a human embryo. He added that it would be "grossly unethical" to transfer these cells into a woman's uterus to try to answer this question. Would it not also be grossly unethical to simply ignore this question and pursue such embryonic stem cell research, particularly if NIH admits that it may violate the law?

Finally, your letter makes no reference to the precedent established by current law on the use of fetal tissue from induced abortions. Under this law, which also specifically covers cells and tissue obtained from embryos, the harvesting procedure itself must not destroy prenatal life, and the timing and method for taking life must not be influenced solely by the needs of the federally funded research project. These principles are violated by the Administration's proposal for stem cell research.

Madam Secretary, because these are complex and important issues, we urge you once again to address our very serious concerns. For three years the ban on taxpayer funding of harmful research involving human embryos was enforced clearly and appropriately. The change in policy proposed by Dr. Varmus, based on the faulty reasoning in your General Counsel's memo, would violate the funding ban and mark a tragic step backward in federal standards for research involving human subjects.

Sincerely,





SPECIAL

03-16-99-0062

Congress of the United States

Washington, DC 20515

Statement of Members of the House of Representatives
to the Working Group of the Advisory Committee to the Director of the National Institutes of Health
APRIL 8, 1999

When Dr. Harold Varmus announced in January that he would reverse current policy and begin using taxpayer funds for research on stem cells taken from living human embryos, we -- together with many of our colleagues -- wrote to Health and Human Services Secretary Donna Shalala to protest. As the ban on such funding originated in Congress, and has been consistently opposed by this Administration, we believe we have something to contribute to today's proceedings, particularly with regard to the legality of Dr. Varmus's plan.

Put simply, any NIH action to initiate funding of research which relies on the mutilation and destruction of human embryos would violate both the letter and spirit of the federal law banning federal support for research in which human embryos are harmed or destroyed. We believe the memorandum from HHS General Counsel Harriet Rabb to Dr. Varmus supporting the claim that taxpayer funds may be used for experiments on embryonic stem cells is wrong. Rather than providing guidance on how best to implement the law that Congress passed and the President signed, the memorandum appears to be a carefully worded effort to justify transgressing that law.

The General Counsel unilaterally narrows the meaning of "research in which a human embryo or embryos are destroyed" and states that it prohibits only direct federal funding of the specific act of destroying the embryo. While the *act* of destroying or injuring an embryo would certainly be ineligible for federal funding, the law has a broader application. It also bars the use of tax dollars to fund research which follows or depends upon the destruction of or injury to a human embryo.

Congress could have structured paragraph (2) of subsection (a) of the law like paragraph (1) and simply prohibited the use of funds for the destruction or discarding of human embryos. We did not do that, and by well-established rules of statutory construction, HHS may not construe the law's provision on "research in which" embryos are destroyed as narrowly as its provision on the creation of embryos. The Supreme Court of the United States has ruled that two parallel clauses of a law may not be interpreted in the same way if Congress expresses one provision narrowly and the other broadly. Had Congress intended only to ban the use of funds for the specific act of destroying or discarding embryos, Congress would have done that. Instead, Congress prohibited funding of "research in which" embryos are destroyed or discarded.

In fact, the Secretary's conclusion that the ban was not intended to cover "research preceding or following" such destruction contradicts NIH's own policy and practice ever since the funding ban was first enacted. In 1997, for example, researcher Mark Hughes was found to be in violation of this law and dismissed from NIH because he had used NIH-funded equipment to analyze genetic material obtained from human embryos. NIH funds were used in research which followed the harvesting of a cell from an embryo; in cases where a genetic defect was found, the analysis may also have preceded the discarding of an embryo. There was never any indication that the NIH equipment was used to destroy embryos. Yet in testimony before the House Commerce Subcommittee on Oversight and Investigations on June 19, 1997, NIH Director Varmus agreed that the ban had been violated, and he assured Congress that NIH had taken "several steps to further diminish the risk of subsequent violations." Now NIH proposes that these types of violations become the norm.

We would also point out that the context in which the funding ban was enacted supports NIH's enforcement of the law from its first enactment in January 1996 until Dr. Varmus's announcement in January 1999. Congress passed the law in response to a 1994 report from the NIH Human Embryo Research Panel. The panel recommended taxpayer support of "research involving the development of embryonic stem cells" as part of its recommendations on funding of "various areas of research involving the ex utero preimplantation human embryo." The panel treated embryonic stem cell research as a form of embryo research because it knew that the cells would have to be obtained by destroying embryos. When Congress rejected the recommendations of the NIH panel by enacting the current funding ban, it did not make any exceptions. It rejected this form of experimentation as well.

Even members of the National Bioethics Advisory Commission (NBAC) criticized Ms. Rabb's memo as "disingenuous" for attempting to draw a line between actually destroying embryos for research purposes and using the cells derived from that destruction.

According to a news report, NBAC member Alex Capron, co-director of the Center for Health Policy and Ethics at University of Southern California, was quoted as saying, "I don't believe use and derivation can be separated." John Fletcher, a biomedical ethicist from the University of Virginia expressed the belief that HHS and NIH were relying on an excessively legalistic interpretation and said the legal argument "is not an ethical argument. It is an opinion that use can be separated from derivation, as if derivation is not relevant." He continued, "As a moral construct I think that is very weak and evasive." (Source: *Washington FAX*, March 4, 1999)

Dr. Varmus's plan and the Rabb memorandum also ignore the policy reflected in current law on fetal tissue transplantation research using tissue from intentionally aborted children. While that law is itself open to criticism, it at least bans the use of fetal tissue in federally funded research if abortion was induced for the purpose of providing the tissue. Under current law, which also specifically covers cells and tissue obtained from embryos, federal funds may not be used for fetal tissue transplantation experiments following an abortion if the timing and method of the abortion were altered solely for the purpose of providing usable tissue for research. Yet, in the embryonic stem cell research which NIH proposes to fund, the timing, method and procedures for destroying the embryonic child would be determined solely by the federally funded researcher's need for usable stem cells.

Finally, both Ms. Rabb's memorandum and Dr. Varmus's testimony before a Senate subcommittee present a new definition of "human embryo" that would undermine both the congressional funding ban on embryo research, and the President's own 1994 directive against using federal funds to create human embryos for research purposes. Ms. Rabb states that "a human embryo, as that term is virtually universally understood, has the potential to develop in the normal course of events into a living human being." She declares on behalf the Department of Health and Human Services, with an appeal to no authority in science or law, that virtually no one considers a human embryo to actually be a living human being. This position simply contradicts the definitions which Ms. Rabb used a few lines before this in her memo to establish that a human embryo is an organism, and, as such, is an "individual constituted to carry out all life functions" of a human being. In other words, an embryo is a human being.

The position that an entity is an "embryo" only if one can show that it is capable, if implanted in the womb, of becoming a born "human being" has no support whatsoever in federal law. Nevertheless, researchers are already offering to use damaged human embryos in their destructive research, or even to engineer lethal defects in advance into the embryos they create for such research, in order to take advantage of this Administration cover and ignore the congressional and presidential directives altogether.

This new and arbitrary use of the term "human being" also contradicts the entire history of federal regulations on human experimentation which, since 1975, have treated the child in the womb at every stage of development as a "human subject" to be protected from harmful research. In commissioning studies of ethical issues in genetics, Congress has urged respect for "the essential equality of all human beings, born and unborn" (42 USC §300v-1). Clearly, in science and law, a human embryo has no need to "develop into" a human being because it already is a human being. The fact that a particular embryo may ultimately have a longer or shorter life span is irrelevant in this regard. It would be akin to HHS claiming that a seriously ill infant is not really an infant because he or she most likely will not "develop into" a live adult.

Even if HHS's arbitrary definition were valid, the General Counsel's statement that pluripotent stem cells "do not have the capacity to develop into a human being, even if transferred to a uterus" is open to question. On January 26, Dr. Varmus testified that he does not know whether these stem cells may sometimes recongregate in culture to begin developing as a human embryo. He added that it would be "grossly unethical" to transfer these cells into a woman's uterus to try to answer this question. Would it not also be grossly unethical to simply ignore this question and pursue such embryonic stem cell research, particularly if NIH admits that it may violate the law?

For more than 20 years, Federal laws and regulations have protected the human embryo and fetus from harmful experimentation at the hands of the Federal government -- regardless of whether the embryo is "perfect" or damaged, wanted or unwanted, intended for abortion or intended for live birth. This area of law has provided a bulwark against government's misuse and exploitation of human beings in the name of medical progress. It would be a travesty for this Administration to attempt to unravel this accepted ethical standard.

We urge you to recommend that the Director rescind his decision to begin funding research involving the manipulation and destruction of living human embryos and continue to enforce the embryo research funding ban as Congress intended.

Respectfully,

The Honorable Jay Dickey, M.C.
The Honorable Christopher H. Smith, M.C.
The Honorable Rick Hill, M.C.
The Honorable Steve Largent, M.C.
The Honorable Ron Lewis, M.C.
The Honorable Kevin Brady, M.C.
The Honorable Mark E. Souder, M.C.
The Honorable Bob Ney, M.C.
The Honorable Gary G. Miller, M.C.
The Honorable Ron Paul, M.C.
The Honorable Tom A. Coburn, M.C.
The Honorable John T. Doolittle, M.C.
The Honorable Richard H. Baker, M.C.
The Honorable Bob Schaffer, M.C.
The Honorable Jim Ryun, M.C.

February 19, 1999

The Honorable Tom Harkin
United States Senate
731 Hart Senate Office Building
Washington D.C. 20510

Dear Senator Harkin:

The undersigned organizations applaud the determination by the Department of Health and Human Services that current law permits the use of federal funds to support research utilizing human pluripotent stem cells.

Human pluripotent stem cells have the ability to give rise to other more specialized types of cells, such as muscle, skin, nerve, pancreas or blood cells. This ability to produce specialized cells opens a tremendous avenue of research with enormous potential for the treatment of many diseases. For example, human stem cells could be used to produce different kinds of specialized cells and tissues for use in transplantation to treat many diseases and conditions, including neurological disorders such as Parkinson's and Alzheimer's diseases, heart disease and stroke, diabetes, osteoarthritis, rheumatoid arthritis, and spinal cord injury.

Stem cell research also offers great promise for use in drug development and testing, to evaluate and understand both the beneficial and toxic effects of drugs on different human cell types, thus potentially reducing the need for animal studies and enabling fewer and more sharply focused human clinical trials. Research on human stem cells will open exciting new pathways by which to strengthen our understanding of normal human cell and tissue development. This, in turn, will accelerate our insights into the mechanisms of abnormal growth and development, and could lead to the discovery of radically new approaches to the prevention and treatment of birth defects and cancer.

The Federal government has an important role in funding and in overseeing the conduct of this research so that the talent and creativity of the nation's scientists -- both privately and federally funded -- can be applied to this valuable line of research. Federal involvement creates a more open research environment, promoting the free exchange of ideas and data among scientists, and ensuring greater public engagement and the protections of federal regulatory oversight. Federal support will also increase fiscal resources and expand the pool of well-trained investigators engaged in this area of research, both of which will speed the pace of scientific discovery.

We concur with the National Institutes of Health's plans to move forward to develop clear guidelines to address the special scientific, legal, and ethical issues surrounding this research. We are confident that this process will have appropriate public input, as well as the advice of the National Bioethics Advisory Commission and NIH's newly

established Council of Public Representatives. NIH has made clear that it will not support any research using human pluripotent stem cells until the appropriate guidelines have been developed and disseminated and an oversight process is in place.

Given the tremendous promise this research holds for millions of Americans, indeed all humankind, we strongly urge you to work with the NIH to ensure that this research can move forward with the support and oversight of the Federal government.

Sincerely,

Alliance for Aging Research
American Academy of Allergy, Asthma and Immunology
American Academy of Orthopaedic Surgeons
American Academy of Otolaryngology - Head and Neck Surgery
American Association for Cancer Research
American Association for Dental Research
American Association for the Study of Liver Diseases
American Association of Colleges of Pharmacy
American Association of Dental Schools
American Association of Immunologists
American College of Cardiology
American Heart Association
American Lung Association
American Medical Association
American Pediatric Society
American Psychiatric Association
American Society for Biochemistry and Molecular Biology
American Society for Cell Biology
American Society for Microbiology
American Society for Pharmacology and Experimental Therapeutics
American Society for Reproductive Medicine
American Society of Clinical Oncology
American Society of Hematology
American Society of Tropical Medicine and Hygiene
American Thoracic Society
American Veterinary Medical Association
Americans for Medical Progress
America's Blood Centers
Association of Academic Departments of Otolaryngology - Head and Neck Surgery
Association of American Medical Colleges
Association of Independent Research Institutes
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Association of Medical School Pediatric Department Chairs
Association of Professors of Dermatology

Citizens for Public Action
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Society for the Advancement of Women's Health Research
Society for Pediatric Research
Society for Reproductive Endocrinology and Infertility
The Genome Action Coalition
The Health, Safety and Research Alliance of New York State, Inc.
The Protein Society
Tourette Syndrome Association

THE AMERICAN SOCIETY FOR CELL BIOLOGY

NATIONAL OFFICE: 9650 Rockville Pike · Bethesda, Maryland 20814-3992
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March 4, 1999

To the President of the United States and Members of the United States Congress:

We, the undersigned, urge you to support the decision to permit federally-funded biomedical scientists to conduct research with human "pluripotent" stem cells. This critical research can be advanced while simultaneously protecting the moral sensibilities of the American people.

Human pluripotent stem cells are not embryonic cells because they cannot become a human being nor can they undergo embryological development. It is likely, however, that further research will reveal how to induce these cells to form certain specialized cell types that can be used for the treatment of human disease. A large body of successful work with mouse pluripotent stem cells encourages us to believe that as we progress to studies with human stem cells we will learn how to induce these cells to become bone marrow for treatment of cancer and other hematopoietic diseases, pancreatic cells for alleviating diabetes, and neuronal cells for treating Parkinson's disease, Alzheimer's and various forms of brain and spinal cord disorders. Treatments using these stem cells could be much more effective than existing therapies because they may be engineered to be less susceptible to rejection.

There are serious negative consequences of not allowing federally funded scientists to work with human pluripotent stem cells. The net effect will be to bar the majority of the Nation's most prominent researchers who are supported by the National Institutes of Health and the National Science Foundation at universities and non-profit institutions throughout the country from engaging in this critical research. Excluding these investigators will close off scientific opportunities to those most qualified to make dramatic advances towards using stem cells for the treatment of disease. Moreover, the new scientific understanding that emerges would not flow into the public domain and may be restricted to the commercial sector. Permitting peer-reviewed federal funds to be used for this research, combined with public

oversight of these activities, is our best assurance that research will be of the highest quality and performed with the greatest dignity and moral responsibility. We hope that the President and the Congress together will make the informed and courageous decision to guarantee that those scientists who are most prepared and qualified to conduct safe, ethical and invaluable stem cell research be enabled to do so.

Stem cell research has enormous potential for the effective treatment of human disease. There is, therefore, a moral imperative to pursue it. Those who seek to prevent medical advances using stem cells must be held accountable to those who suffer from horrible disease and their families, why such hope should be withheld.

Sincerely yours,

Kenneth J. Arrow
Professor of Economics and
Operations Research Emeritus
Stanford University
Nobel Prize in Economics, 1972

David Baltimore
President
California Institute of Technology
Nobel Prize in Physiology or Medicine, 1975

Baruj Benacerraf
Fabyan Professor of Comparative Pathology
Emeritus
Harvard Medical School
Nobel Prize in Physiology or Medicine, 1980

Paul Berg
Stanford University School of Medicine
Cahill Professor of Cancer Research
Department of Biochemistry
Nobel Prize in Chemistry, 1980

J. Michael Bishop
University Professor
Chancellor, University of California, San Francisco
Nobel Prize in Physiology or Medicine, 1989

Steven Chu
Professor of Applied Physics
Stanford University
Nobel Prize in Physics, 1997

Stanley Cohen
Distinguished Professor of Biochemistry
Vanderbilt School of Medicine
Nobel Prize in Physiology or Medicine, 1986

E. J. Corey
Professor of Chemistry
Harvard University
Nobel Prize in Chemistry, 1990

Edmund H. Fischer
Professor, Emeritus of Biochemistry
University of Washington
Nobel Prize in Physiology or Medicine, 1992

Robert Furchgott
University Distinguished Professor Emeritus
State University of New York
Health Science Center at Brooklyn
Nobel Prize in Physiology or Medicine, 1998

Alfred G. Gilman
Regental Professor and Chairman
University of Texas Southwestern Medical Center
Department of Pharmacology
Nobel Prize in Physiology or Medicine, 1994

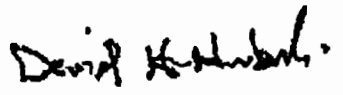
Donald A. Glaser
Professor of Physics and of Neurobiology in the
Graduate School
University of California at Berkeley
Nobel Prize in Physics, 1960

Joseph L. Goldstein
Professor and Chairman
Department of Molecular Genetics
University of Texas Southwestern Medical Center
at Dallas
Nobel Prize in Physiology or Medicine, 1985

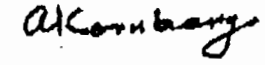
Roger Guillemin
Distinguished Research Professor
The Salk Institute for Biological Studies
Nobel Prize in Physiology or Medicine, 1977

Dudley Herschbach
Baird Professor of Science
Harvard University
Nobel Prize in Chemistry, 1986

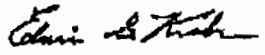
ASCB Stem Cell Research Position/Page 3



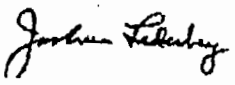
David H. Hubel
John Franklin Enders University Professor of Neurobiology
Harvard Medical School
Nobel Prize in Physiology or Medicine, 1981



Arthur Kornberg
Professor of Biochemistry
Stanford University Medical Center
Nobel Prize in Physiology or Medicine, 1959

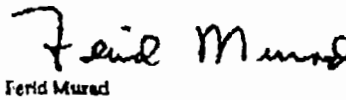


Edwin G. Krebs
Professor Emeritus
Department of Pharmacology
University of Washington
Nobel Prize in Physiology or Medicine, 1992



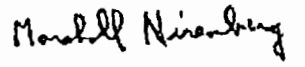
Joshua Lederberg
President Emeritus
The Rockefeller University
Nobel Prize in Physiology or Medicine, 1958

Leon M. Lederman
Pritzker Professor of Science
Illinois Institute of Technology
Nobel Prize in Physics, 1988



Ferid Murad
Professor and Chair, Department of Integrative Biology & Pharmacology
Director, Institute of Molecular Medicine
John Dunn Distinguished Chair in Medicine and Physiology
Regental Professor, University of Texas, Houston
Nobel Prize in Physiology or Medicine, 1998

Daniel Nathans
University Professor of Molecular Biology and Genetics
The Johns Hopkins University
Senior Investigator, the Howard Hughes Medical Institute
Nobel Prize in Physiology or Medicine, 1978



Marshall Nirenberg
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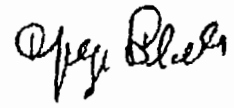
National Heart Lung & Blood Institute
The National Institutes of Health
Nobel Prize in Physiology or Medicine, 1968



George Olah
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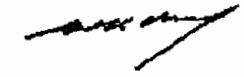
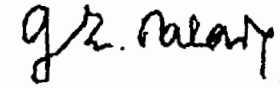
University of Southern California
Nobel Prize in Chemistry, 1994



Douglas D. Osheroff
J.G. Jackson and C.S. Wood Professor of Physics
Stanford University
Nobel Prize in Physics, 1996



George Palade
Professor, Department of Medicine, Division of Cellular and Molecular Medicine
Dean, Scientific Affairs
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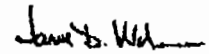
Nobel Prize in Physiology or Medicine, 1974

Burton Richter
Paul Pigott Professor of Physics
Stanford University
Nobel Prize in Physics, 1976

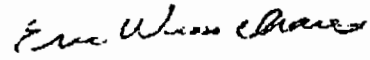
Richard J. Roberts
Research Director
New England Biolabs
Nobel Prize in Physiology or Medicine, 1993

Phillip A. Sharp
Professor and Head
Department of Biology
Massachusetts Institute of Technology
Nobel Prize in Physiology or Medicine, 1993

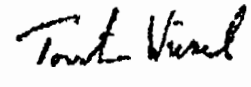
E. Donnall Thomas
Member
Fred Hutchinson Cancer Research Center
Nobel Prize in Physiology or Medicine, 1990



James D. Watson
President
Cold Spring Harbor Laboratory
Nobel Prize in Physiology or Medicine, 1962



Eric F. Wieschaus
Professor of Molecular Biology
Princeton University
Nobel Prize in Physiology or Medicine, 1995



Torsten Wiesel
President Emeritus
The Rockefeller University
Director, the Shelby White & Leon Levy Center for Mind Brain & Behavior
Nobel Prize in Physiology or Medicine, 1981

NATIONAL BIOETHICS ADVISORY COMMISSION

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March 9, 1999

Harold E. Varmus, M.D.
Director
National Institutes of Health
Building 1, Room 126
Bethesda, MD 20892

Dear Harold:

In my January 22nd letter to you I provided an outline of NBAC's plans for completing our report on research involving human stem cells, and our hope to provide the President (and others) with the benefit of any conclusions we might come to along the way. Given your own interest in NBAC's work, I wanted to share with you some of the commission's thinking at this point, even though no specific conclusions have been reached. This thinking is preliminary and is based on our most recent meeting (March 2-3), and reflects my views.

We seem to be coming to general agreement that federal funding for research involving the derivation and use of human embryonic stem (hES) cells should be permitted for at least the following categories of research: research using hES cells obtained from fetal tissue, and research using hES cells obtained from embryos in excess of those needed from infertility treatments. The commission is less close to agreement on the appropriateness of using federal funds to use (or derive) hES cells from embryos intentionally produced for research purposes (for example from somatic cell nuclear transfer), but I am confident that we will have something to say about this.

I am also enclosing a working draft, "Points to Consider," for your information. I had asked NBAC staff to prepare this document for two reasons: first, it may provide a useful summary of many of the ethical issues that might arise in research involving hES cells; second, it could, eventually, be included in our report as a suggestion for use (or adoption) by others. The commission has taken no position on this document at this time, but you may find it useful as you continue your thinking on how NIH will consider ethical issues. I recognize that this document reflects the model utilized by the Recombinant DNA Advisory Committee, but we took no position on whether it should be used by any particular group in that way.

We remain on target for completing our report by June, and I hope you will continue to follow our deliberations. I would be pleased to provide any clarification on any of these points.

Sincerely,

Harold T. Shapiro
Chair

168933

NBAC STAFF DRAFT

Points To Consider
In Evaluating Basic Research Involving Human Stem Cells

The following *Points to Consider* are presented not to prejudge the question whether human stem cell research should be conducted using federal funds. Rather, this document describes some of the ethical, clinical, scientific, and legal issues that could be considered when designing and/or reviewing studies that involve access to and use of human stem cells. These *Points to Consider* are only relevant for designing and evaluating studies where the role of the individual(s) who provide gametes, fetal tissue or embryos is limited to providing these materials for research that is intended to develop generalizable new knowledge. *These Points to Consider do not apply to situations in which an individual would be the recipient of a stem cell-based therapy, nor do they apply to studies involving human/animal hybrids.*

I. Scientific and Research Design Considerations

Several issues arise when designing research involving human stem cells, consideration of which would help ensure that research is well-designed, important, feasible, and timely. These issues are of particular significance given the nature of the materials.

A. The Source From Which The Human Stem Cells Will Be Obtained
   1. From existing cell lines (such as neuronal or hematopoietic stem cells)
   2. From aborted fetal tissue (following spontaneous or induced abortion or surgical termination of ectopic pregnancy)
   3. From stored/spare embryos obtained from infertility treatment
   4. From embryos produced for research purposes (including somatic cell nuclear transfer)

B. Previous Research Involving Animals

C. Alternatives To Using Human Stem Cells

D. Future Plans And Conservation Of Gametes, Fetal Tissue, and Embryos
   1. Will stem cells be produced and stored for later use?
   2. If a particular protocol is being proposed using stored embryos, does it use only the number of embryos necessary?
   3. What plans exist in the event that additional stem cells are needed?

E. The Research Setting
   1. Are the investigators scientifically qualified to carry out the proposed research?
   2. Is the research environment (including facilities) appropriate for the conduct of research involving stem cells?

II. Identification of Providers and Donors, Recruitment Practices, and Compensation

Several issues in identifying individuals (or couples) who may be asked to consider providing gametes, fetal tissue, or embryos for research involving human stem cells, consideration of these issues could help to ensure that no inappropriate burden, inducement or exploitation would occur.

A. Identification And Recruitment Practices
   1. Are potential donors or providers identified through advertisements to the general public? Are they identified through direct solicitation? Do they self-select?
   2. Is the selection of such individuals equitable and fair?

3. Are these individuals vulnerable to undue influence, coercion or exploitation? Does the recruitment method raise concerns about undue influence or coercion of the prospective donors? embryos?
4. Are the potential donors capable of giving an informed consent?
5. In which circumstances is it appropriate to identify and recruit an individual as well as his or her partner?

B. Compensation And Reimbursement

1. Will any financial compensation be paid to individuals (or couples) who provide source material ?
2. Does the compensation exceed the costs already being incurred (for example, the cost of embryo storage)? Will this fact be disclosed?
3. Does the compensation reimburse the individual (or couple) for specific services (e.g., gametes, infertility services)?
4. When is the offer of compensation made relative to individual's (or couple's) decision to make available the materials from which stem cells will be derived?

III. Informed Consent

Several issues arise in the process of informed consent (including the content of consent forms); considering these issues would help to ensure that ensure prospective donors or providers of source materials would receive timely, relevant and appropriate information to make informed and voluntary choices

A. General Considerations For Individuals (or Couples) Who Provide Gametes, Fetal Tissues or Embryos

1. Who will obtain informed consent? Will a clinician and researcher be available to answer questions?
2. Is it appropriate for others to participate in the consent process (e.g., partner or family member)?
3. Will psychological support mechanisms be in place when needed?
4. Are the purposes of stem cell research (in general) fully described?
5. If a specific research protocol is being contemplated with stem cells obtained, is the protocol fully described?
6. What are the possible risks to the woman (or partner) from the procedure to obtain stem cells, and how will these be minimized?
7. Will the consent form clearly disclose that stem cell research is not intended to benefit them directly?
8. Is it clear that decisions to consent to or refuse the procedures to obtain stem cells will not enhance the quality of care they will receive?
9. Will individuals be informed that no medical or genetic information about the gametes, fetal tissue, embryos, or stem cells derived from these sources will be provided?
10. What measures will be taken to protect the privacy and confidentiality of individuals who provide gametes, fetal tissue or embryos?
11. Is the source of funding for research (public, private, public/private, philanthropic) disclosed?
12. What known commercial benefits, if any, are expected to arise for the investigators seeking to obtain human stem cells?

B. Issues Specific To Consenting To The Use of Fetal Tissue

1. Is there a description of what is usually done with fetal tissue at the institution at which individuals are undergoing termination of pregnancy? Is this information available in written form and provided to the individuals?
2. Is there a description that the decision to permit research will entail that research may begin immediately.

C. Issues Specific To Consenting To The Use of Embryos Obtained From Infertility Treatments

1. Is there a description of what is usually done with spare embryos at the institution at which individuals are undergoing infertility treatment? Is this information available in written form and provided to the individuals?
2. Will information be made available about whether the spare embryo was viable and normal or non-viable and abnormal?
3. Is there a description of options available (e.g., permit material to be used in research, cryopreserve, discard, donate to another couple for infertility treatment)?
4. Is it clear that the embryos used in research will not, under any circumstances, be transferred to any woman's uterus?
5. Is it clear that the research will result in the destruction of the embryo? Is the method described?

D. Issues Specific To Consenting To The Use of Gametes[1]

1. Will individuals be informed whether embryos will be produced with the gametes (e.g., using *in vitro* fertilization, or somatic cell nuclear transfer?)
2. Is there a description of what is usually done at this institution with gametes not used for research?
3. Is there a description of options available (e.g., permit materials to be used in research, cryopreserve, discard, donate to another couple for fertilization and transfer)?
4. Is it clear that the embryos produced for research purposes (whether by IVF or somatic cell nuclear transfer) will not, under any circumstances, be transferred to any woman's uterus?

IV. Review Issues

Several issues arise in the review and oversight of research involving human stem cells; consideration of these issues will provide assurance that, regardless of the source of funding, appropriate compliance with applicable regulations, guidelines and other standards will occur. These considerations would supplement, not replace, applicable federal and state regulations.

A. Applicability of Relevant Regulations

1. What current guidelines, regulations, rule, or policies apply to the conduct of this research?
2. What mechanisms are in place to assure compliance with these regulations?

B. Applicability of Professional Practice Standards

C. IRB Review

D. Submission of Research Findings for Publication

E. Other Responsibilities of Investigators and Collaborating Clinicians

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[1] Note: For persons who provide sperm anonymously, the details of the consent form and the specificity of the informed consent process may vary—EMM 2/15/99

Office of the Secretary
Washington, D.C.

DATE: Mon May 24 12:04:29 1999

FAX TO: Devorah Adler

FROM: Lauren

SUBJECT: Stem Cell Qs

FAXED FROM THE OS NETWORK!

If you need this fax to be retransmitted, please call the originator above.

---------- MESSAGE ----------

Q&As on Stem Cell Research
FOR INTERNAL USE ONLY
May 24, 1999

Q: What is your response to reports that the National Bioethics Advisory Commission is considering recommending that Federal funding should be made available for research on embryos made by in vitro fertilization?

A: The Commission has not submitted or even written their report on this issue, so it would be premature and unwarranted to comment on it at this time.

Background: Current law prohibits Federal funding of the destruction of embryos. However, HHS's Office of the General Counsel has determined that the statute permits the funding of research using stem cells.

FOLLOW UP QUESTION

Q. What do you think of the Commission's proposed recommendation?

A. The Administration's position is clear; we will not fund research in which human embryos are destroyed, discarded, or subjected to impermissible risk. Because the Commission has not made its final recommendation yet, any other comments on this report are premature.

2 parts of law

DRAFT 2/22/99

Supplemental Stem Cell Q and A for the Secretary's Testimony during the Week of 2/22/99

File: stem.rt

Q. Since even Dr. Varmus agrees that federal funds can't be spent on research that destroys embryos in the process of deriving stem cells, how can you justify federal funding for the use of those stem cells once derived?

A. It is entirely legal in the private sector to do research that derives stem cells from embryos. Federal law does not allow federal funding for that activity. We are talking about funding research using these stem cells that could lead to treatments for Parkinson's disease, heart disease, diabetes, stroke, burns, arthritis and other very serious medical conditions. The potential for this research is very great. It is important, too, to remember that, once derived, a line of stem cells can support many many research projects.

Q. Do you agree with your General Counsel that the human embryo research ban in your Department's 1999 appropriation allows federal funding of stem cell research?

A. I do. I am not a lawyer, but I have read the opinion and the words of the human embryo research ban, and the reasoning seems correct to me. We would not fund research in which human embryos are destroyed, discarded or subjected to impermissible risk.

I want to add that we have been careful to adhere to the human embryo research ban from the outset. We have given notices to NIH grantee scientists and to intramural scientists reminding them of the law and its constraints. We have every intention to continue to follow the law and to obey its mandate.

Q. The human embryo research ban forbids federal funding for "...research in which ... human embryos are destroyed, discarded or knowingly subjected to risk of injury or death...". Since embryos had to be destroyed to get the stem cells, shouldn't the bar apply?

A. No. The research that derived the stem cells was not federally funded. That was privately-funded research in which embryos were destroyed. The stem cell research will not destroy any embryos. It will not be research in which embryos are destroyed.

Q. If we look at the standard rules of statutory construction, didn't your counsel apply the prohibition too narrowly -- given the difference in the drafting of the prohibition on creating embryos vs. destroying or discarding them?

A. The General Counsel's office, as is normal practice, conducted a full review of the law, examining the words of the statute itself and looking for any legislative history that would shed light on the subject. The words of the statute are clear. I am told that there is no legislative history on this subject that casts any doubt on the clear words of the law. There is no indication that Congress intended to ban research utilizing stem cells derived in privately funded research Under those circumstances, I am bound to follow the law as it is written.

Q. By defining embryo according to its ability to develop into a human being, aren't you encouraging the development of and research on defective or deformed embryos in order to evade the law?

A. First, let me point out that the Counsel did not define the term "embryo"; the statute defined the term. And the statute defined "embryo" as an "organism". You asked if a diseased or damaged embryo is subject to the human embryo research ban and the answer is, if it is an organism, yes, there can be no federal funding of research in which such an embryo would be destroyed, discarded or subject to impermissible risk.

Q. Well, in your view, is a defective or deformed embryo an organism?

A. As my Counsel and the NIH Director have said, the definition of what is an "organism" is taken from science. I am not a scientist, but my scientists have said that during its development, such an embryo would meet the definition of the statutory term "organism" and thus be subject to the law.

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Federal Embryo Research Is Backed

By Rick Weiss
Washington Post Staff Writer
Sunday, May 23, 1999; Page A1

A presidentially appointed ethics panel has decided to recommend that the federal government begin funding some research on human embryos, saying the moral cost of destroying embryos in research is outweighed by the social good that could come from the work.

Citing recent evidence that some human embryo cells have the potential to grow into replacement tissues to treat a wide variety of chronic diseases, the National Bioethics Advisory Commission has concluded that it is essentially unfair to millions of patients for Congress to continue its broad, four-year-old funding ban on human embryo research.

Instead, federal rules should be written that ensure an appropriate measure of protection and respect for human embryos, according to a draft version of the report and interviews with commissioners and others. Those rules would allow federally financed researchers to conduct studies on leftover embryos from fertility clinics if the embryos were no longer wanted by the parents who made them.

"These are very difficult judgments to make, but it's a balancing act," said Harold T. Shapiro, chairman of the bioethics commission and president of Princeton University. "We have moral obligations to the future health and welfare of people, and we need to balance these with, at the very least, the symbolic moral obligation we have to the embryo."

The recommendations go further than those recently proposed by the National Institutes of Health. Those call for federally funded research on laboratory-grown human embryo cells, but not on human embryos themselves.

The more conservative NIH recommendations already have drawn fire from some members of Congress. Observers said the bioethics commission's report is likely to escalate the long-standing political tussle over the moral status of embryos and the wrenching national debate over abortion.

"I have a sense that this is going to be one of the liveliest debates on the Senate and the House floors this session," said Sen. Arlen Specter (R-Pa.), who last fall held a hearing on stem-cell research.

Contentious as the issue is, there are signs that public opinion may be moving toward support of at least limited embryo research.

"Patients and their families faced with life-threatening and

chronically disabling diseases want science to move as quickly as possible," said Daniel Perry, executive director of the Alliance for Aging Research and chief of a new coalition of patient groups advocating research on human embryonic stem cells, the embryo-derived cells that have generated so much recent excitement.

The new group, Patients' Coalition for Urgent Research, or CURe, includes more than two dozen national organizations, such as the American Cancer Society and the Christopher Reeve Paralysis Foundation. At an inaugural event last week, the group released poll results indicating that 74 percent of Americans support human embryonic stem-cell research.

"We're not naive and we know there's not going to be a cure tomorrow," Perry said. "But it's a good thing for federal funding to be there because it means the research will be done more quickly and it will be more accountable to the public."

The commission's report, due to be released next month, is the second federal ethics analysis in less than five years to conclude that certain kinds of research on human embryos warrant federal support. The previous one, by a panel convened by the NIH, was partially approved by President Clinton in 1994 but then rejected by Congress, which passed an appropriations rider blocking all such funding and has renewed that ban annually ever since.

The 17-member bioethics commission calls for a more limited range of embryo experiments than did the 1994 panel. It does not support the use of federal funds to create new human embryos just for research, for example – the single provision that Clinton rejected in 1994 – and it offers specific policy guidelines to keep studies within narrow scientific and ethical bounds.

But the biggest difference between 1994 and 1999, experts said, is that the benefits of embryo research are now far less theoretical. If the morality of human embryo research is pegged in part to the benefits that are likely to accrue to sick and dying people, as many ethicists, religious leaders and others believe, then the tipping point of acceptability appears to have been reached, the report concludes.

"This research is allied with a noble cause," the draft report states, "and any taint that might attach from the source of the stem cells diminishes in proportion to the potential good which the research may yield."

The commission's report is still undergoing revisions. But interviews with commissioners and others involved in its crafting indicate that a clear consensus exists for some basic recommendations.

For now, the report will say, federal funding should be made available only for research on embryos made by in vitro fertilization for infertile couples. A single cycle of IVF can result in the creation of a dozen or more embryos, of which three or four typically are transferred to the womb. The rest are frozen for later efforts. Under the report's recommendation, if any are left over when the couple stops trying to get pregnant, the couple could donate them for federal research (or have them destroyed or keep them frozen indefinitely).

Federally funded scientists would be allowed to ask parents for permission to conduct studies on their embryos only after the parents had independently decided to abandon them. And if any compensation were to be allowed, it would be very limited.

With protections such as these in place, the commission concludes, parents – and not the federal government – would be "morally responsible" for the embryos' demise.

Most commissioners also favor creation of a national oversight board that would be responsible for ensuring that only those embryo experiments deemed most worthy get federal support.

The commission concedes that it cannot settle the debate over embryos' intrinsic moral value. But for the purposes of making public policy, it seeks to find an ethical middle ground by balancing the potential harm to embryos against the potential benefits to patients.

The commission notes, for example, that even many conservatives support abortion under certain circumstances. "Conservatives who accept that killing a fetus is permissible where it is necessary to save the life of the mother should agree with liberals that it is also permissible to destroy embryos where it is necessary to save people."

The new analysis comes at a time of growing public clamor for full-bore pursuit of research into human embryonic and fetal stem cells – cell types discovered just last year that have the potential to grow into many kinds of tissues. Researchers envision cultivating the cells into replacement neurons for patients with Parkinson's disease, insulin-secreting cells for diabetics, and heart muscle cells for victims of heart attacks, among other uses.

But it wasn't only advances in science that led the commission to decide it is time to invite federal investment in embryo research, said Eric Meslin, the commission's executive director. Since the 1994 NIH report, Meslin said, people have been reconsidering their feelings about embryo research. A growing number seem to have found room within their personal belief systems to justify limited amounts of such research – including many religious leaders who testified to the commission.

"The community has been coming to the view that these sources of cells are ethically acceptable with a number of protections put in place," Meslin said.

Many also favor a federal presence in the stem-cell field so research priorities will be selected on the basis of what is best for the nation's health and welfare, instead of on the basis of maximum profitability for the companies now pursuing the technology with private money.

The American Society for Reproductive Medicine, the professional organization that oversees fertility clinics, where most of the nation's uncounted thousands of spare embryos are stored in freezers, expressed support for the commission's conclusions.

"We would certainly welcome federal funding and oversight for

research involving human embryos and human embryonic stem cells, and we would hope that Congress would act on the commission's recommendation," said Sean Tipton, a spokesman for the organization in Washington.

But others, including antiabortion activist John Cavanaugh-O'Keefe of the Laytonsville, Md.-based Eugenics Watch, vowed to fight the move. And congressional support is hardly assured. Rep. Jay Dickey (R-Ark.), a co-author of the rider that has banned embryo research since 1995, said through a spokesman that he strongly opposes the commission's views.

"Any NIH action to initiate funding of such research would violate both the letter and spirit of the federal law banning federal support for research in which human embryos are harmed or destroyed," Dickey wrote in a recent letter to Health and Human Services Secretary Donna E. Shalala.

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1. don't know final recommendation
2 what is Admin position on this—
this will harm other activities on
the Hill — not distinguishing
btwn 2; are we? if we are,
we need to work on this.
Can't send any signal to contrary
on this.

Health - stem cell research

cc: Bruce, Chris

from Rich T. 70 senator letter

February 11, 1999

The Honorable Donna E. Shalala
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Shalala:

Last month, the General Counsel at HHS, Harriet Rabb, issued a memorandum to Dr. Harold Varmus, Director of the National Institutes of Health, supporting the legality of using taxpayer funds for research on stem cells taken from living human embryos. Shortly thereafter, and using the Rabb memo as a basis, Dr. Varmus announced that NIH will reverse current federal policy and begin funding research which relies on the mutilation and destruction of human embryos.

We wish to express to you, in the strongest possible terms, our objection to Ms. Rabb's memo and to Dr. Varmus's decision. Any NIH action to initiate funding of such research would violate both the letter and spirit of the Federal law banning federal support for research in which human embryos are harmed or destroyed.[1] Rather than providing guidance on how best to implement the law that Congress enacted and the President signed, the memorandum appears to be a carefully worded effort to justify transgressing that law.

In her memorandum Ms. Rabb makes significant errors on the way to her conclusion that it would be permissible for NIH to fund research using stem cells harvested from human embryos. We call upon you to correct the General Counsel's interpretation and to reverse Dr. Varmus's decision.

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[1] Since January 1996, Congress has included in the annual Labor, Health and Human Services, Education Appropriations Act a section prohibiting funding for this type of research. Section 511 of the most recently enacted research funding bill, Public Law 105-277, provides (in part) that--

> (a) None of the funds made available in this Act may be used for--
> (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 utero under CFR 46.208(a)(2) and section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)).

The Honorable Donna E. Shalala

At the start of her analysis, the General Counsel unilaterally narrows the meaning of "research in which a human embryo or embryos are destroyed" and states that it prohibits only direct federal funding of the specific act of destroying the embryo. In this way she limits the scope of the law passed by Congress and signed by the President. While the *act* of destroying or injuring an embryo would certainly be ineligible for Federal funding, the law has a broader application. It also bars the use of tax dollars to fund research which follows or depends upon the destruction of or injury to a human embryo.

Congress could have structured paragraph (2) of subsection (a) of the law like paragraph (1) and simply prohibited the use of funds for the destruction or discarding of human embryos. We did not do that, and by established rules of statutory construction, HHS may not construe the law's provision on "research in which" embryos are destroyed as narrowly as its provision on the creation of embryos.[2] Instead, we prohibited the funding of research projects in which the lethal dissection or harmful manipulation of living human embryos is a necessary prerequisite, including projects where the material used in the experiments is obtained by destruction of an embryo that would not otherwise be done (or not otherwise done in the same way). In congressional testimony, Dr. Varmus has confirmed that it is impossible to obtain stem cells from embryos for these experiments without destroying the embryos.

The Rabb memo also ignores the policy reflected in current law on fetal tissue transplantation research using tissue from intentionally aborted children. While that law is itself open to criticism, it at least bans the use of fetal tissue in federally funded research if abortion was induced for the purpose of providing the tissue. Under current law, federal funds may not be used for fetal tissue transplantation experiments following an abortion if the timing and method of the abortion were altered solely for the purpose of providing usable tissue for research. Yet, in the embryonic stem cell research which NIH proposes to fund, the timing, method and procedures for destroying the embryonic child would be determined solely by the federally funded researcher's need for usable stem cells.

Finally, both Ms. Rabb's memorandum and Dr. Varmus's testimony before a Senate subcommittee present a new definition of "human embryo" that would undermine both the congressional rider on embryo research, and the President's own 1994 directive against using federal funds to create human embryos for research purposes. They now say that an entity is an "embryo" only if one can show that it is capable, if implanted in the womb, of becoming a born "human being." This narrow definition has no support whatsoever in federal law.

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[2]When a law has two parallel clauses, one of which is deliberately written in broader terms than the other, it may not be interpreted to have the same meaning as the narrower clause. See *Russello v. United States*, 464 U.S. 16, 23 (1983), and cases cited therein.

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Nevertheless, researchers are already offering to use damaged human embryos in their destructive research, or even to engineer lethal defects in advance into the embryos they create for such research, in order to take advantage of this Administration cover and ignore the congressional and presidential directives altogether.

For more than 20 years, Federal laws and regulations have protected the human embryo and fetus from harmful experimentation at the hands of the Federal government – regardless of whether the embryo is "perfect" or damaged, wanted or unwanted, intended for abortion or intended for live birth. This area of law has provided a bulwark against government's misuse and exploitation of human beings in the name of medical progress. It would be a travesty for this Administration to attempt to unravel this accepted ethical standard.

We urge you to review this issue carefully, and to put a stop to a proceeding which so clearly does violence to the meaning and intent of Federal law.

Sincerely,